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Catalysis of Symmetry-disallowed Reactions

V.I.Labunskaya, A.D.Shebaldova, and M.L.Khidekel'

Opportunities for applying the principle of the conservation of orbital symmetry to catalytic processes are surveyed. Current views on the role of a transition metal in the catalysis of symmetry-disallowed reactions are reported, and possible mechanisms are discussed. Close attention is paid to the correlation of the catalytic activity of metal-containing catalysts with the electron configuration of the transition metal, the structure of the complex, and the nature of the ligands. Examples of catalytic reactions disallowed by the Woodward-Hoffmann rules—valency isomerisation of hydrocarbons, hydrogenation and disproportionation of alkenes, cyclo-oligomerisation—are considered in the light of ideas on concerted and stepwise mechanisms. A list of 137 references is included.

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I. INTRODUCTION

The study of catalysis as a method for conducting chemical processes has always made use of ideas developed in solid-state physics, organic, coordination, inorganic, and polymer chemistry, and enzymology. Many general theories of catalysis—physical, multiplet, semiconductor, supersaturation, etc. theories—were constructed in various historic periods on the foundation of advances in solid-state physics. From Sabatier to the present time the concept of intermediate compounds has been of the greatest assistance in the selection of new catalysts; such ideas were based on achievements in the preparation of various types of coordination and organometallic compounds. Generalisations such as the theory of "soft" and "hard" acids and bases, electronic theories developed in organic chemistry, etc. have proved extremely useful for catalysis. "Catalytic bionics"—whose aim is to create novel highly efficient and specific catalysts—has been constructed from data on the structure and the mechanism of the action of enzymes and the general principles of the action of biological catalysts.

One of the most important recent achievements of theoretical organic chemistry has been to elaborate rules for the conservation of orbital symmetry in concerted reactions (called the Woodward–Hoffmann rules). The directions of many chemical processes have been explained and predicted by means of these rules during recent years. It appeared useful to examine their application to the catalysis of reactions that are disallowed for

reasons of symmetry. Several possibilities of interpreting the mechanism of the process and describing (in isolated cases predicting) the nature of the action of a transition-metal catalyst are discussed for such important reactions as the valency isomerisation of hydrocarbons, the hydrogenation and disproportionation of alkenes, and cyclo-oligomerisation.

II. MAIN RULES FOR THE CONSERVATION OF ORBITAL SYMMETRY IN CONCERTED REACTIONS

The Woodward–Hoffmann rules[1-6] are based on the hypothesis that the direction of a synchronous reaction is determined by the symmetry of the highest occupied orbitals†. The view that these orbitals determine the reactivity of molecules had been expressed earlier by other workers. In this connection we must note the papers by Fukui and his collaborators on the theory of frontier electrons[13-15], which provide a basis for correlations between the position of the reaction centre and the maximum electron densities in the highest occupied orbitals and the lowest vacant orbitals of a molecule. Longuet-Higgins and Coulson[16,17] as well as Dewar[18] used the theory of perturbations to explain aromatic substitutions. The merits and defects of these methods have been analysed in detail in Salem's review[19].

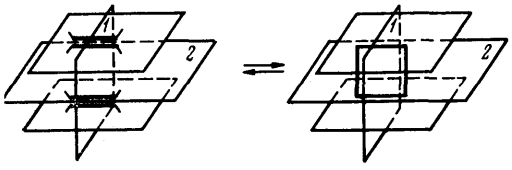


Figure 1. Symmetry elements for the coplanar combination of two ethylenic bonds to form cyclobutane.

The Woodward–Hoffmann method consists essentially in constructing correlation diagrams for the energy levels of products and reactants, and analysing them with respect to symmetry. If the symmetry of the highest occupied orbitals in the ground state of the products correlates with the symmetry of the ground state of the reactants, the reaction is thermally allowed. If the ground state of the products correlates with an excited state of the reactants, the reaction is thermally forbidden, but is allowed photochemically. The fundamental principle was formulated by Woodward and Hoffmann: "Orbital symmetry is conserved in synchronous reactions"[6].

Since we shall be interested mainly in synchronous cycloaddition and electrocyclic reactions, let us examine as example two correlation diagrams—of two ethylenic bonds for the cycloaddition, and of butadiene and cyclobutene for the cyclisation—for which purpose we make use of the arguments in Ref. 6. In the simultaneous combination of two ethylenic bonds to form a cyclobutane ring four π-levels of the two ethylene molecules, the latter lying in two parallel planes, and four σ-levels of cyclobutane are classified as symmetric S or antisymmetric A relative to the plane located midway between the carbon atoms of ethylene (plane *1* in Fig. 1) and the plane parallel to those of the molecules and located midway between them (plane *2*).

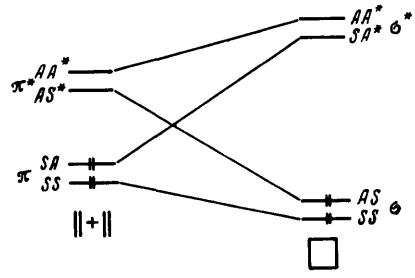


Figure 2. Correlation diagram of levels in the transition ethylene + ethylene → cyclobutane.

The correlation diagram for the transition ethylene + ethylene → cyclobutane shows (Fig. 2) that the reaction is thermally prohibited for reasons of symmetry, since the ground state of ethylene correlates with an excited state of cyclobutane. For reactions of this type the general rule of the conservation of symmetry can be written: reaction is thermally allowed provided that $m + n = 4q + 2$ (where m and n are the numbers of π-electrons in the reactants, and $q = 1, 2, 3, \ldots$); reaction is thermally forbidden for a system in which the number of electrons $m + n = 4q$.

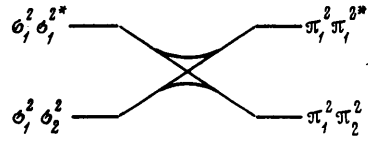


Figure 3. Diagram of states for cyclobutane and ethylene.

With forbidden reactions lines joining levels of similar symmetry intersect. Owing to electronic interaction, however, the system may cross from the adiabatic curve to the ground state of the product[20]. The diagram for the states of cyclobutane and two ethylene molecules shows that in this case symmetry prohibition is responsible for the high energy barrier opposing the transition ethylene + ethylene → cyclobutane (Fig. 3). No barrier due to symmetry is present with symmetry-allowed reactions (e.g. the Diels–Alder reaction).

A similar application of symmetry analysis to the cyclisation of butadiene (an electrocyclic reaction) shows[6]

†Numerous examples of concerted reactions obeying the rules of orbital symmetry (electrocyclic, sigmatropic reactions, cycloadditions, eliminations, etc.) are cited in Woodward and Hoffmann's monograph[6] as well as in reviews[7-12].

that conversion of a π-bond into a σ-bond may occur by either conrotatory or disrotatory motion of the ends of the molecule (Fig. 4). The corresponding symmetry elements are the axis of the molecule and a reflecting plane. The conrotatory path is thermally allowed with respect to symmetry, whereas the disrotatory path is forbidden (Fig. 5).

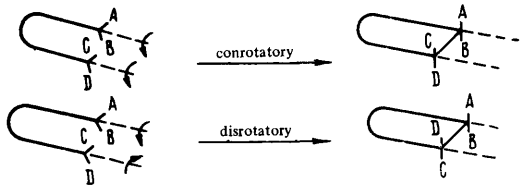


Figure 4. Conrotatory and disrotatory cyclisation of butadiene.

The general formulation of the prohibition rules for electrocyclic reactions is that the latter are thermally permitted with conrotatory motion if $k = 4q$ (where k is the number of π-electrons) and photochemically permitted when $k = 4q + 2$ (tne opposite relation applies with disrotatory motion).

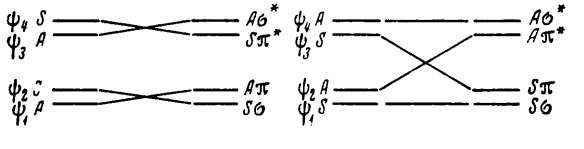


Figure 5. Correlation diagrams of levels for the transition butadiene → cyclobutane.

Correlation diagrams can be applied only to systems that possess symmetry. A different method of analysis was suggested for asymmetric systems [21]. A more general method (mapping) was proposed by Trindle [22] for a wide range of reactions, including those to which the Woodward–Hoffmann rules do not apply.

III. ROLE OF A TRANSITION METAL IN THE CATALYSIS OF SYMMETRY-DISALLOWED REACTIONS

Many symmetry-disallowed thermal reactions involving the cycloaddition of two ethylenic bonds with the formation of cyclobutane or the concerted opening of a cyclobutane ring (the valency isomerisation of strained σ-bonds, the disproportionation of alkenes, cyclo-oligomerisation) take place readily in the presence of complexes of transition metals. At the present time there is no generally accepted view on the role of the metal in catalysing such symmetry-disallowed reactions. The main problem consists in deciding whether such reactions are concerted or non-concerted (stepwise) in character.

A non-concerted mechanism involves essentially redox addition with formation of an intermediate complex, and can usefully be considered for specific examples of catalysed symmetry-disallowed reactions (Section IV). With a concerted mechanism the influence of the metal is apparent in a change in the symmetry of the highest occupied orbitals of the organic substrate.

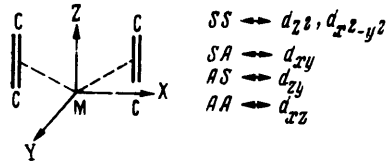


Figure 6. Metal–dialkene complex.

The correlation diagram (Fig. 2) shows that the orbitals of symmetry *SA* and *AS* play the main part in the concerted combination of two ethylenic bonds to form a cyclobutane ring. Occurrence of the thermal reaction requires conformity in symmetry between the ground states of cyclobutane and the two alkene molecules, which can be obtained by the mixing of metal and alkene orbitals in complexes of a transition metal with the alkene and with cyclobutane. Correlation diagrams for such complexes were first given by Mango and Schachtschneider [23] for the suprafacial $(2s + 2s)$‡ cycloaddition of two alkenes.

The concerted addition of two alkenes requires that their antibonding *AS* orbital should be populated (Fig. 2). Since the highest occupied ethylenic π-orbital is *SA*, formation of a metal–alkene complex involves transfer of an electron pair from this orbital to a metallic *d*-orbital of suitable symmetry, whereas an *AS** orbital obtains an electron pair from a *d*-orbital of the same symmetry (*AS*) [24,25].

Fig. 6 shows the symmetry relations between metal and alkene orbitals for a metal–dialkene complex in the given coordinate system. The interaction between metal and alkene orbitals results in their occupation in such a way that the symmetry-disallowed reaction ethylene + ethylene → cyclobutane becomes allowed in the presence of the metal, as follows from the correlation diagram (Fig. 7).

The ligand field of the non-reacting ligands has been disregarded in the construction of this correlation diagram: i.e. the diagram has been drawn for a metal–dialkene complex. In this case all the *d*-orbitals are degenerate. Nevertheless, the presence of non-reacting ligands creates a ligand field which splits the *d*-orbitals; this must be taken into account in studying the catalysis of symmetry-disallowed reactions [26]. Formation of an intermediate complex $ML_nAlkene_2$ in actual catalytic systems is accompanied by splitting of the *d*-levels, the degree of splitting and the distribution of the levels depending on the nature of the ligand and the structure of the complex. The symmetry of the highest occupied orbital of the complex is determined by its geometry. With strong ligand fields, where the splitting of the *d*-orbitals

‡Here and subsequently the symbols *s* and *a* denote suprafacial and antarafacial addition [7].

is large, the highest occupied orbital of the metal–cyclobutane complex may be of either *SA* or *AS* symmetry. Fig. 8 shows that the transition ethylene + ethylene → cyclobutane remains disallowed by symmetry: i.e. a ligand-field symmetry restriction operates in this case [26].

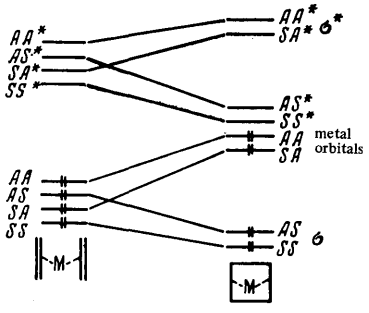


Figure 7. Correlation diagram for the conversion of the complexes metal–dialkene → metal–cyclobutane.

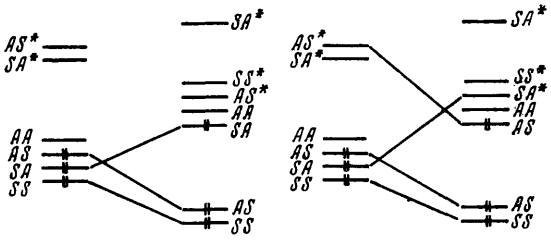


Figure 8. Correlation diagrams for the conversion of the complexes metal–dialkene → metal–cyclobutane for strong ligand fields.

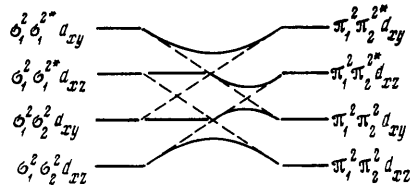


Figure 9. Diagram of states of metal–dialkene and metal–cyclobutane complexes.

The interaction between the orbitals of reactant and metal in electrocyclic reactions catalysed by transition metals produces the same effect as with cycloaddition of type 2 + 2.

A different view, that the metal acts by lowering the activation barrier to the disallowed reaction, not by changing the symmetry of the orbitals in the reactants, has been put forward by van der Lugt [27]. This view is supported by the correlation diagram of states for the concerted opening of the cyclobutane ring in the case of the square planar complex ML_2Cyclobutane and ML_2Alkene, where the metal has a d^8 shell. However, Mango has shown [28] that this example is a particular case of catalysis in which, owing to the effect of the ligand field, the splitting of the *d*-orbitals is such that the reaction remains disallowed by symmetry, but its activation barrier is greatly lowered by the mixing of the occupied orbitals with lower excited orbitals (Fig. 9).

IV. SYMMETRY-DISALLOWED REACTIONS CATALYSED BY TRANSITION-METAL COMPLEXES

Numerous examples of reactions, forbidden by the rules of the conservation of orbital symmetry but catalysed by transition metals, have become known since the publication of the Woodward–Hoffmann correlations [1–5]. They include the valency isomerisation of strained cyclic systems, the disproportionation and hydrogenation of alkenes, and also cyclo-oligomerisations. Examination of these catalytic reactions in the light of the conservation rules is extremely useful for determining the conditions under which such processes may be expected to occur.

Three views are currently held on the mechanism of symmetry-disallowed reactions catalysed by transition metals. Firstly, the reaction can be regarded as a concerted process of type 2 + 2, which becomes symmetry-allowed as a consequence of interaction between the electron levels of organic substrate and metal [26]. Another opinion [27] is that the introduction of orbitals of the metal intermediate in energy between the highest occupied and the lowest vacent orbital of the substrate lowers considerably the activation energy of the reaction, which remains symmetry-disallowed. Finally, a non-concerted process is possible, in which an organometallic intermediate is formed by oxidative addition of the metal to the substrate [29,30].

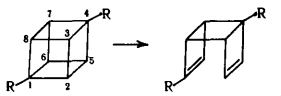
1. Valency Isomerisation of Strained Cyclic Systems

Valency isomerisations of cyclic systems having highly strained σ-bonds are of great interest among the symmetry-disallowed reactions known at the present time. While being in most cases "thermally forbidden" according the Woodward–Hoffmann rules, these reactions take place extraordinarily readily under mild conditions in the presence of compounds of transition metals; they are characterised also by high selectivity and by stereospecificity. Apart from the theoretical significance of valency isomerisations in developing the principle of the conservation of orbital symmetry, they are also useful for organic preparations, since they provide routes to the synthesis of several unique hydrocarbons (e.g. cuneane and semibullvalene).

Extraordinarily interesting examples of the catalytic valency isomerisation of strained σ-bonds are provided by cubane [31,32] and by homocubyl [33,34], 1,1′-bishomocubyl [33–38], and secocubane [39,40] systems, information on which has appeared quite recently. The very existence and the thermal stability of highly strained cubane compounds can probably be explained by the Woodward–Hoffmann rules, according to which thermal rearrangements of the type $\sigma 2a + \sigma 2a$ are not allowed for these molecules in the ground state.

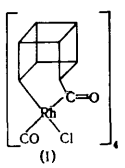
Ions and complexes of several transition and non-transition metals—rhodium, silver, palladium, copper, magnesium, zinc, iron, and mercury—have been examined as catalysts for the isomerisation of cubane and its derivatives. However, only silver(I), rhodium(I), and palladium(II) compounds were found to catalyse this

process, and their catalytic activity was varied and highly specific. In the presence of catalytic quantities of diene complexes of the type $(RhCl\,dien)_2$ (where diene represents norbornadiene, cyclo-octa-1,5-diene, or *syn*-tricyclo-octadiene) cubane undergoes rapid and quantitative isomerisation into *syn*-tricyclo-octadiene[31]:



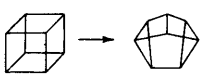
This process can be regarded as a concerted opening of the cyclobutane fragment of type $\sigma 2s + \sigma 2s$, i.e. as concerted rupture of the $C_{(1)}-C_{(2)}$ and $C_{(5)}-C_{(6)}$ bonds allowed by the participation of a transition metal of suitable electron configuration (d^8), which donates electrons to antibonding cubane orbitals of appropriate symmetry. However, no experimental evidence in support of a concerted mechanism was obtained.

Cassar et al.[31] quote certain results indicating a non-concerted mechanism for the isomerisation of cubane into tricyclo-octadiene. The rate-determining step in this mechanism is the rupture of one carbon–carbon bond by the oxidative addition of the metal to the cubane. Oxidative addition is well known with rhodium and other d^8 complexes[29,30]. A non-concerted route is supported by kinetic data, the distribution of isomeric products from a monosubstituted cubane, and above all the isolation of an intermediate rhodium complex in the stoichiometric reaction of cubane with the dimer of the dicarbonylrhodium chloride. The tetrameric structure of the intermediate complex



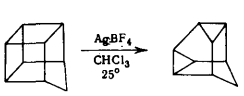
which corresponds to the tetragonal structure of the rhodium atom, is quite soundly based on its chemical reactions and infrared spectra[31].

The silver ion is an efficient catalyst for the isomerisation of cubane and its derivatives[32,34]. The valency rearrangement of cubane itself (catalysed by silver perchlorate in benzene) yields the saturated isomer cuneane (pentacyclo[3,3,0,$0^{2,4}$,$0^{3,7}$,$0^{6,8}$]octane), a representative of important natural ring systems (the cuneane molecule should be ~30–40 kcal mole^{-1} less strained than cubane):

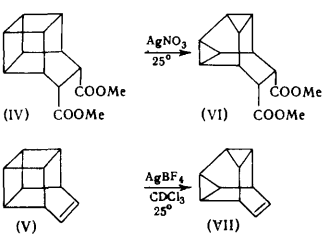


Cubane undergoes an analogous transformation under the influence of palladium(II) complexes (e.g. $[PdCl_2(C_6H_5CN)_2]$).[32]

The remarkable ability of the silver ion to promote symmetry-disallowed skeletal rearrangements is clearly apparent in the valency, isomerisation not only of cubane but also of its derivatives—homocubyl, 1,1′-bishomocubyl, and secocubane systems. In particular, homocubane (II) is converted in the presence of silver tetrafluoroborate into pentacyclo[4,3,0,$0^{2,4}$,$0^{3,8}$,$0^{5,7}$]nonane (III):[33]

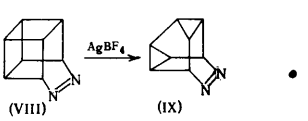


Although the homocubane structure is more strained than the pentacyclononane structure by about 45 kcal mole^{-1}, the purely thermal rearrangement ($\sigma 2a + \sigma 2a$) of (II) into (III) is not allowed by the Woodward–Hoffmann rules. The ease of the silver-catalysed process is probably due to mixing of the orbitals of the metal with the strained σ-orbitals of homocubane, resulting in the appearance of new occupied molecular orbitals, whose symmetry properties are compatible with the permitted isomerisation. Examples of the valency isomerisation of 1,1′-bishomocubyl derivatives are provided by the rearrangement of compounds (IV) and (V) into the corresponding pentacyclic isomers (VI) and (VII)[33–35]:



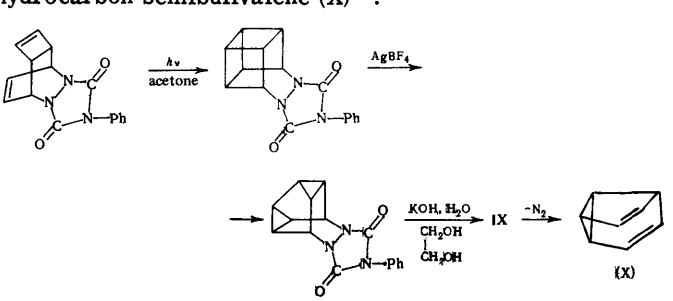
Formation of the pentacyclic diester (VI)has been observed also in thermal isomerisation. This suggests that here the effect of the transition metal is to lower the energy barrier to reaction, especially as four cyclobutane rings are converted into the thermodynamically more stable system comprising two cyclopropane and two cyclopentane rings. This reaction was not catalysed by compounds of mercury, copper, zinc, iron, and rhodium, nor by mineral acids.

It is noteworthy that a redistribution of σ-bonds occurs with compound (V), while the π-bond of the cyclobutene ring, having a greater tendency to coordinate with a metal, remains unchanged[33]. Nevertheless, the azo-derivative (VIII) does not isomerise into (IX)



under conditions of catalysis by the silver ion, probably owing to the presence of the lone pairs of electrons on the nitrogen atoms, which interact readily with the metal[36].

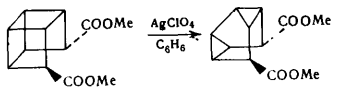
The silver-catalysed rearrangement of 1,1′-bishomocubyl systems has been used for preparative purposes, in particular to obtain the hitherto almost inaccessible hydrocarbon semibullvalene (X)[36]:



Although attempts to obtain this difficultly accessible hydrocarbon by the valency isomerisation directly of compound (VIII) were unsuccessful[36], use of its *NN*′-disubstituted derivatives (e.g. an *NN*′-diester) gave positive results[37].

The stereospecificity of catalytic valency isomerisations of cubane systems is excellently illustrated by the

silver-catalysed rearrangement of secocubane compounds[39,40]. Thus the *endo-endo*-diester (XI) gives a quantitative yield of the *endo-endo*-tetracyclo[3,3,0,$0^{2\ 8}$,$0^{4\ 6}$]-octane derivative (XII), and the *exo-exo*-diester is correspondingly converted into *exo-exo*-isomer[40]:



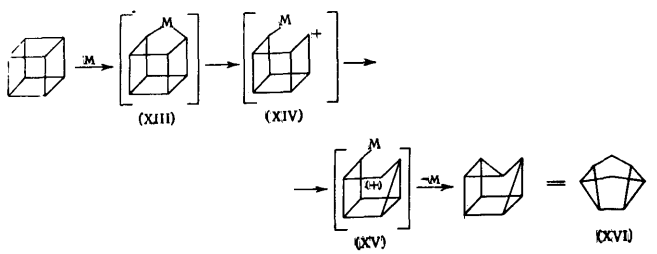
(XI) (XII)

Similar stereoselectivity has been observed also with tetra-substituted derivatives[39].

From the distribution of reaction products and a comparison of the rates of isomerisation of various *exo-endo*-isomers it is concluded[39] that substituted σ-bonds ($C_{(1)}$–$C_{(2)}$, $C_{(5)}$–$C_{(6)}$, $C_{(2)}$–$C_{(3)}$, and $C_{(4)}$–$C_{(5)}$) are not involved in the reaction. Furthermore, numerous examples of the isomerisation of homocubyl, 1,1′-bishomocubyl, and secocubane systems have shown convincingly that the presence of the $C_{(2)}$–$C_{(5)}$ bond is not necessary for the reaction.

The marked difference in catalytic properties shown by rhodium(I) compared with silver(I) and palladium(II) in the valency isomerisation of cubane and its derivatives cannot be explained in terms of electron configurations, since palladium(II) ($4d^8$) resembles silver(I) ($4d^{10}$) more closely than the isoelectronic rhodium(I) ($4d^8$). The reaction mechanism in this case is most probably determined by the oxidising properties of the metals or the effect of the ligand field.

The most general view of the valency isomerisation of cubane and related compounds catalysed by silver(I), palladium(II), and rhodium(I) has been given by Cassar et al.[41] on the basis of a non-concerted carbonium-ion mechanism involving a stage of oxidative addition:



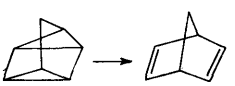
The oxidative addition of a metal ion (Ag^+, Pd^{2+}, or Rh^+) to the cubane molecule yields an organometallic adduct (XIII), which is obviously converted by the ions Ag^{2+} and Pd^{4+} into a cyclobutylcarbonium ion (XIV) (because of the strongly degenerate oxidative character of these metal ions). The ion (XIV) would in turn rearrange into the more stable cyclopropylcarbonium ion (XV). Subsequent reductive elimination of the metal ion should yield the final product, e.g. cuneane (XVI). In the case of catalysis by rhodium(I) further conversion of the organorhodium compound into a carbonium ion probably cannot occur owing to the lower oxidising power of rhodium(III)—compared with silver(II) and palladium(IV).

A stepwise mechanism is supported also by the influence of the positions and electronic effects of substituents on the rates of isomerisation of cubane systems[39,40,42]. Thus a linear free-energy correlation has been established[42] between the rate constants of the rearrangement of 1,4-disubstituted cubanes and the Taft polar δ* constants: rearrangement takes place more slowly the more negative is this constant (the greater the electron-repelling effect of the substituent). The closely similar rates of isomerisation of all stereoisomers of the secocubane ester (XI) and of reaction of the more strained dimethyl cubane-1,4-dicarboxylate probably indicate that electronic factors have a greater influence than geometric factors, which can be explained only in terms of a stepwise mechanism.

In spite of the above fairly convincing arguments in support of a non-concerted pathway for the valency isomerisation of cubane systems, interpretation of these reactions on the basis of a concerted mechanism cannot be finally rejected.

We can try to explain certain facts as due to the effect of the ligand field. The difference in catalytic activity between the isoelectronic palladium(II) and rhodium(I) is obviously associated, not with filling of the *d*-shells, but with the difference in the effects of the field due to the ligands (e.g. $[PdCl_2(C_6H_5CN)_2]$ and $[(RhCl\,dien)_2]$. Substitution of the ligands even in the rhodium complex may lead to a loss of activity towards the isomerisation of cubane (such an effect is produced in particular by replacing the diene ligands by triphenylphosphine ligands[31]). An intermediate complex of rhodium with cubane and its derivatives could be isolated only in the case of the dimer of carbonylrhodium chloride, which cannot be related to the specific properties of carbon monoxide as a ligand. Mango and Schachtschneider showed[26] that this ligand imposes a considerable ligand-field type of restriction on the concerted opening of the cyclobutane ring. They do not recommend the use of carbonyl-containing complexes as catalysts for valency isomerisations. The mechanism of the valency isomerisation of cubane and its derivatives catalysed by transition metals—silver(I), palladium(II), and rhodium(I)—has not yet been finally established. This problem may be solved when additional experimental results appear, and have been subjected to detailed analysis taking into account the orbital symmetry with the construction of correlation diagrams in each specific case.

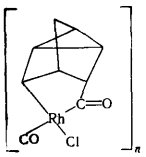
The conversion of quadricyclene into norbornadiene



is especially noteworthy among the valency isomerisations of strained cyclic systems disallowed by the Woodward–Hoffmann rules[43-45]. This skeletal rearrangement has been the object of the most thorough study of the dependence of the catalytic activity of transition-metal complexes on the filling of their *d*-shell and on the geometric configuration of the complexes[45]. The quantitative conversion of quadricyclene into norbornadiene has been effectively catalysed by mono- and di-alkene complexes of rhodium, palladium, and platinum—di-μ-chloro-dibicyclo-[2,2,1]hepta-2,5-dienedirhodium, di-μ-chloro-tetraethylenedirhodium, dichloro-cyclo-octa-1,5-dienepalladium, di-μ-chloro-bis-π-methylallyldipalladium, and dichloro-bicyclo[2,2,1]hepta-2,5-dieneplatinum—as well as by complexes of several transition metals with phthalocyanine and a tetraphenylporphyrin[45].

Two views are held on the mechanism of this reaction, as in the case of cubane: either the cyclobutane ring undergoes concerted opening, or a non-concerted process involves initial cleavage only of one carbon–carbon bond of the cyclobutane fragment by oxidative addition. A telling argument in support of a non-concerted mechanism is the formation of a rhodium complex of quadricyclene[43] by reaction of the dimer of dicarbonylrhodium chloride

with excess of quadricyclene. The structure of this complex



resembles that of the corresponding cubane complex (I).[31] However, a concerted mechanism is also quite likely, since the molecule could easily coordinate with the metal as a consequence of the π-character of the cyclopropane bonds common to the three- and four-membered rings[44].

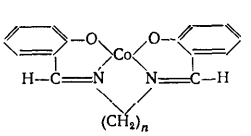
Table 1. Catalytic activity of square planar complexes of bivalent metals in the isomerisation of quadricyclene*.

Electronic structure	d^5	d^6	d^7	d^8				d^9		d^{10}
Metal ion	Mn^{2+}	Fe^{2+}	Co^{2+}	Ni^{2+}	Pt^{2+}	Rh^{1+}	Pd^{2+}	Cu^{2+}	Ag^{2+}	Zn^{2+}
	−	+	+	+	+	+	+	−	−	−

*+ = active; − = inactive.

Manassen has shown[45] that the ability of metals to catalyse the isomerisation of quadricyclene is primarily connected with the filling of the d-shell. Ions of metals with d^6, d^7, and d^8 electron shells are active in this process, whereas d^9 and d^{10} ions do not catalyse the reaction (Table 1). Such correlation is readily explained in terms of a concerted mechanism. In the d^8 complexes of rhodium, palladium, and platinum the d_{xy} orbital (i.e. the orbital of symmetry AS) should be vacant, or the highest unoccupied p-orbital should be quite close in energy to the occupied d-orbital. In the d^{10} complexes of copper(I) and silver(I) all the orbitals are occupied, and these ions are evidently incapable of catalysing the concerted opening of the cyclobutane ring.

The effect of ligands on the catalytic activity of the complexes (Section III) is due to splitting of the metal orbitals. In a study of complexes with quadridentate ligands (phthalocyanine, tetraphenylporphyrin, and certain Schiff bases) Manassen showed that a square planar configuration is the main condition for catalytic activity in the isomerisation of quadricyclene[45]. This configuration possesses vacant octahedral sites for the coordination of quadricyclene molecules with formation of an intermediate complex of symmetry such that concerted opening of the cyclobutane ring becomes permitted. As soon as the configuration of the catalytic complex ceases to be planar, the symmetry of the intermediate complex changes, and concerted opening of the ring remains symmetry-disallowed. For example, the most active catalyst for the rearrangement of quadricyclene was the square planar cobalt complex of a Schiff base



(XVII)

having $n = 2$. Complexes in which $n > 2$, whose configuration is non-planar, do not catalyse this isomerisation. Furthermore, the need for vacant octahedral sites in the square planar complexes is supported by the inhibition of their catalytic activity by pyridine bases, which are known to coordinate at octahedral sites in metal porphyrins[46].

Thus the important factor in the catalysis of symmetry-disallowed reactions is the field due to the ligands, together with the filling of the d-orbitals of the metal. On the whole the catalytic activity of each metal in concerted addition (or rupture of bonds) depends on its ability to form complexes of definite symmetry. That is why some metals possess catalytic activity, while others do not.

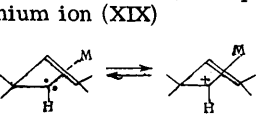
A detailed study has been made of the isomeric changes undergone by bicyclo[1,1,0]butane, which occurs as a structural unit in several polycyclic molecules. Available experimental results indicate that the direction of the valency isomerisation of bicyclobutanes catalysed by transition-metal complexes and ions is determined by the type of metal, the nature of the ligands, and also the positions of alkyl substituents in the bicyclobutane system.

Under the influence of the silver ion alkylated bicyclobutanes undergo almost quantitative and largely stereospecific conversion into dienes[47-50]. Thus *exo-exo*- and *endo-exo*-2,4-dimethylbicyclobutanes are converted mainly into *trans-trans*- and *cis-trans*-hexa-2,4-dienes respectively[47,48]. Under similar conditions 1,2,2-trimethylbicyclobutane yields not only hexa-2,4-dienes but also the corresponding vinylcyclopropane[49], whereas unsubstituted bicyclobutane is converted into butadiene[47].

Isomerisation proceeds differently in the presence of catalysts containing palladium[50,51]. Thus both 2,4- and 1,3-dimethylbicyclobutanes are converted under the influence of dichlorodibenzonitrilepalladium mainly into 2-methylpenta-1,3-diene[50]. Study of this complex together with bischloro-π-allylpalladium shows[51] that the nature of the ligand attached to the transition metal has a substantial influence on the direction of the isomerisation of bicyclobutanes. When small quantities (~ 0.2 mole %) of the catalyst are used, ligand exchange may occur during the reaction, which can lead to anomalous products[51].

In the presence of carbonyl complexes of rhodium, iridium, and ruthenium, alkylbicyclobutanes are converted into dienes and vinylcyclopropane. The structure and the proportions of the products are determined by the position of the alkyl substituents in the initial bicycle[50,52,53].

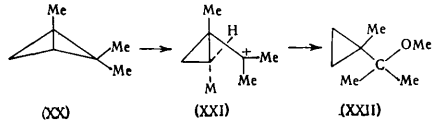
The mechanism of the valency isomerisations of the bicyclobutane system has been a matter of great debate. Several alternative mechanisms have been suggested. Paquette et al.[48,54] originally regarded the silver-catalysed rearrangement of bicyclobutanes into a 1,3-diene system as a concerted process of type $\sigma 2a + \sigma 2a$. However, later work[49,53,55,56] has led to rejection of a concerted mechanism for such processes. A silver–carbonium ion, resulting from rupture of the central $C_{(1)}$–$C_{(3)}$ bond of bicyclobutane followed by complex formation with the silver ion, was suggested[49] as intermediate. According to Gassman et al.[53] the intermediate compound is a transition-metal carbene complex (XVIII) in equilibrium with the hydride–carbonium ion (XIX)



(XVIII) (XIX)

These workers have since obtained[57,58] direct evidence that the interconversion (XVIII) ⟷ (XIX) is a stepwise

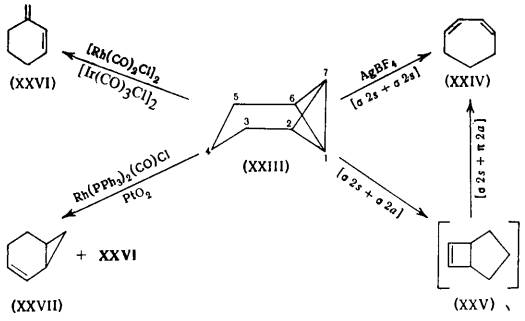
process involving successive rupture of the $C_{(1)}-C_{(2)}$ and $C_{(1)}-C_{(3)}$ bonds of bicyclobutane under the influence of the transition-metal complex. Formation of a cyclopropylmethyl cation (XXI) preceding appearance of the structures (XVIII) ⟷ (XIX) is supported by production of the corresponding methoxycyclopropane (XXII) from 1,2,2-trimethylbicyclobutane (XX) in the presence of bischlorodicarbonylrhodium in a strongly nucleophilic solvent (methanol):



(XX) (XXI) (XXII)

However, these workers [58] do not exclude the possibility of a different stepwise mechanism depending on the solvent.

The valency isomerisation of tricyclo[4,1,0,$0^{2,7}$]heptane (XXIII) is catalysed by a wide range of transition metals, the direction of the reaction being determined by the type of catalyst employed:

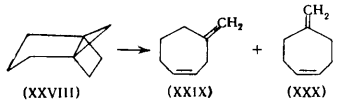


(XXVI) (XXIII) (XXIV) (XXVII) (XXV)

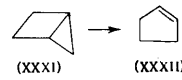
In the presence of silver tetrafluoroborate (XXIII) is converted rapidly and quantitatively into cyclohepta-1,3-diene (XXIV). [47,54] In view of the part played by the silver ion in several concerted processes, this reaction can be regarded as resulting from a symmetry-disallowed concerted ring opening of type $\sigma 2s + \sigma 2s$. With a non-concerted mechanism a two-step process can occur, involving as initial stage the thermally allowed rearrangement $\sigma 2s + \sigma 2a$ of (XXIII) to bicyclo[3,2,0]hept-6-ene (XXV) [59] followed by ring opening of type $\sigma 2s + \pi 2a$.

When (XXIII) isomerises in the presence of catalysts containing rhodium, iridium, platinum, ruthenium, palladium, and copper, the sole (or main) product is 3-methylenecyclohexene (XXVI), the yield of which is determined by the type of ligand [60,61]. Small quantities bicyclo[4,1,0]hept-2-ene (XXVII) are also formed. We must not overlook the fact that palladium(0), platinum(IV), and rhodium(I) were similar in their catalytic effects on this reaction, but the reason is still obscure. The ability of heterogeneous catalysts based on noble metals (PtO_2, Pd/C) to catalyse the isomerisation of tricycloheptane suggests that isomerisation is possible in their presence even during the hydrogenation of highly strained rings.

Examples of the valency isomerisation of polycyclic systems are the conversion of tricyclo[3,2,1,$0^{1,5}$]octane (XXVIII) into 4- and 5-methylenecycloheptenes (XXIX) and (XXX) [62] and the isomerisation of bicyclo[2,1,0]pentane (XXXI) into cyclopentene (XXXII) [63], which should take place in the presence of carbonyl complexes of rhodium, iridium, and ruthenium:



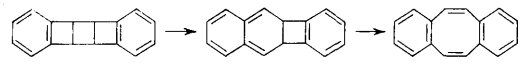
(XXVIII) (XXIX) (XXX)



(XXXI) (XXXII)

By analogy with the isomerisation of bicyclobutane and tricycloheptane the above changes are regarded [62] as stepwise processes with intermediate formation of a metal–carbene complex similar to structures (XVIII) ⟷ (XIX).

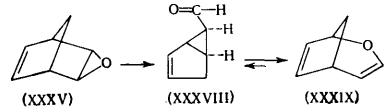
Several valency isomerisations involve the opening of a cyclobutene ring forming part of a bicyclic or tricyclic system. In the presence of silver ions at room temperature, for example, dibenzotricyclo-octadiene (XXXIII) isomerises to dibenzocyclo-octatetraene (XXXIV) [64–66]:



(XXXIII) (XXXIV)

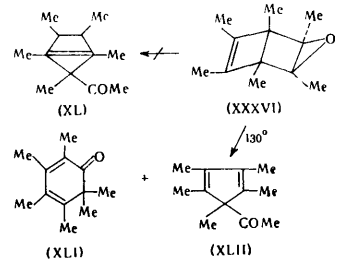
The forbidden disrotatory ring-opening (XXXIII) ⟷ (XXXIV) obviously becomes allowed thanks to the additional orbitals of the metal catalyst.

Papers have appeared recently [67,68] on the isomerisation of the epoxides of norbornadiene (XXXV), Dewar hexamethylbenzene (XXXVI), and cyclo-octatetraene (XXXVII). Under the influence of the dimer of dicarbonylrhodium chloride the first of these epoxides (XXXV) is converted quantitatively into the aldehyde (XXXVIII) and the cyclic ether (XXXIX):



(XXXV) (XXXVIII) (XXXIX)

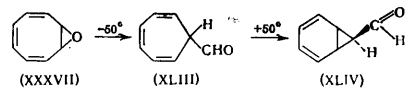
Thermal rearrangement of (XXXVI) is permitted and is a concerted process $\pi 2a + \sigma 2s + \sigma 2a$, which should yield the very strained cyclic system (XL). The actual products of thermal isomerisation, however, are the cyclohexadienone (XLI) and the cyclopentadienyl methyl ketone (XLII):



(XL) (XXXVI) (XLI) (XLII)

Catalytic isomerisation is more specific and gives mainly the latter product (XLII).

Cyclo-octatetraene epoxide (XXXVII) in the presence of the same rhodium complex is readily converted into the aldehyde (XLIII), which when heated to 50°C isomerises into the *exo*-aldehyde (XLIV) (probably as a result of disrotatory opening of the ring):



(XXXVII) (XLIII) (XLIV)

The rhodium-catalysed rearrangement of the epoxides (XXXV)–(XXXVII) is regarded [67,68] as a non-concerted process involving a step of oxidative addition to the metal with fission of a carbon–oxygen bond.

Despite the great attention paid to the valency isomerisation of strained cyclic systems catalysed by transition metals, it has not yet become generally accepted

whether the mechanism is concerted or stepwise. Sufficient experimental data are evidently not yet available to settle this question.

2. Disproportionation of Unsaturated Compounds

The disproportionation of a carbon–carbon double bond [69,70]

$$\begin{matrix} RCH{=}CHR' \\ RCH{=}CHR' \end{matrix} \rightleftarrows \begin{matrix} RCH \\ \| \\ RCH \end{matrix} + \begin{matrix} CHR' \\ \| \\ CHR' \end{matrix}$$

catalysed by transition-metal complexes, can be regarded as conforming to the Woodward–Hoffmann rules for the conservation of orbital symmetry [6]. The mechanism which is currently accepted involves intermediate formation of a "quasi-cyclobutane" four-membered ring (XLVI), which can break down in two ways with formation either of products or of the starting materials [71]:

$$\begin{matrix} RCH{=}CHR' \\ RCH{=}CHR' \\ \text{(XLV)} \end{matrix} \rightleftarrows \left[\begin{matrix} RHC\text{——}CHR' \\ | \quad\quad | \\ RHC\text{——}CHR' \end{matrix}\right] \rightleftarrows \underbrace{\begin{matrix} RCH \\ \| \\ RCH \end{matrix} + \begin{matrix} CHR' \\ \| \\ CHR' \end{matrix}}_{\text{(XLVII)}}$$
$$\text{(XLVI)}$$

Experiments with labelled alkenes confirmed [72–74] that redistribution of the double bonds took place via a four-centre state. Hence disproportionation can be regarded as a suprafacial cycloaddition (and cyclodecomposition) of type $\pi 2s + \sigma 2s$, disallowed by the Woodward–Hoffmann rules.

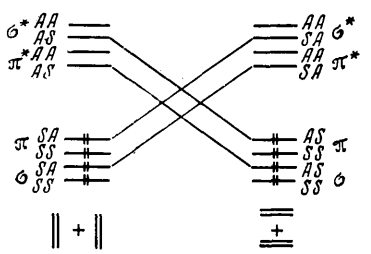
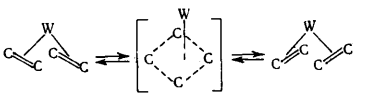


Figure 10. Correlation diagram for the disproportionation of alkenes.

The correlation diagram (Fig. 10) shows that occurrence of the reaction (XLV) → (XLVII) [26] requires that either orbitals of symmetry *SA** in the reaction products (XLVII) or those of symmetry *AS** in the initial alkenes (XLV) should be filled. Only under these conditions can the intermediate cyclobutane structure be formed, and then two new alkene molecules (Fig. 11).

The disproportionation of unsaturated hydrocarbons can take place under conditions of either homogeneous or heterogeneous catalysis [69,70]. Inspection of the correlation diagram shows (Fig. 11) that interaction of alkenes with a metal may make disproportionation a symmetry-allowed process provided that the metal–dialkene complex has lower filled orbitals of symmetry *AS* and *SA*. Satisfaction of this condition depends on the geometry of the intermediate complex and on the relative effect of the fields due to the unchanged ligands.

In the early work on homogeneous disproportionation Calderon et al. [75] assumed that the intermediate complex was a tetragonal pyramid on a square base formed by two alkene molecules, with the metal atom (tungsten) located at the vertex:



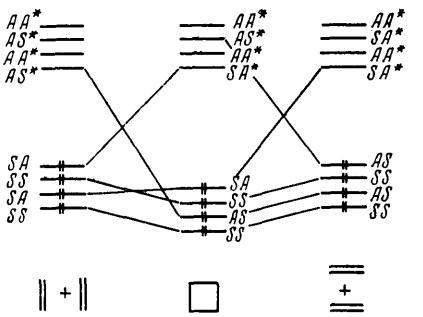


Figure 11. Correlation diagram for the transitions alkene → cyclobutane → alkene.

The position of the remaining ligands remained obscure. The double bonds were supposed to be weakened by coordination of the alkenes with the metal, so that exchange of the alkylidene groups became possible.

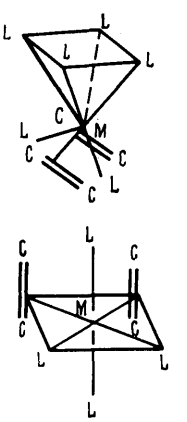


Figure 12. Possible structures of the intermediate metal–dialkene complex in disproportionation.

More precise geometries were suggested for the intermediate complex by Wang and Menapace [76] (for the catalytic system WCl_6 + n-C_4H_9Li) and also by Hughes [77] (for nitrosyl complexes of molybdenum). The intermediate complex can be regarded as an octahedron with the alkene ligands in the *cis*-position or as an Archimedean antiprism (Fig. 12).

Galdow and MacGregor [78] made calculations on the reactions alkenes → cyclobutane → alkenes [1] catalysed by d^6 and d^8 metals, and drew the corresponding correlation diagrams. They found that, in the presence of strong ligand fields and low-spin configurations, the most favourable geometry for the intermediate complex was (Fig. 13).

trigonal bipyramid (D_{3h}) ⇌ square pyramid (C_{4v}) ⇌ ⇌ trigonal bipyramid

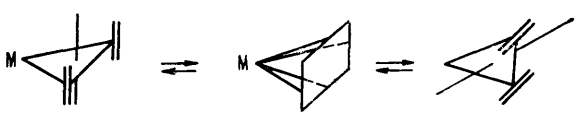
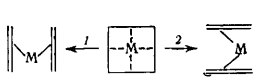


Figure 13. Geometry of the intermediate complex in the disproportionation of alkenes for low-spin d^6 and d^8 metal configurations.

A tetrahedral or square planar configuration imposes strong field restrictions on the redistribution of double bonds in alkenes. Quantum-mechanical calculations for d^6 and d^8 metals show [26,78] that the transition alkenes ⇌ ⇌ cyclobutane is impossible in the presence of a strong ligand field. With weak ligand fields, when splitting of the d-levels is small, such conversion is made possible by mixing of the orbitals of the ground state with lower excited orbitals.

Mango and Schachtschneider [26] constructed correlation diagrams, based on calculations by the extended Hückel method, for carbonyl and chloride complexes of iron and nickel. They examined square planar and tetrahedral configurations for the complexes ML_2alkene$_2$ and ML_2cyclobutane. They found that the transition dialkene ⇌ cyclobutane with preservation of the square planar configuration of the whole complex was restricted with respect to symmetry, since the ground state of the reactants correlated with an excited state of the products. The tetrahedral configuration showed no symmetry disallowance, but the cyclobutane ring can open only in one direction (*1* or *2*):

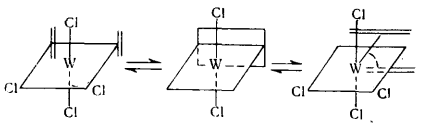


In particular, path *1* is symmetry-allowed for d^6 and d^8 metals, and path *2* for d^{10} metals.

When the complex contains a carbonyl ligand, the strong splitting of the d-orbitals results in the appearance of an energy barrier along the allowed path of the transition. Hence cycloaddition can be expected to occur—not disproportionation—when complexes with strong ligands are used as catalysts, since the latter process would require that the cyclobutane ring could break down in both directions. Such conditions can be achieved in weak ligand fields, where splitting of the d-orbitals is small.

Disproportionation of alkenes in the presence of the WCl_6 + RMgHal catalytic system [79] probably takes place by a four-centre mechanism, since a chloro-ligand does not produce strong fields. The reduction of tungsten hexachloride to the tetrachloride followed by coordination of two alkene molecules to the tungsten atom in the d^2 state suggests the transition

Alkenes ⇌ Cyclobutane ⇌ Alkenes



Attempts at the catalytic decomposition of cyclobutane into alkenes on disproportionation catalysts proved unsuccessful, which led Lewandos and Pettit [80,81] to suggest a four-centre mechanism of disproportionation but without cyclobutane as intermediate. They assumed the formation of a tetramethylene intermediate complex by interaction of the d-orbitals of the metal with four methylene orbitals of the alkene. This interaction is also severely restricted by symmetry: i.e. transitions are permitted only between orbitals of the same symmetry. Such interaction leads to formation of the four-centre system (XLVIII) (Fig. 14), which can break down to yield either (1) the initial substances or (2) disproportionation products.

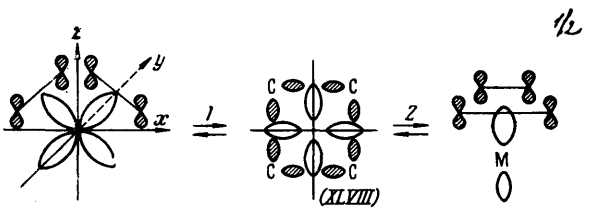


Figure 14. Possible mechanism of disproportionation.

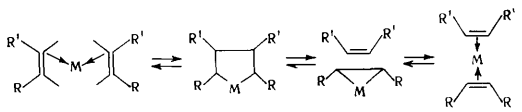
A significant difference between this mechanism and that involving formation of cyclobutane is that here the carbon σ-bonds of the initial alkenes are broken at the same time as the π-bonds. Coordination of the tetramethylene intermediate with the metal takes place at four sites: i.e. the metal must be in a low state of oxidation. Pettit [81] supports his hypothesis by results for the disproportionation of pent-2-ene and non-4-ene under the influence of an arene–$W(CO)_3$ complex. It is suggested that, when tricarbonyltungsten is used, the removal of one carbonyl group is the decisive factor in formation of the tetramethylene–$W(CO)_2$ complex, since only in this case does the tungsten have four vacant coordination sites. Disproportionation does not take place in the presence of excess of carbon monoxide, owing to an insufficient number of free sites for coordination of the tetramethylene complex.

In the Reviewers' opinion a configuration of the intermediate M–alkene complex that is unfavourable for the alkene ⇌ cyclobutane transition is obtained with excess of carbon monoxide, and furthermore carbonyl produces a strong ligand field. The existence of a tetramethylene complex as intermediate also seems improbable, since the proposed [81] symmetry analysis will not give satisfactory results for the simultaneous disproportionation of alkenes with an inner and a terminal double bond.

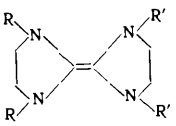
All the above mechanisms for the disproportionation of alkenes presuppose, independently of the structure of the intermediate complex, that the process is concerted.

Recently, however, data have appeared indicating that this reaction may have a non-concerted mechanism, as postulated earlier by Cassar et al.[31]

Formation of a metal ring as intermediate has been suggested[82]:



Carbene complexes have been isolated as intermediates (under the influence of rhodium(I) complexes)[83] in the disproportionation of "electron-rich" alkenes of the type



Thus the mechanism of the disproportionation of alkenes still remains a matter of controversy.

3. Hydrogenation of Alkenes

Special interest attaches to application of the conservation rules of orbital symmetry to a process of such theoretical and practical importance as the catalytic hydrogenation of unsaturated compounds in the presence of transition-metal complexes. Although many papers (including reviews[84-87]) have been published on homogeneous catalytic hydrogenation, many aspects of the reaction mechanism and of the action of the catalysts remain matters of debate. In particular, the sequence of the interrelated stages of activation of molecular hydrogen and activation of the substrate has not been established. Convincing explanations of the selective action of complex catalysts have not appeared.

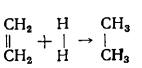
In the Reviewers' opinion, regarding catalytic hydrogenation as the concerted addition of molecular hydrogen to the double bond of an alkene allows us to postulate that the first stage of homogeneous hydrogenation is complex formation between alkene and metal. The selectivity of the action of complex catalysts should be related to the way in which the unsaturated substrate is coordinated with the metal.

Uncatalysed hydrogenation

The uncatalysed hydrogenation of a carbon–carbon double bond can occur in two ways. A free-radical mechanism involves dissociation of the hydrogen molecule followed by addition of the hydrogen atoms at the double bond:

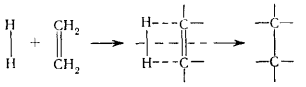
$$H_2 \rightarrow H + H$$
$$CH_2=CH_2 + H \rightarrow CH_3-CH_2^{\cdot}$$
$$CH_3-CH_2^{\cdot} + H \rightarrow CH_3-CH_3$$

The hydrogen molecule may undergo concerted addition to the alkene:

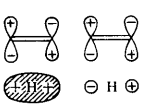


The first of these mechanisms is symmetry-allowed[88,89] according to the Woodward–Hoffmann rules[6], but the reaction has a high activation barrier owing to the large dissociation energy of the hydrogen molecule (104 kcal mole^{-1}). Extreme conditions—high temperatures and pressures—are therefore necessary for the uncatalysed hydrogenation of alkenes[90].

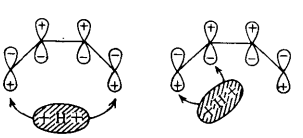
The second pathway—concerted addition—presupposes formation of an intermediate four-centre state followed by simultaneous cleavage of H–H and C=C bonds with formation of new C–H bonds:



Monoalkenes and alkenes having non-conjugated multiple bonds, like the hydrogen molecule, belong to the D_{nh} point group; the highest occupied orbitals in the ground state are the A_{1g} orbital of hydrogen and the B_{3u} orbital of the alkene. In the transition state for concerted addition (four-centre configuration, point group C_{2v}) the highest occupied orbitals have symmetry A_1 and B_2, while the B_{3u} orbital passes into B_1 and is an excited orbital. Thus the ground state of the reactants correlates in symmetry with an excited state of the intermediate configuration, so that the concerted addition of hydrogen to monoalkenes and alkenes having isolated double bonds is disallowed by symmetry[88,89]. According to the Woodward–Hoffmann rules[6] thermally forbidden reactions can be accomplished photochemically. Hence the photochemical hydrogenation of alkenes is fully able to occur by a four-centre mechanism:



The hydrogenation of conjugated dienes is symmetry-allowed when hydrogen adds at the 1,4 (or 2,3) positions, and disallowed in the case of 1, 2 (or 3, 4) addition[88,89]:

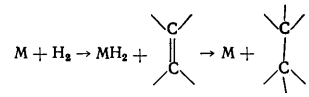


Catalytic homogeneous hydrogenation of alkenes

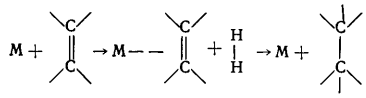
Homogeneous hydrogenation is currently regarded as being generally a stepwise process with successive addition of hydrogen atoms to the double bond of an alkene. The first stage is assumed to be activation of molecular hydrogen by its interaction with the metal (homolytic fission with formation of a mono- or a di-hydride or heterolytic fission with formation of a monohydrate). The H–H bond can be weakened both by transfer of electrons from a filled *d*-orbital of the metal to an antibonding orbital of the hydrogen molecule[91] and by redistribution of electron density between an occupied bonding orbital of the hydrogen molecule and a vacant orbital of the metal[87,92]. Aspects of the activation of molecular hydrogen by simple and complex ions of transition metals have been discussed in detail[84,85,87,91].

The possibility of the concerted addition of a hydrogen molecule to a carbon–carbon double bond was first pointed out by Pearson[88,89]. As already mentioned, a symmetry-forbidden reaction may become allowed by the participation of a transition metal[23]. If catalytic hydrogenation is regarded as a concerted process, three possible reaction paths can be distinguished—(1) formation

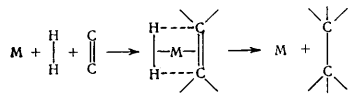
of a complex MH_2 and its subsequent interaction with the substrate



(2) formation of a metal–alkene complex followed by its interaction with hydrogen



and (3) simultaneous coordination of hydrogen and alkene molecules with the metal followed by interaction of hydrogen with the alkene in the complex



The formation of two new carbon–hydrogen bonds in the hydrogenation of a double bond requires the preliminary interaction of an unoccupied orbital of the hydrogen molecule A_{1u} with an occupied orbital of the alkene B_{3u} or of an occupied orbital of hydrogen A_{1g} with a free orbital of the alkene B_{2g}. In the absence of a transition metal such interaction between orbitals of the hydrogen molecule and of the substrate is symmetry-forbidden. When a hydrogen or an alkene molecule coordinates with a metal, interaction of a filled d-orbital of the metal with an unoccupied orbital of the molecule (Fig. 15) removes the symmetry restriction, independently of the geometry of the resulting complex. In both cases the given fragment of the complex has symmetry C_{2v}. With simultaneous coordination of hydrogen and alkene molecules with a metal concerted addition is impossible if the two molecules lie in the same plane (Fig. 15). Departure from a planar configuration may bring one hydrogen atom closer to the alkene molecule than the other, in which case there is no sense in considering a concerted process.

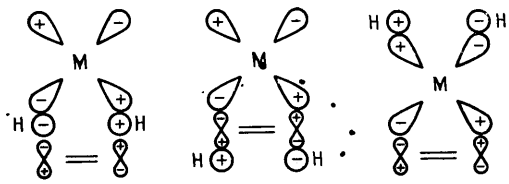
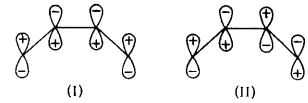


Figure 15. Possible intermediate configurations in the catalytic hydrogenation of alkenes.

Thus, depending on the suggested mechanism for homogeneous hydrogenation, the metal either activates molecular hydrogen (in the stepwise scheme) or changes the symmetry of the highest occupied orbitals of the reactants by interaction with the substrate, so that the forbidden reaction becomes allowed (concerted addition).

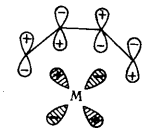
Regarding the hydrogenation of a double bond as a concerted process will explain the selective action of transition-metal complexes in the hydrogenation of conjugated dienes. As mentioned above, addition of a hydrogen molecule at the 1,4 (or 2,3) positions is a symmetry-allowed process. Such addition should result in monoalkenes having an internal double bond. The effect of the metal catalyst is then merely to lower the activation barrier without changing the symmetry of the system [27,93].

Conjugated dienes have two antibonding π-orbitals

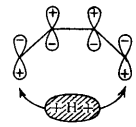


(I) (II)

Coordination of the diene with a metal and formation of a dative bond take place when the orbital (II) interacts with a filled d-orbital of the metal

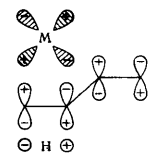


It has been shown in the formation of a metal–butadiene complex that the electron density is displaced from the periphery towards the centre of the diene molecule [93]. The antibonding π-orbital (I) remains vacant, but is allowed by its symmetry to interact with a filled σ-orbital of hydrogen: i.e. addition of hydrogen will occur at the 1,4 positions to form monoenes having an internal double bond



Thus interaction of a metal with a substrate does not change the symmetry of the highest occupied orbitals involved in the formation of carbon–hydrogen bonds, but merely removes the energy difference between them.

A different pattern is found in the hydrogenation of conjugated dienes at the 1,2 positions. As with monoalkenes, the concerted addition of a hydrogen molecule to this double bond is symmetry-forbidden. Interaction of the substrate with a metal may make the 1,2-addition symmetry-allowed, but only provided that coordination of the diene with the metal occurs only at the site of the hydrogenated bond. Thus the electron density of the metal–diene bond would be displaced towards the end of the diene molecule:



In this case the reaction products should be terminal alkenes.

The high selectivity exhibited by complexes of metals of the fourth period in the hydrogenation of conjugated dienes to monoalkenes (Table 2) is evidently connected with the mode of coordination of the diene molecule with the metal. When chromium and vanadium complexes are used as catalysts, for example, monoenes with a terminal double bond are almost completely absent from the products [98,99,101], which must definitely be related to the paucity of complexes of these metals with monoenes

and non-conjugated alkenes. The hex-2-ene and hex-3-ene obtained by the hydrogenation of hexadienes in the presence of tricarbonylchromium do not isomerise, which probably indicates the inability of these metals (especially of chromium) in a particular state of oxidation to coordinate alkenes at only one double bond.

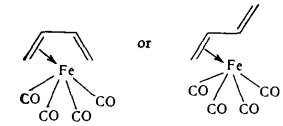
Table 2. Hydrogenation of conjugated dienes in the presence of complex catalysts.

Catalyst	Substrate	Hydrogenation product	Yield, %	Ref.
$CoCl_2$—KCN(CN/Co>6)	butadiene	but-1-ene	80—85	95
$CoCl_2$—KCN(CN/Co<5,5)		*trans*-but-2-ene		
		cis-but-2-ene	86	
$CoH(Ph_2PEt)_2$	butadiene	but-1-ene	11	96
		cis-but-2-ene	50	97
$Co(acac)_3 + Et_2AlCl + Ph_2PPr$	butadiene	*cis*-but-2-ene	38.7	
		but-1-ene	39.7	
$(C_5H_5)_2Cr(CO)_3$	isoprene	2-methylbut-2-ene	95	98
$PhCOOCH_2Cr(CO)_3$	hexa-1,3-diene	*cis*-hex-2-ene	66	99
		cis-hex-3-ene	40	
$PhCOOCH_2Cr(CO)_3$	hexa-2,4-diene	*cis*-hex-2-ene	90	99
		cis-hex-3-ene	10	
$PhCOOCH_2Cr(CO)_3$	methyl sorbate	methyl *cis*-hex-3-enoate		99
$RuCl_2$	isoprene	2-methylbut-2-ene		100
		3-methylbut-1-ene		
$(C_5H_5)_2VCl_2$	isoprene	2-methylbut-2-ene	97	101
$FeCl_3 + PPh_3 + AlEt_3$	butadiene	butadiene	22	102
		but-2-ene	13	
		but-1-ene	56.9	
		butane	83	
Ru-N-phenylanaline	isoprene	isopentane	8.4	103
		3-methylbut-1-ene	15.4	
		2-methylbut-1-ene	40.7	
		2-methylbut-2-ene	35.4	

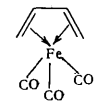
The possibility of the concerted addition of a hydrogen molecule to conjugated dienes at both the 1,4 and 1,2 positions can be illustrated by the hydrogenation of butadiene in the presence of pentacyanocobalt [94,95,104-115]. Kwiatek et al. [95] showed that the composition of the hydrogenation products depends on the CN/Co ratio. When the ratio is ≤ 5.5 the main product is *trans*-but-2-ene (70–86%), but dominant formation of but-1-ene (80–85%) takes place at ratios > 6. Such variation in the yields of the isomers was explained [95,107,115] by the possible formation of π-allyl and σ-allyl intermediate complexes at low and high ratios respectively.

An explanation of the above results in terms of concerted addition is that, at low ratios of the cyanide ion to cobalt, butadiene is probably coordinated on the complex ion $[Co(CN)_5]^{3-}$ (the activity of this ion has been demonstrated) [116-118], and a complex is formed in which the electron density of the metal–diene bond is localised in the region of the second and third carbon atoms of the diene: i.e. the diene acts as a bidentate ligand. In this case addition of hydrogen at the 1,4-positions will be symmetry-allowed, with the formation of but-2-ene. At high ratios an additional coordination site of the metal is occupied by a cyano-group ($[Co(CN)_6]^{4-}$ is probably formed), and the diene can be coordinated only through one double bond (the butadiene acts as a unidentate ligand). Addition of hydrogen at the 1,2-bond then becomes symmetry-allowed, with the predominant formation of but-1-ene.

Some support for the above arguments is provided by the existence of a butadiene complex of iron tetracarbonyl, in which the diene behaves as a unidentate ligand:



Nevertheless, butadiene occupies two coordination sites in the iron tricarbonyl complex:



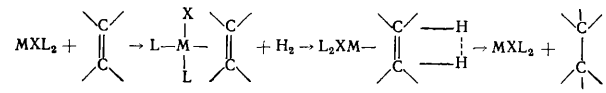
Considering the hydrogenation of a carbon–carbon double bond as a concerted process enables us to suggest complex formation between metal and alkene as the first stage in homogeneous hydrogenation. This view may be supported by several experimental results on the hydrogenation of monoalkenes and non-conjugated dienes in the presence of individual complexes of transition metals and complex organometallic compounds (catalysts of the Ziegler–Natta type).

The first stage in the hydrogenation of alkenes on phosphine complexes of rhodium and iridium is the detachment of one phosphine group, i.e. the freeing of one coordination site [119-121]:

$$MX(PPh_3)_3 \rightleftarrows MX(PPh_3)_2 + PPh_3$$

The second stage would be complex formation between the metal and one of the reactants, to give either the metal hydride or a metal–alkene complex.

The hypothesis that a dihydro-complex of the metal is an intermediate in this reaction was based on the isolation of iridium dihydride [122,123]. In a kinetic study of the hydrogenation of ethylene in the presence of hydrocarbonyltristriphenylphosphineiridium, however, Burnett and Morrison [124] found that the trihydrocarbonylbistriphenylphosphineiridium formed is an inhibitor of the reaction. Kinetic data on the hydrogenation of dimethyl maleate [125] indicate that the first stage is formation of an iridium complex of the substrate, which then reacts with hydrogen. Kinetic investigations of the hydrogenation of alkenes in the presence of chlorotristriphenylphosphinerhodium and hydrocarbonylbistriphenylphosphinerhodium also led Wilkinson et al. [126-128] to regard formation of a metal–alkene complex as the initial stage (the kinetic order with respect to the alkene varies from the first to zero). These results suggest concerted addition of hydrogen by the scheme



Complex organometallic catalysts of the Ziegler–Natta type are active in the hydrogenation of monoalkenes and non-conjugated dienes [84,85]. The decrease in reducing power of the organoaluminium component in the sequence

$$(AlEt_3 \geqslant Al(i\text{-}Pr)_3 > AlEt_2Cl > AlEtCl_2 > Al(OEt)Et_2)$$

leads to a fall in the catalytic activity of the system [129]. The sequence of transition metals with respect to their activity in catalysing the hydrogenation of alkenes is

$$Co \geqslant Ni > Fe > Mn \simeq Cr > V > Ti$$

i.e. their efficiency increases with increase in the number

of *d*-electrons. The calculated overlap integrals of the metal–alkene bond showed [130] that the energy of this bond diminishes in the same sequence

$$Ni<Co<Fe<Mn<Cr<V<Ti.$$

Hence the formation of a metal–alkene complex is an important stage in the hydrogenation of an isolated double bond, and permits the concerted addition of hydrogen.

No selectivity is observed when Ziegler–Natta catalysts are used in the hydrogenation of conjugated dienes [102,131]: monoenes having internal and terminal double bonds and also alkenes can be found among the reaction products. The whole process can be represented by the scheme

$$\text{Diene} + M \rightarrow (M\text{-Diene}) + H_2 \begin{cases} \nearrow M\text{-Monoene-1} \\ \searrow M\text{-Monoene-2} \end{cases} \xrightarrow{H_2} \text{Alkane} + M.$$

The absence of selectivity is probably due to the possibility of coordinating the resulting monoalkenes with Group IV metals in a low state of oxidation.

4. Cyclo-oligomerisations

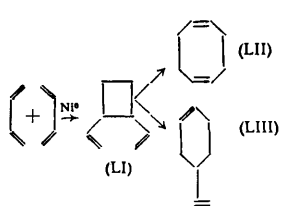
Among cyclo-oligomerisations of alkenes catalysed by transition-metal complexes that of butadiene is of the greatest scientific and practical interest. This reaction can be regarded as a concerted addition, in contrast to polymerisation, which involves closing the chain at the third unit. Concerted addition is supported by the fact that the larger and intermediate rings are formed by the polymerisation of butadiene only on strong dilution, whereas cyclo-oligomerisation takes place only at high concentrations of the monomer.

The formation of cyclododecatriene and cyclo-octatetraene from butadiene is symmetry-disallowed, 2 + 2 + 2 and 2 + 2. In the presence of a transition metal, e.g. nickel, this process becomes allowed, thanks to the coordination of butadiene on the metal and the formation of complexes of π-allyl type [132–135]

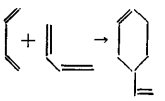
(XLIX) (L)

which have been isolated [134–136].

Heimbach and Brenner [133] studied the dimerisation of butadiene on nickel complexes, and found that, in the presence of zerovalent nickel, butadiene is converted via divinylcyclobutane (LI) mainly into cyclo-octa-1,5-diene (LII) together with some 4-vinylcyclohexene (LIII):



Up to 40% of (LI) appears among the reaction products at low concentrations of butadiene. Reaction of butadiene with isoprene in the presence of the same catalysts yields cyclododecatriene [134], which can also be explained by concerted addition. The formation of (LIII) can be regarded as resulting from the symmetry-allowed interaction of two π-bonds of one butadiene molecule with one π-bond of a second molecule:



The low yield of (LIII) is probably connected with the small probability of such relative orientation of the molecules. If the number of coordination sites is limited, the action of the metal may be to facilitate such orientation and form a complex of type

In particular, examples are known [132,135] in which the introduction of an additional ligand (e.g. triphenylphosphine or carbonyl) leads to the formation solely of (LIII). Vinylcyclohexene is also the sole product of the oligomerisation of butadiene in the presence of rhodium complexes in solvents of high complexing power (e.g. dimethylformamide) [137].

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Equilibrium Acidity of Carbon - Hydrogen Bonds in Organic Compounds

O.A.Reutov, K.P.Butin, and I.P.Beletskaya

A survey is made of experimental results on the equilibrium acidity of CH acids in the gas phase and in aqueous solution, as well as in dimethyl sulphoxide, cyclohexylamine, benzene, ether, and other aprotic solvents. Reasons are discussed for the sharp difference between CH and OH acids that appears on passing from the gas phase to aqueous solutions. Various acidity scales for CH acids in aprotic solvents—the McEwen, Streitwieser, Cram, Breslow, and polarographic scales, and the acidity scale in dimethyl sulphoxide—are compared. A list of 114 references is included.

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I. INTRODUCTION

Under the influence of a base (a proton acceptor) of suitable strength almost all organic compounds are capable of ionising with the formation of carbanions, i.e. negatively charged species in which the charge—or more often part of the charge—is concentrated on a carbon atom. This permits the occurrence of a multitude of organic reactions—e.g. carbonyl–methylene condensations, transmetallations, allyl rearrangements under the influence of bases, etc.—in which the limiting step is detachment of a proton. Even saturated hydrocarbons exhibit acidic properties, though fairly weak[1]. Several reviews have recently appeared on CH acids and carbanions[2-4], among which Cram's monograph[2] is of primary importance.

In the present paper we shall use the term *acidity* instead of the alternative "acid ionisation constant", in order to stress the connection

$$RH + B^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^- + HB;\ pK_a = -\lg K_a = -\lg \frac{k_1}{k_{-1}}$$

between the *equilibrium* (thermodynamic) acidity, i.e. the acid ionisation constant K_a, and the *kinetic* acidity, i.e. the rate of detachment of a proton from the molecule of the acid k_1. A linear relation is quite often observed between equilibrium and kinetic acidities, i.e. between pK_a and $\lg k_1$, when Brønsted's principle is valid. We shall consider only data on the equilibrium acidity of CH acids, which is independent of the mechanism of detachment of the proton and best represents the thermodynamic stability of carbanions in a given system. Since a correction for the energy of solvation should be made to the energy of every species involved in acid–base equilibrium in solution, we shall first examine the acid–base equilibrium in the gas phase, which best corresponds to the "intrinsic" acidity of the CH acid and is due solely to structural factors. Acid–base equilibrium in various solvents will be discussed subsequently.

II. ACID IONISATION IN THE GAS PHASE AND IN WATER

1. Acidity in the Gas Phase

The acidity of any acid in the gas phase can in principle be determined from the thermodynamic cycle[3,5]

$$\begin{array}{c} AH \rightarrow A^{\cdot} + H^{\cdot};\ DH \\ A^{\cdot} + e^- \rightarrow A^-;\ -EA \\ H^{\cdot} \rightarrow H^+ + e^-;\ IP \\ \hline AH \rightarrow A^- + H^+;\ \Delta H = DH - EA + IP \end{array}, \qquad (1)$$

where DH is the A—H dissociation energy, EA the electron affinity of the A· radical, IP the ionisation potential of the hydrogen atom, and ΔH the enthalpy of ionisation of the acid. Investigation of the dependence of acidity on the structure of the acid is of the greatest interest for organic chemistry. With such an approach the ionisation potential IP cancels out, and the variation in acidity in a series of CH acids can be predicted from a knowledge merely of DH and EA.

Brauman et al.[5], as well as several other workers[6], have used pulsed ion–cyclotron resonance to determine experimentally the electron affinities of several radicals, and have then employed the thermodynamic cycle (1) to calculate values of ΔH for the ionisation of the hydrides of several elements. The results (Table 1) indicate[5] that the acidity of hydrides in the gas phase increases from left to right in a period, and downwards in a group:

$$\begin{array}{ccccccccc} CH_4 & < & NH_3 & < & H_2O & < & HF \\ \wedge & & \wedge & & \wedge & & \wedge \\ SiH_4 & < & PH_3 & < & H_2S & < & HCl \\ & & \wedge & & \wedge & & \wedge \\ & & AsH_3 & < & HBr & & \\ & & & & \wedge & & \\ & & & & HI & & \end{array}.$$

The main factor determining the variation relative acidity is the electron affinity along a period, and the dissociation energy down a group (Table 1). A ready explanation of

this rule is that the A—H molecular orbital ψ is a combination of the atomic orbitals φ_A and φ_H, and will be the more stable relative to φ_A the closer the energies of φ_A and φ_H, i.e. the smaller the difference in electronegativity between the given element and hydrogen. With increase in the electronegativity of the element φ_H becomes more stable, the mixing coefficient of the orbitals decreases, and the energy of ψ approaches that of φ_A. Since Pauling's electronegativity shows a greater variation along a period than down a group and is a function of the electron affinity, the acidity of hydrides will be more strongly dependent on *EA* along a period than down a group in the Periodic System.

Table 1. Bond dissociation energies, electron affinities, and calculated enthalpies of ionisation for simple hydrides in the gas phase[5,6] (ionisation potential of hydrogen *IP* = 316 kcal mole^{-1}).

Hydride	*DH*	*EA*	ΔH	Hydride	*DH*	*EA*	ΔH
	kcal mole^{-1}				kcal mole^{-1}		
CH_4	104			H_2S	90	53	350
NH_3	110	17	407	HCl	103	83	333
H_2O	119	42	390	AsH_3		29.3	
HF	136	80	370	HBr	88	78	324
SiH_4	80			HI	71	71	314
PH_3	80	28.8	364				

The weakest acid among the above examples is methane; this in particular is a consequence of the low electron affinity of the methyl radical. However, replacing a hydrogen atom in methane by a group which increases the electron affinity of the corresponding radical, i.e. which stabilises the carbanion, leads to an increase in the acidity. Introduction of the inductively electronegative chlorine makes the enthalpy of ionisation for the carbon—hydrogen bond smaller than the value for ammonia: $CH_3Cl > NH_3 > CH_4$. Toluene, whose phenyl group stabilises the negative charge by a conjugation mechanism, is a stronger acid than is water[7].

Existing experimental results can be summarised by the sequence

$$n\text{-}C_4H_9SH > CH_3NO_2 > \text{cyclo-}C_6H_6 \geqslant CHCl_3 > CH_3COCH_3 > CH_3CN > CH_2Cl_2,\ CH_3SOCH_3 \geqslant C_2H_6,\ t\text{-}C_4H_9OH,\ i\text{-}C_4H_9OH > C_2H_5OH > CH_3OH > C_6H_4,\ C_6H_5CH(CH_3)_2 > C_6H_5CH_3 > C_3H_8 > H_2O > C_6H_6 > H_2 > NH_3 > C_2H_4,\ C_6H_{12} > (CH_3)_3,\ CH_4$$

in which various Brønsted acids are arranged in order of diminishing acidity (in the gas phase in a flowing afterglow at 300°K).[8] This sequence evidently destroys completely our usual ideas of the relative acidities of various compounds, based on the study of aqueous or alcoholic solutions.

It is interesting that in the gas phase alkyl substituents increase the acidity of a molecule: i.e. like halogens they possess a $-I$ effect. Thus the acidity of alcohols in the gas phase increases in the opposite sequence

propan-2-ol > ethanol > methanol > water

to the acidity of the same compounds in aqueous solution[9,10]. The reason is, of course, solvation. The ionisation of hydrogen chloride, for example, is endothermic in the gas phase (ΔH = +333 kcal mole^{-1}—Table 1), but in water ΔH = −16 kcal mole^{-1}.[11]

The energy parameters listed in Table 1, as well as the qualitative series given in the text, show that no sharp distinction exists between CH acids and other types of acids in the gas phase. This is indicated also by Ritchie and King's theoretical calculations[12] of potential-energy surfaces for a series of simple gas-phase proton transfers from the molecules—hydrogen, hydrogen fluoride, water, ammonia, and methane—to the hydride ion. As expected, the lowest energy corresponded in every case to that reaction path involving attack by the hydride ion along the axis of the X—H bond:

$$X{-}H \leftarrow\!-\!-H^- \ (X = H,\ F,\ OH,\ NH_2,\ CH_3)\ .$$

Water, ammonia, and methane were found to behave similarly, the only distinction between them consisting in a quantitative energy difference between reactants and products of proton transfer.

Thus hydrocarbons and their derivatives (i.e. CH acids) are inherently just as likely to exhibit acid properties as are hydrides of other elements and their substituted derivatives†. In hydroxylated solvents, however, the acidic properties of hydrides and substituted hydrides of electronegative elements (e.g. hydroxyl acids) are far more strongly developed than are those of CH acids. It has now been found that the ability of hydroxylated solvents to promote the acid ionisation of hydrides of electronegative elements is due to their specific property of forming hydrogen bonds with these elements. In the next subsection we shall compare the acidities of CH and OH acids in water.

2. Acidity of CH Acids in Water—Comparison with OH Acids

In the gas phase toluene possesses more strongly developed acidic properties than does water[7]. We shall examine what occurs in the acid ionisation of these two compounds in a hydroxylated solvent. Acid—base equilibria in the two systems can be written

$$H_2O\cdot solv. + B\cdot solv. \rightleftharpoons HB^+\cdot solv. + OH^-\cdot solv.$$
$$PhCH_3\cdot solv. + B\cdot solv. \rightleftharpoons HB^+\cdot solv. + PhCH_2^-\cdot solv.$$

The calculation of ionisation constants in solution must take into account the solvation of all species involved in the equilibrium, on both sides of the equations. If the proton acceptor B is the same in these two examples and reaction takes place in the same solvent, calculation of the relative acidity of water and toluene in solution will allow for the solvation energies only of water and toluene on the left-hand side of the equilibria, and of hydroxide and benzyl anions on the right-hand side.

The difference between the solvation of water and that of toluene in hydroxylated solvents is due to the fact that the latter solvate molecules and anions mainly by hydrogen bonding. Eigen gives the sequence

$$OH\cdots O > OH\cdots N,\ NH\cdots O > NH\cdots N > SH\cdots X,\ RH\cdots S > PH\cdots X,\ XH\cdots P > CH\cdots X,\ XH\cdots C$$

(where X is any element) of diminishing ability of elements to form hydrogen bonds[13], with OH and CH acids located at opposite ends: the former are the strongest, and the latter the weakest, hydrogen-bond donors. Hence on passing from the gas phase to a hydroxylated solvent,

† Acetic acid, for example, can be regarded as oxygen hydride substituted by an acetyl group.

e.g. water, the energy of the water molecule shows a greater decrease than that of the toluene molecule. Similarly, oxygen bases are the strongest, and carbon bases the weakest, hydrogen-bond acceptors. On passing from the gas phase to aqueous solutions, therefore, the energy of a hydroxide ion will also decrease far more strongly than that of a benzyl anion.

The principal factor determining the relative acidity of water and toluene in water is the difference between the solvation of the anions. According to results obtained by Parker[14] the most important energy contribution in reactions and equilibria involving anions is made by the difference in solvation of the anions on passing from an aprotic to a protic solvent (in the present case from the gas phase to water). The hydroxide ion, which is small and has a localised charge, is strongly solvated by water, whereas the benzyl anion, with a delocalised charge, is more poorly solvated‡. Hence it follows that the difference between the solvation energies of the hydroxide ion and of water considerably exceeds the difference between those of toluene and the benzyl anion: in other words, a hydroxylated solvent promotes strongly the process $H_2O \rightarrow OH^-$ and only weakly the process $C_6H_5CH_3 \rightarrow C_6H_5CH_2^-$. As a result, equilibrium involving water is far more strongly displaced to the right than the equilibrium involving toluene, in water compared with the gas phase, an effect illustrated by Table 2.

Table 2. Effect of solvation on change in relative acidity of water and toluene on passing from the gas phase to aqueous solution.

Molecule or ion solvated		Net change in acidity
H_2O	OH^-	
well	very well	strong increase
$PhCH_3$	($PhCH_2^-$)	
poorly	(poorly)	slight*

* The anion is therefore "instantly" protonated in water.

Thus solvation effects greatly enhance the acidity of water in aqueous medium, whereas toluene does not exhibit acid properties. This leads to the conclusion that the benzyl anion is "strongly basic", although it would be more correct to say "strongly basic in water", since in the gas phase all bases are strongly basic, as we have already seen.

The above example enables us to understand why, in water, CH acids are far weaker than OH acids. This is further illustrated in Table 3, which compares the acidities of acids of the two types of similar structure. It may be concluded that CH acids in water are on the average weaker than the corresponding OH acids by $\Delta pK_a = 20$.

However, some CH acids are quite strong even in water (pK_a values in Table 4). Appreciable dissociation in water is shown only by those CH acids which contain so called *acidifying* groups such as nitro, acyl, cyano, etc., capable of stabilising the carbanions formed by dissociation. The introduction of more than one such group adjacent to the ionised bond leads to a still greater increase in acidity. The ionisation constants of such CH acids in water can be determined by the usual methods--potentiometrically, spectrophotometrically, conductometrically, etc.

‡ This follows also from Pearson's principle of hard and soft acids and bases[15].

Table 3. Effect of substituents on acidity ($pK_a = -\lg K_a$) of related hydroxyl and methine acids (difference in acidity ΔpK_a) determined from the equilibria (other than methane):

$$H-OR + H_2O \rightleftarrows OR^- + H_3O^+$$
$$H-CH_2R + H_2O \rightleftarrows CH_2R^- + H_3O^+$$

Acid	pK_a	Ref.	ΔpK_a	Acid	pK_a	Ref.	ΔpK_a
H—OH	15.7	2	25	H—OCN	3.7	17	20
H—CH_2Ph	40*	2		H—CH_2CN	24	2	
H—OCOCH$_3$	4.7	16	16	H—ONO_2	(—7)	18	(17)
H—CH_2COCH$_3$	21	2		H—CH_2NO_2	10.2	(Table 4)	

* On Cram's scale (Section III, 2).

Table 4. Acidity of CH acids in water at 25°C.

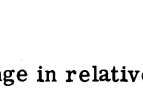
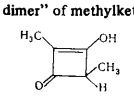
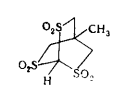
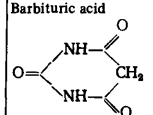
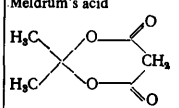
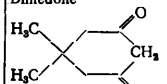
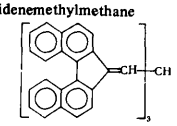
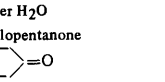
No.	Compound	pK_a	Determination	Ref.
1	Pentacyanocyclopentadiene 	(<—11)	spectroscopic	19
2	Tricyanomethane $CH(CN)_3$	(—5.13)	spectroscopic	20
3	Trinitromethane $CH(NO_2)_3$	0.17	spectroscopic, at 20°C	21
4	"Acid dimer" of methylketen 	2.8	potentiometric	22
5		3.30	potentiometric	23
6	Dinitromethane $CH_2(NO_2)_2$	3.57	conductometric, spectroscopic	24, 25
		3.60	spectroscopic at 20°C	26
		3.47	spectroscopic at 20°C	27
7	Barbituric acid 	4.0 (pure CH acidity)	relaxation	28
8	1,1,1-Trifluoropentane-2,4-dione $CF_3.CO.CH_2.CO.CH_3$	4.7	potentiometric	29
9	Meldrum's acid 	4.83 (mixed acid) enol 2.49	relaxation	28
10	1,1-Dinitroethane $CH_3CH(NO_2)_2$	5.21	spectroscopic	26
11	Nitroacetone $CH_3.CO.CH_2.NO_2$	5.1	potentiometric	29
12	Dimedone 	5.23 (pure enol)	spectroscopic	30
13	Cyclohexane-1,3-dione	5.26	conductometric	31
14	Triacetylmethane $CH(COCH_3)_3$	5.81	potentiometric	32

Table 4 (contd.)

No.	Compound	pK_a	Determination	Ref.
15	Tris-7*H*-dibenzo[*c,g*]fluorenylidenemethylmethane 	5.9	spectroscopic	33
16	Ethyl fluoronitroacetate $NO_2CHF.COOC_2H_5$	6.28	spectroscopic	34
17	Phenylnitromethane $C_6H_5CH_2NO_2$	6.8 aci-form 3.89	potentiometric, polarographic	35
18	Dibenzoylmethane $C_6H_5COCH_2COC_6H_5$	8.95	spectroscopic	36
19	$(CH_3)_2\overset{+}{S}-CH_2-\overset{+}{S}(CH_3)_2$	9.00	potentiometric	37
20	Pentane-2,4-dione $CH_3COCH_2COCH_3$	8.94 enol 8.13	spectroscopic	30, 32
21	Nitromethane CH_3NO_2	10.21 10.24 10.1	potentiometric potentiometric spectroscopic	38 39 40
22	Ethyl acetoacetate $CH_3COCH_2COOC_2H_5$	10.49 enol 8.09	potentiometric at 20°C	30
23	Malononitrile $CH_2(CN)_2$	11.19	potentiometric	29
24	Diphenylsulphonylmethane $C_6H_5SO_2CH_2SO_2C_6H_5$	11.21	spectroscopic	41, 42
25	Ethyl malonate $CH_2(COOC_2H_5)_2$	13.30	potentiometric	29
26	Water H_2O	15.7		
27	Cyclopentanone 	16.7 enol 11.8	bromine method	43
28	Tri-*p*-nitrophenylmethane $(p\text{-}NO_2C_6H_4)_3CH$	17.44 (in alcohol)	potentiometric	44

The CH acids listed at the start of Table 4 are comparable in strength with mineral acids, e.g. hydrochloric and sulphuric acids. The weakest CH acid whose acidity could be measured in aqueous solution (cyclopentanone) has $pK_a = 16.7$. It is noteworthy that Table 4 contains barely a single "pure" hydrocarbon, i.e. a CH acid containing no acidifying group. The only exception is Kuhn's hydrocarbon (No. 15), but it occupies a special position, since the dibenzofluorenylidenemethyl group is a strongly acidifying substituent (other such groups and their effect on acidity have been discussed[33]).

Water is unsuitable as a solvent for determining the equilibrium acidity of alkanes, alkenes, arenes, cycloalkanes, and other hydrocarbons. It is not in general an ideal solvent for studying the ionisation equilibria of CH acids, since it has in water a fairly high acidity (for H_2O in water $pK_a = 15.7$). Methods have therefore been developed for determining the acidity of hydrocarbons in aprotic solvents, and will be considered below.

III. METHODS FOR DETERMINATION OF IONISATION EQUILIBRIUM OF CH ACIDS

The equilibrium acidity is determined by the position of equilibrium between acids and conjugate bases. Most of the data on the equilibrium acidity of hydrocarbons have been obtained from the study of *transmetallations*

$$R-H+R'-M \rightleftarrows R-M+R'-H$$
(M=Li, Na, K, Cs; R=Alk, Ar, Aralkyl, etc; R'=Alk, Ar, cyclo-$C_6H_{11}NH$, NH_2, etc.)

in solvents of low polarity and low proton-donating activity (ether, benzene, liquid ammonia, cyclohexylamine, dimethyl sulphoxide, etc.).

In 1908 Shorygin showed that ethylsodium metallates benzene, toluene, and diphenylmethane[45], which indicated that ethane was a weaker acid than the latter three hydrocarbons. Many similar qualitative results have since been obtained: it was shown[46], for example, that potassamide in liquid ammonia metallates diphenylmethane but not toluene, pentylsodium reacts with benzene, and phenylsodium in turn reacts with toluene[47]. These results enabled the sequence of increasing acidity to be constructed[48]:

pentane (or ethane) < benzene < toluene < ammonia < diphenylmethane.

Gilman et al. established that the yield of transmetallation product obtained with dibenzothiophen depends on the nature of the organolithium compound RLi with which it reacts (Table 5).[49] These results show that the acidity of the hydrocarbons RH should increase in the above sequence.

Table 5.

R	n-C_4H_9	C_6H_5	1-$C_{10}H_7$	p-$CH_3OC_6H_4$
Yield, %	55	12	7.6	0

By the end of the 1930s many data of this type had been obtained[50-54], enabling a qualitative assessment to be made of the relative strengths of CH acids. However, quantitative comparison of CH acidities began only with the work of Conant and Wheland[55,44,57] and of McEwen[56]. These papers are now regarded as classics.

1. Quantitative Assessment of Acidity of Weak CH Acids

Conant and Wheland[55] used a colorimetric method and the carboxylation of organosodium and organopotassium compounds to estimate the relative acidity of hydrocarbons; McEwen also used polarimetry[56]. This work involved study of the equilibrium of the sodium or potassium salts of the CH acids

$$R-M+R'H \underset{\text{ether or benzene}}{\overset{25^\circ}{\rightleftharpoons}} R-H+R'-M \qquad (2)$$

in ether by Conant and Wheland, in benzene by McEwen. The salts RM and R'M absorb at different wavelengths, so that their concentrations can be estimated colorimetrically. The change in colour usually occurs rapidly, but in some cases, especially when sodium salts are used, many days are required to reach equilibrium. The equation

$$pK_a(RH) - pK_a(R'H) = -\lg\frac{[RM]}{[RH]} + \lg\frac{[R'M]}{[R'H]} \qquad (3)$$

holds for the equilibrium (2). McEwen originally assumed that the salts RM and R'M were dissociated to the same extent, whereas the CH acids were not dissociated at all. With these postulates formula (3) becomes

$$pK_a(RH) - pK_a(R'H) = -\lg\frac{[R^-]}{[RH]} + \lg\frac{[R'^-]}{[R'H]}.$$

It was subsequently shown, however, that at 25°C the sodium and caesium salts of fluorene exist as internal ion-pairs, whereas the lithium salt occurs as separated ion-pairs, which have the same spectrum as intimate

ion-pairs in the visible region, but differ in the ultraviolet spectrum[58]. Electrical conductivity data show that these fluorene salts are only slightly dissociated. Thus the change in colour observed by McEwen is due to the formation not of dissociated compounds but of ion-pairs: i.e. Eqn. (3), proposed by Cram[2], is valid.

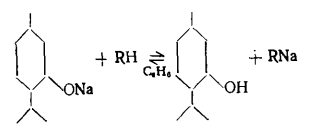
It follows from Eqn. (3) that, with equal initial concentrations of RM and R'H, visual observation of 91% (more precisely 90.9%) metallation will correspond to a difference between the acids RH and R'H of $\Delta pK_a = 2$. If such a degree of metallation is reached with a fivefold excess of R'H, the corresponding difference between the acids will be only 0.4.

McEwen compared various pairs of CH acids, which involved many cross experiments. An additional method of checking the correctness of the colorimetric results was provided by carbonation. The position of equilibrium between two acids and their salts was assessed from the relative yield of carboxylic acids obtained after carbonation of the equilibrium mixture

$$\begin{array}{ccc} RH + R'M & \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} & RM + R'H \\ \downarrow CO_2\ k_2 & & \downarrow CO_2\ k_3 \\ R'COOM & & RCOOM \end{array} \quad . \qquad (4)$$

Obviously, the method is applicable only when both $k_2 \gg k_1$ and $k_3 \gg k_1$ (Eqn. 4). The two methods gave mutually consistent values of ΔpK_a for various pairs of CH acids.

McEwen used a polarimetric method to determine the position of equilibrium between sodium mentholate and various CH and OH acids, as well as between menthol and the sodium salts of the CH and OH acids (in benzene):



$[\alpha]_D^{23} = -12.2°$ Na *laevo*-mentholate

$[\alpha]_D^{23} = -45.6°$ *laevo*-menthol

It thus proved possible to interrelate the acidities of OH, CH, and NH acids, and to construct a general scale covering acids from methanol to cumene. McEwen adopted the value $pK_a = 16$ [59] for methanol, and on this basis determined values for weaker acids. He noted that his values were minima, because of the postulates made in the colorimetric determinations. Table 6 gives McEwen's scale, which remained the only one for a long time.

In 1959 Streitwieser et al. began to elaborate another scale of equilibrium acidity[60,61], also based on transmetallations. He measured the equilibrium constant between lithium or caesium cyclohexylamide and the CH acids, or between the lithium and caesium salts of the CH acids and cyclohexylamine, with cyclohexylamine as solvent:

$$RH + \text{cyclo-}C_6H_{11}\overset{\delta-}{N}H\overset{\delta+}{M} \rightleftharpoons \overset{\delta-}{R}\overset{\delta+}{M} + \text{cyclo-}C_6H_{11}NH_2 \, . \qquad (5)$$

In order that equilibrium transmetallation data can be used without correction as a measure of relative acidities, the organometallic compounds should correspond as closely as possible to the free carbanion. Streitwieser et al.[61,62] adduce the following arguments indicating that this condition is satisfied for the lithium and caesium salts of polyarylmethanes in cyclohexylamine.

Firstly, the salts absorb at far longer wavelengths than do the corresponding hydrocarbons: i.e. conjugation increases on passing to the salt. Secondly, solutions of most of these salts obey the Lambert–Beer law over a wide concentration range. Thirdly, a diminution in the polarity of the solvent is accompanied by a hypsochromic shift in the spectra (by 30–70 nm), probably due to breakdown of the solvation of the cation in the ion-pair[62]. The most significant aspect, however, is that, despite the sharp difference between lithium and caesium cations in electronegativity and ionic radius, the spectra are almost independent of the nature of the cation. The electrical conductivity of fluorenyl-lithium in cyclohexylamine is very close to that of lithium perchlorate in this solvent[63].

Table 6. McEwen acidity scale.

Compound	pK_a	Compound	pK_a
Methanol (standard)	16	Diphenylamine	23
Pyrrole	16.5	Fluorene	25
Benzyl alcohol	18	Aniline	27
Ethanol	18	*p*-Toluidine	27
Diphenylmethanol	18	*p*-Anisidine	23
Propan-2-ol	18	Xanthen	29
Triphenylmethanol	19	9-Phenylxanthen	29
t-Butyl alcohol	19	Biphenylyldiphenylmethane	31
t-Pentyl alcohol	19	Triphenylmethane	33
Methol	19	1-Naphthyldiphenylmethane	34
Acetophenone	19	Diphenylmethane	35
9-Phenylfluorene	21	1,1-Diphenylethane	36
9-1'-Naphthylfluorene	21	Cumene	37
Phenylacetylene	21		
Indene	21		

The spectral data obtained by Streitwieser et al. will be found in Ref. 60. On the basis of these results they assumed that lithium and caesium salts exist as ion-pairs in cyclohexylamine, and that interaction leading to the formation of a covalent bond could be neglected. In such case equilibrium constants (Eqn. 5) determined spectroscopically are an absolute measure of the difference in acidity[60]. These constants were linked with the pK_a values by relating them to the arbitrary standard 9-phenylfluorene (in aqueous sulpholan $pK_a = 18.5 \pm 0.1$ [64])§. The values obtained by Streitwieser et al. are listed in Table 7.

Table 7. Streitwieser acidity scale.

Compound	pK_a	Compound	pK_a
9-Phenylfuorene	(18.5)	1,1,3-Triphenylpropene	26.4
3,4-Benzofluorene	19.4	Dihydro-9,9-dimethyl-10-phenylanthracene	28.0
1,2-Benzofluorene	20.0	*p*-Biphenylyldiphenylmethane	30.2
4,5-Methylenefluorene	22.6	Triphenylmethane	31.5
Fluorene	22.8	Diphenylmethane	33.1
2,3-Benzofluorene	23.2		

The Streitwieser scale is more precise than the McEwen scale by an order of magnitude, but it covers a narrower class of hydrocarbons, being restricted to polyarylmethanes and structurally similar compounds. Comparison of Tables 6 and 7 shows that polyarylmethanes have almost the same affinity in ether, benzene, and cyclohexylamine: i.e. solvation factors have only a slight effect

§ Choice of this compound as standard may not be altogether correct, since in dimethyl sulphoxide 9-phenylfluorene has $pK_a = 16.4$ (Table 12).

on the pK_a in these solvents. Both scales have the disadvantage of not extending to very weak CH acids, including monoarylmethanes, alkenes, arenes, and alkanes. The two scales can be used to assess the acidity of methine acids having $pK_a < 33$ (on the Streitwieser scale).

Filler and Wang used Streitwieser's system (cyclohexylamine + lithium cyclohexylamide) to determine the equilibrium acidity of polyfluorinated tri- and di-phenylmethanes and several other compounds[65]. The results are given in Table 8.

Table 8. Equilibrium acidity of polyfluorinated aromatic compounds on the Streitwieser scale[65].

Compound	pK_a
$(C_6F_5)_3CH$	15.8
$(C_6F_5)_2CH_2$	21.3
$(p\text{-}CH_3C_6F_4)_3CH$	17.9
$(p\text{-}CH_3OC_6H_4)_3CH$	19.3
$(C_6F_5)_2CHCH(C_6F_5)_2$	22.7

Shatenshtein et al.[66,67] used the Streitwieser and McEwen scales to assess the acidities of derivatives of *o*-, *m*-, and *p*-carboranes in various solvents (ether, dimethoxyethane, and cyclohexylamine). The pK_a values obtained for these methine acids varied little with the nature of the solvent. Table 9 gives the acidities of carboranes in dimethoxyethane on the Streitwieser scale.

Table 9. Equilibrium acidity of carboranes in dimethoxyethane with potassium fluorenylide[a] as base at 25°C.

Compound	pK_a	Compound	pK_a
9,10-Dichloro-1,2-carborane	16.3[b]	1-Phenyl-1,7-carborane	27.5[c]
1-Phenyl-1,2-carborane	22.6	1-Methyl-1,7-carborane	27.9[c]
1-Methyl-1,2-carborane	23.1	*m*-Carborane	27.9[c]
o-Carborane	23.3	*p*-Carborane	30.0[c,d]
1-Isopropyl-1,2-carborane	23.9		

[a] Use of lithium fluorenylide gives pK_a values 1–2 units smaller than those in the Table.

[b] Lithium fluorenylide as base.

[c] Potassium 9-phenylxanthylide as base.

[d] In cyclohexylamine $pK_a = 31.0$.

Transfer from dimethoxyethane to ether as solvent has hardly any effect on the acidity of carboranes[68]. A wider range of ethereal solvents has been studied for the acid ionisation of 9,10-dihydroanthracene ($pK_a = 30.4$ on the Streitwieser scale) and biphenylyldiphenylmethane[69]. Values of pK_a for these two hydrocarbons in diglyme, dimethoxyethane, diethoxyethane, ether, and cyclohexylamine vary within the range $\Delta pK_a = 0.5$. Shatenshtein et al. have also determined the acidity of potassium nido-(3)-1,2-dicarbaundecaborate[70]. Hydrogen attached to five atoms (three boron atoms and two carbon atoms) in the pentagonal plane of a truncated icosahedron probably possesses acidic mobility.

$$B_9C_2H_{13}^-K^+ + A^-K^+ \rightleftharpoons B_9C_2H_{11}^{2-}K_2^+ + HA$$

(where HA represents fluorene or indene). On the Streitwieser scale this compound has $pK_a = 21.3$: i.e. it is a fairly strong CH acid, in spite of the presence of an integral negative charge.

Although the McEwen and Streitwieser acidity scales have found wide practical application, they nevertheless have the above defect of not extending to such hydrocarbons as monoarylalkanes, arenes, alkenes, and alkanes. This is solely because of experimental difficulties in determining the ionisation equilibrium positions of these hydrocarbons. Indirect methods of estimating the acidities of very weak CH acids are therefore attracting attention. The first attempt to set up a universal acidity scale for CH acids, covering all classes of hydrocarbons, was made by Cram[2], who used McEwen's and Streitwieser's transmetallation equilibrium data, together with original investigations by Dessy et al. and by Applequist and O'Brien, which will be discussed below.

2. Cram's MSAD Scale

The direct determination of the ionisation equilibrium of alkanes, alkenes, and other weak CH acids encounters serious experimental difficulties. A method for solving this problem was suggested by Applequist and O'Brien[71], who measured the equilibrium constants between iodobenzene and various lithium alkyls, alkenyls, aryls, and aralkyls in ether and in ether–pentane mixtures at −70°C. Table 10 lists the negative logarithms of the constants K_{Ap} for the equilibrium

$$RLi + PhI \overset{K_{Ap}}{\rightleftharpoons} RI + PhLi\,.$$

Table 10. Logarithms of equilibrium constants between iodobenzene and RLi and between diphenylmercury and R_2Mg (K_{Ap} and K_{De} respectively—see text).

R	$\lg K_{Ap}$	$\lg K_{De}$	R	$\lg K_{Ap}$	$\lg K_{De}$
cyclo-C_5H_9	6.90	—	CH_3	—	2
cyclo-C_4H_7	6.14	—	cyclo-C_3H_5	0.98	0.9
neo-C_5H_{11}	5.46	—	C_6H_5	0	0
iso-C_4H_9	4.59	—	$CH{=}CH_2$	−2.41	0.5
iso-C_3H_7	—	6	$CH_2CH{=}CH_2$	—	−0.2
n-C_3H_7	3.88	—	$CH_2C_6H_5$	—	−0.4
C_2H_5	3.50	4			

Another method for assessing the equilibrium acidity of very weak CH acids was proposed by Dessy et al.[72,73], who estimated the constants K_{De} of the equilibrium

$$R{-}Hg{-} + Ph'{-}Mg{-} \overset{K_{De}}{\rightleftharpoons} R'{-}Hg{-} + R{-}Mg{-}$$

between various dialkyl-, dialkenyl-, and diaryl-magnesium compounds and diphenylmercury in oxolan at 25°C. Table 10 includes the relative logarithms of the equilibrium constants for this reaction.

The data obtained by Applequist and by Dessy were used by Cram[2] to determine the relative stability of anions formed from very weak CH acids. Cram felt, in his own words, "inner consistency" (Ref. 2, p. 29) between these

workers' results and certain data on the kinetic acidity of alkanes. Making a rational approach to these data, he set up the first universal acidity scale, covering such weak acids as saturated hydrocarbons. Cram's scale, which he termed the MSAD (McEwen–Streitwieser–Applequist–Dessy) scale, is given in Table 11. As already noted, the Applequist and Dessy data show good mutual agreement with the exception of the values for the vinyl group. According to Dessy ethylene is more acidic, but according to Applequist benzene (Table 10). Preference was given to the Dessy scale in setting up the MSAD scale.

Table 11. Cram's MSAD scale[2].

Methine acid	pK_a	Methine acid	pK_a
Fluoradene	11	Ethylene	36.5
Cyclopentadiene	15	Benzene	37
9-Phenylfluorene	18.5	Cumene (α)	37
Indene	18.5	Triptycene (α)	38
Phenylacetylene	18.5	Cyclopropane	39
Fluorene	22.9	Methane	40
Acetylene	25	Ethane	42
1,3,3-Triphenylpropene	26.5	Cyclobutane	43
Triphenylmethane	32.5	Neopentane	44
Propene (α)	35.5	Propane (s-)	44
Toluene (α)	35	Cyclopentane	44
Cycloheptatriene	36	Cyclohexane	45

Cram's MSAD scale undoubtedly requires refinement, especially in the region of the alkanes. It gives for methane $pK_a = 40$; the same value had been suggested in 1944 by Morton[48], and later by Pearson and Dillon[29]. However, the value for methane on Kosower's scale[74] is 47. Furthermore, calculation based on the equation[75,76]

$$pK_{CH_4} - pK_{NH_4^+} = pK_{NH_3} - pK_{OH_3^+}$$

with $pK_{NH_3} = 35$ [76] yields $pK_{CH_4} = 58$. On the polarographic scale the value for methane is 57 (see below). Maksič and Eckert-Maksič calculated pK_a values for several CH acids from the degree of *s*-character of the carbon–hydrogen bond undergoing ionisation; their scale has the value 50 for methane[77]. Streitwieser suggested that, in the case of planar unsaturated hydrocarbons, the equilibrium acidity is proportional to the difference between the energies of delocalisation of π-electrons in the carbanion and in the initial hydrocarbon $E_{\pi A^-}$ and $E_{\pi AH}$.[78] Assuming that the resonance integral β (in the molecular-orbital method) remains constant on passing from one system to another, and disregarding the difference in solvation and change in bond angles on passing from the hydrocarbon to the carbanion, we can use the equation

$$\Delta E_\pi = E_{\pi A^-} - E_{\pi AH} = 2\alpha + \Delta M\beta$$

(where α is the Coulombic integral in the molecular-orbital method) to calculate the parameter ΔM, and hence values of pK_a for planar hydrocarbons using the equation

$$pK_a = a + b\Delta M .$$

The dependence of ΔM on pK_a for toluene, fluorene, and indene is a straight line on the McEwen scale. The resulting graph gives $a = 48$ and $b = -15.5$. The former can be regarded as the pK_a of methane, since all these hydrocarbons are derivatives of methane, for which $\Delta M = 0$.

Thus the MSAD scale gives minimum pK_a values for the alkanes, and their true equilibrium acidities are probably smaller by factors of ~10^{10}. Ritchie[79] reached a similar conclusion by a different line of reasoning—from the difference in the solvation of anions having delocalised and non-delocalised charges.

3. Equilibrium Acidity of CH Acids in Dimethyl Sulphoxide

In contrast to many other dipolar aprotic solvents, dimethyl sulphoxide remains unchanged on treatment with its conjugate base (the dimsyl anion $CH_3SOCH_2^-$).[80] Kolthoff and Reddy showed that a glass electrode can be used for titration in pure dimethyl sulphoxide[81], and that acid ionisation constants up to $pK_a \simeq 30$ can be determined potentiometrically. For dimethyl sulphoxide itself the value is 33.1.[82,83]

Table 12. Acidity of CH acids in dimethyl sulphoxide, water, and cyclohexylamine[83].

No.	Acid	pK_{dmso}	pK_{cha}	pK_{H_2O}
1	9-Cyanofluorene	8.4	—	14.2 (methanol)
2	1,3-Difluorenylpropane	8.7	—	—
3	Methyl fluorene-9-carboxylate	10.3	—	12.9*
4	Fluoradene	10.5	—	17 (methanol)
5	Malonitrile	11.0	—	11.1
6	Benzoylacetone	12.1	—	9.6
7	Tri-*p*-nitrophenylmethane	12.2	—	14.3*
8	Hydrogen cyanide	12.9	—	9.1
9	Pentane-2,4-dione	13.4	—	9.0
10	Nitromethane	15.9 16.9[85]	—	10.2
11	9-Phenylfluoroene	16.4	(16.4)	18.2*
12	Indene	18.5	17.8	18.2*
13	1,2-Benzofluorene	17.9	17.9	—
14	9-Methylfluorene	19.7	20.6	—
15	4,5-Methylenephenanthrene	20.0	20.5	—
16	Fluorene	20.5	20.6	21.0*
17	Benzyl cyanide**	21.3[86]	—	—
18	1,1,3-Triphenylpropene	23.1	24.5	—
19	9-Phenylxanthen	25.5	26.4	—
20	*p*-Biphenylyldiphenylmethane	26.9	28.1	—
21	Methyl phenyl sulphone	27[87]	—	—
22	Triphenylmethane	28.3	29.4	~34 (methanol)
23	Diphenylmethane	30.0	31.0	—
24	Dimethyl sulphoxide	33.1	—	—
	Acidity of alcohols			
	Methanol	27.0	—	18.3 (methanol)
	Ethanol	27.4	—	20.4 (ethanol)
	Propan-1-ol	28.0	—	—
	t-Butyl alcohol	29.2	—	—
	Water	29	—	—

* Values of pK measured with respect to the acidity function and related to the standard state in aqueous solution.

** In dimethyl sulphoxide containing ~1% of water.

The first acidity scale in dimethyl sulphoxide, including CH and NH acids, whose acidity was determined by titration with potassium dimsylate in the presence of triphenylmethane as indicator (which gave a coloured anion), was proposed by Steiner and Gilbert[84]. This scale has since been modified by Ritchie[83] and by Ritchie and Uschold[82]. Table 12 gives the acidity scale in dimethyl sulphoxide.

It is interesting to compare the acidity of CH acids in dimethyl sulphoxide with their acidity in water (last column in Table 12). Benzoylacetone and tri-*p*-nitrophenylmethane have the same acidity in dimethyl sulphoxide, but in water these compounds exhibit a difference

ΔpK_a = 4.7: the acidity of benzoylacetone increases on passing from dimethyl sulphoxide to water, whereas that of tri-*p*-nitrophenylmethane decreases. Nitromethane and 9-phenylfluorene have similar pK_a values in dimethyl sulphoxide, but in water nitromethane is more acidic and 9-phenylfluorene less acidic. The acidity of malononitrile, fluorene, and indene remains almost unchanged on passing from aqueous solutions to solutions in dimethyl sulphoxide. The remaining CH acids in Table 12 can be divided into two groups: the first group comprises 9-cyano-, 9-methoxycarbonyl-, and 9-phenyl-fluorene derivatives, fluoradene, triphenylmethane, and trisnitrophenylmethane, which have lower pK_a values in dimethyl sulphoxide than in aqueous solution; the second group includes benzoylacetone, acetylacetone, hydrogen cyanide, and nitromethane, which are more acid in water than in dimethyl sulphoxide. The first group obviously contains CH acids that form anions with a delocalised charge, whereas CH acids of the second group yield anions having their negative charge localised on the heteroatom.

The above results are easily interpreted on the basis of Parker's theory[14], according to which the change in equilibrium constants and rate constants on passing from protic to dipolar aprotic solvents is attributable mainly to solvation of the anions. We have noted earlier that anions with a localised charge are well solvated by hydroxylated solvents. Dimethyl sulphoxide, in contrast, will well solvate strongly polarisable anions with a delocalised charge[14]. Thus the solvation of the latter anions will improve on passing from water to dimethyl sulphoxide, whereas that of anions having a localised charge will deteriorate. As a consequence, the acid ionisation equilibrium will shift to the right in the first case, and to the left in the second case. These arguments are valid, of course, provided that the difference in solvation of all other species involved in the ionisation equilibrium can be neglected.

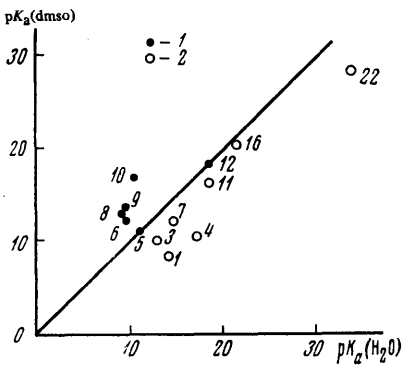


Figure 1. Dependence of acidity in dimethyl sulphoxide on acidity in water for carbanions: 1) well solvated by hydrogen bonds; 2) poorly solvated in water. Numbering as in Table 12. Straight line drawn at unit slope.

The relation between pK_a values in dimethyl sulphoxide and in water is plotted in Fig. 1 for several CH acids. The identity of pK_a values in water and in dimethyl sulphoxide for malononitrile and the other compounds located on the line of unit slope from the origin is fortuitous. With these compounds the energy of solvation of the anions of the conjugated bases changes little on passing from the solvent to water, although the actual nature of solvation becomes quite different. The fact that in water pentane-2, 4-dione is a stronger acid than malononitrile is due to stronger solvation of the conjugated base of the former by hydrogen bonds in water. In dimethyl sulphoxide the acidities of these two compounds have the "normal" sequence (Table 12). Thus the relative acidity in dimethyl sulphoxide corresponds more closely to the "true" acidity of the molecules (apparent in pure form in the gas phase—Section II)(than does the acidity in water.

The lower part of Table 12 gives pK_a values for water and simple alcohols determined in dimethyl sulphoxide. The acidity of alcohols in this solvent is evidently comparable with that of tri- and di-phenylmethane, which is consistent with qualitative results for ionisation in the gas phase (Section II) and diverges sharply from the "generally accepted" values of pK_a = 16—19 for alcohols[88]. This again is explained by a sharp decrease in basicity of oxygen-containing anions (increase in acidity of hydroxyl acids) in hydroxylated solvents due to hydrogen bonding. The high activity of metal alkoxides in dimethyl sulphoxide, first noted by Cram et al.[89], is now widely used in practical synthesis for accomplishing reactions in which the limiting or pre-equilibrium stage is detachment of a proton[2].

The penultimate column of Table 12 contains pK_a values for CH acids in cyclohexylamine. Here the value 16.4 has been chosen for 9-phenylfluorene[83], not 18.5 as in the Streitwieser scale. Hence the pK_a values for CH acids in cyclohexylamine given in Table 12 are smaller by 2.1 than the corresponding values on the Streitwieser scale. Transfer from dimethyl sulphoxide to cyclohexylamine is seen to have little effect on the relative acidities of the hydrocarbons.

4. Polarographic Acidity Scale

The polarographic method has the considerable merit of enabling acidities to be estimated over a very wide range of pK_a values in any polar solvent, even in one that is more "acidic" than the CH acid. It is based on the correlation between the cathodic reduction parameters of organomercury compounds having the general formula R_2Hg and the pK_a values of the corresponding acids RH

The first attempt to use polarography to assess the stability of carbanions was made by Streitwieser and Perrin[90], who measured the half-wave polarographic reduction potentials of substituted benzyl chlorides and polycyclic arylmethyl chlorides in dimethylformamide. If the transition state of this reduction

$$ArCH_2Cl + 2e^- \xrightarrow{E_{1/2}} ArCH_2^- + Cl^-$$

were structurally similar to the carbanion $ArCH_2^-$, a correlation could have been expected between the reduction potentials of the chlorides and the stabilities of the carbanions (i.e. the pK_a values of the methine acids). However, the slow stage in the reduction of halogenated organic derivatives in these systems proved to be transfer of the first electron, which is characterised by a radical-like transition state, so that the expected correlation was very poor. Dessy et al.[73] tried to use the half-wave potentials for the reduction of organomercury salts

$$RHgX \xrightarrow{\text{1st wave}} RHg \quad (\text{or } R_2Hg_2) \xrightarrow[\text{2nd wave}]{E_{1/2}} R^- + Hg$$

as a measure of the relative acidity of CH acids. However, this attempt also was unsuccessful.

The present Reviewers proposed determining the acidity of CH acids by measuring parameters of the cathodic reduction of symmetrical organomercury compounds

$$R_2Hg + 2e^- \xrightarrow{\alpha E_{1/2}} 2R^- + Hg\,.$$

This method takes into account not only the half-wave potential $E_{\frac{1}{2}}$ but also the change in the so called electrochemical transfer coefficient αn_a on passing from one organomercury compound to another[91,92]. On the assumption that the mechanism of cathodic reduction remains unchanged on passing from one mercury dialkyl to another over a quite large number of compounds, i.e. that only rupture of the carbon–mercury bond takes place in the transition state, with the group R acquiring a partial negative charge (which is probably true in most cases[93]), the tendency of the mercury dialkyl to undergo cathodic reduction can be related by simple reasoning with the acidity of the corresponding CH acid RH.

Three processes can probably be interrelated—(i) acid dissociation of the CH acid

$$RH \overset{K_a}{\rightleftharpoons} R^- + H^+\,, \qquad (6)$$

(ii) dissociation of the organomercury compound

$$R_2Hg \overset{1/K_m}{\rightleftharpoons} 2R^- + Hg^{2+}\,, \qquad (7)$$

and (iii) cathodic reduction of the organomercury compound

$$R_2Hg + 2e^- \rightarrow 2R^- + Hg\,.$$

The equilibrium constants (6) and (7) represent the stability of the carbanions in media containing a proton donor or a donor of the mercury cation respectively.

Deduction of a formula linking the acidity of CH acids with the cathodic reduction parameters of their mercury salts necessarily involved the assumption that the proton affinity of the carbanions was related linearly to their affinity for the mercury cation

$$\Delta \ln K_m = A \cdot \Delta pK_a \qquad (8)$$

(where A is a constant, $\Delta \ln K_m$ is the difference between the values of $\ln K_m$ for two organomercury compounds, and ΔpK_a is the difference between the pK_a values for the corresponding methine acids). The validity of this hypothesis has recently been proved[94] by analysing the nuclear magnetic resonance spectra of organomercury compounds. Scheffold has shown[95] that the spin–spin interaction constants between the magnetic isotope of mercury and the methyl protons $J_{^{199}Hg-CH_3}$ in complexes of the methyl mercury cation with various anions X^- (CH_3HgX) are proportional to the logarithm of the stability constants of these complexes:

$$CH_3Hg^+ + X^- \rightleftharpoons CH_3HgX;\ K'_m = \frac{[CH_3HgX]}{[CH_3Hg^+][X^-]}$$

Thus the (thermodynamic) stability of the bond between the cation CH_3Hg^+ and the anion of X^- can be assessed from the n.m.r. spectra. Scheffold's correlation embraces anions with various donor atoms—oxygen, sulphur, nitrogen, halogens, and, especially important, carbon (the cyanide anion)—and can be used to estimate the stability constants of complexes of the methylmercury cation with carbanions, in particular with alkyl anions.

Fig. 2 shows a plot of the constants $J_{^{199}Hg-CH_3}$ against $\lg K'_m$, representing the affinity of various anions X^- for the methylmercury cation. Values of $\lg K'_m$ for the anions—$CH{:}\,C^-$, CF_3^-, $H_2C{:}\,CH^-$, CH_3^-, and C_2H_5—can be estimated by marking off on this graph points corresponding to compounds having low values of J (the sign of the constant remains unchanged throughout the series[96]).

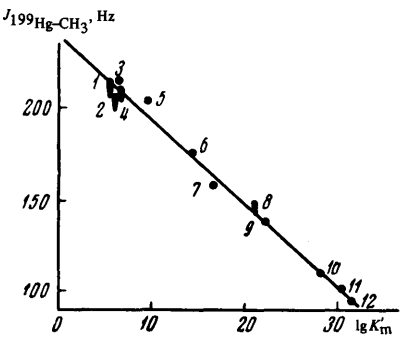


Figure 2. Linear relation between the constants $J_{^{199}Hg-CH_3}$ and $\lg K'_m$ for methylmercury compounds CH_3HgX, where X is: 1) Cl; 2) SCN; 3) $OCOCH_3$; 4) Br; 5) OH; 6) CN; 7) $SHgCH_3$; 8) $C{:}\,CH$; 9) CF_3; 10) $CH{:}\,CH_2$; 11) CH_3; 12) C_2H_5.

The values obtained for $\lg K'_m$ (Table 13) correlate well with the pK_a values for the corresponding hydrocarbons on the Cram scale (Fig. 3). This relation is described by the equation

$$\lg K'_m = 0{,}6 \cdot pK_a + \text{const}\,.$$

Table 13. Affinity of carbanions for methylmercury cation.

No.	Anion	$\lg K'_m$	No.	Anion	$\lg K'_m$
1	CN^-	14.2	4	$CH_2{=}CH^-$	28
2	$HC{\equiv}C^-$	21	5	CH_3^-	30
3	CF_3^-	22	6	$C_2H_5^-$	31.5

By analogy with the above we can assume a linear relation also between the proton affinity of the carbanions and their affinity for the Hg^{2+} cation (Eqn. 8). For the equilibrium reduction of R_2Hg we have

$$\Delta G^0 = -RT \ln K_m + \Delta G_{Hg^0/Hg^{2+}}\,,$$

where the second term on the right-hand side is the redox potential of the Hg^0/Hg^{2+} system. Hence comparison of two organomercuric compounds yields

$$-\Delta\Delta G^0 = RT \cdot \Delta \ln K_m\,. \qquad (9)$$

From Eqns. (8) and (9) it follows that

$$-\Delta\Delta G^0 = RT \cdot A \cdot \Delta pK_a\,. \qquad (10)$$

Rates of reduction of organomercury compounds must be compared at the same potential E, at which each compound will be reduced with a certain overpotential

$$\eta = E - E^0, \tag{11}$$

where E^0 is the equilibrium potential for the given mercury dialkyl. From Eqns. (10) and (11) we obtain for the difference between the overpotentials of two organomercury compounds the formulae

$$\Delta\eta = -\Delta E^0;\ \Delta\eta = \frac{\Delta\Delta G^0}{F},\ \Delta\eta = A^* \cdot \Delta pK_a, \tag{12}$$

where A^* is a constant.

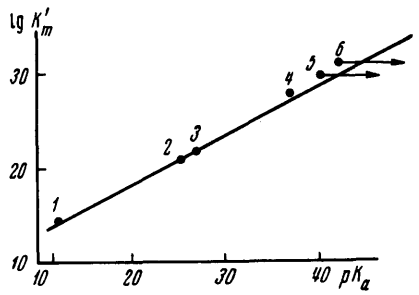


Figure 3. Relation between $\lg K'_m$ and pK_a on MSAD scale. Numbering of compounds as in Table 13.

The cathodic reduction rate constant depends on the overpotential[97]:

$$\ln k_e = \ln k_e^0 - \frac{\alpha n_a F}{RT}\eta, \tag{13}$$

where k_e^0 is the rate constant at the equilibrium potential, n_a the number of electrons involved in the slow stage, and α the electrochemical transfer coefficient¶. Equation (13) presupposes that the transfer coefficient α is independent of the overpotential. If α does depend on the overpotential[98,99], Eqn. (13) can be written, with $n_a = 1$,

$$\ln k_e = \ln k_e^0 - \frac{F}{RT}\int_0^{\eta} \alpha\, d\eta. \tag{14}$$

The difference between the rates for any pair of mercury dialkyls at the same potential, in particular at $E = 0$, is given by the formula

$$\Delta \ln k_e = \Delta \ln k_e^0 - \frac{F}{RT}\int_{\eta_1}^{\eta_2} \alpha\, d\eta.$$

whence

$$\Delta \ln k_e = \Delta \ln k_e^0 - \frac{\alpha_e F}{RT}\Delta\eta \tag{15}$$

in which α_e is the mean transfer coefficient over the range of overpotentials $\eta_1 - \eta_2$.

From Eqns. (12) and (15) we obtain

$$\Delta \ln k_e = \Delta \ln k_e^0 - \alpha_e \cdot A \cdot \Delta pK_a, \tag{16}$$

which shows that the relative rate of reduction of a mercury dialkyl at a given potential depends not only on the relative stability ΔpK_a of the corresponding carbanion R^- but also on the relative rate of reduction of the compound R_2Hg when $\Delta pK_a = 0$, i.e. on the difference between the rates of electron transfer at the equilibrium potentials $\Delta \ln k_e^0$. We may suppose by analogy that $\Delta\eta$ for electron transfer is equivalent to $\Delta pK_a = pK_a(HA) - pK_a(HB)$ for the proton transfer $HA + B^- \rightleftharpoons A^- + HB$, and $\Delta \ln k_e^0$ to the relative rate of proton transfer when $\Delta pK_a = 0$. The quantity $\Delta \ln k_e^0$ is evidently connected with the energy of structural reorganisation of the R_2Hg-R^- system involved in electron transfer. The change in rate of proton transfer when $\Delta pK_a = 0$ observed with change in the structure of the acid may be due to a change in the pK_a of the latter[13] Similarly, in the case of electron transfer we may suppose to a first approximation that $\Delta \ln k_e^0$ varies linearly with $\ln K_m(R_2Hg)$, i.e. with $pK_a(RH)$. If $\ln k_e$ is assumed to be constant over the given range of overpotentials, we find from Eqn. (16) that

$$\Delta \ln k_e = -\rho' \cdot \Delta pK_a \tag{17}$$

It thus remains to measure only the rate constants of cathodic reduction for a series of mercury dialkyls at the same potential, and the problem of determining the acidity of CH acids will be solved. However, since the organomercury compounds R_2Hg are reduced at potentials from 0 to −3 V depending on the nature of R, such measurements are impossible. We are therefore compelled to estimate the rate constants by means of the Koutecky–Delahay equation[100], which, provided that the drop period of the mercury electrode is constant and the diffusion coefficient of the mercury dialkyl varies little with the nature of the alkyl group, is written

$$\frac{\alpha n_a F}{RT} E_{1/2} = \ln k_{E=0} + \text{const}, \tag{18}$$

where $k_{E=0}$ is the rate constant of electron transfer at $E = 0$ relative to some reference electrode, and α is the polarographic transfer coefficient at the half-wave potential $E_{\frac{1}{2}}$. We find from Eqns. (17) and (18) that

$$\Delta(\alpha n_a E_{1/2}) = \rho \cdot \Delta pK_a, \tag{19}$$

where ρ is a constant depending on the experimental conditions. This constant cannot be calculated, and must therefore be determined experimentally each time.

Fig. 4 illustrates diagrammatically the dependence of $\ln k_e$ on the electrode potential[98,99]. The error in the determination of $\ln k_e$ obviously depends on the choice of potential E' at which the rates of reduction of the mercury dialkyls are compared. Thus the quantity $\alpha n_a E(E_{\frac{1}{2}} - E')/RT$, which is determined by linear extrapolation of the tangent at the point $E_{\frac{1}{2}}$ to the potential E' (Fig. 4), does not represent the true value k'_e, and the discrepancy will be larger when the compound is reduced at more negative potentials.

In spite of a number of theoretical limitations, Eqn. (19) was found to hold for a large number of organomercury

¶ This parameter has an analogous significance to the Brønsted coefficient for proton transfer. Change in potential corresponds to a change in equilibrium between oxidised and reduced forms of the substance, just as a change in pK_a corresponds to a change in the position of protolytic equilibrium. The quantity α shows the extent to which potential influences the rate of the forward reaction. The value of αn_a is readily determined from the slope of the polarograms.

compounds corresponding to a series of CH acids with a range of variation in pK_a exceeding 50.[101-107] In this way a polarographic acidity scale was set up, which included CH acids having pK_a values of 7–60 (Table 14).

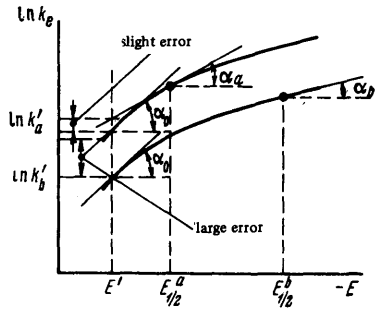


Figure 4. Scheme illustrating dependence of $\ln k_e$ on electrode potential for two different compounds R_2Hg.

Anhydrous dimethylformamide was used as solvent for the polarographic measurements. Half-wave potentials and αn_a were evaluated by means of Heyrovský graphs, and the dependence of the product $\alpha n_a E_{\frac{1}{2}}$ on the pK_a values of the corresponding CH acids was then plotted (Fig. 5).

Table 14. Polarographic acidity scale for CH acids.

Acid	Position of CH bond	pK_a	Acid	Position of CH bond	pK_a
Propane	2	60	Fluoroform		26
Methane		57	Methyl phenyl sulphone	α	25
1,3,5-Trimethylpyrazole	4	38	Ethyl difluoroacetate	α	25
Indole	3	38	Methyl acetate	α	24
	2	35	Pentafluorobenzene		23
Ethylene		37	1,1,1,2,3,3,3-Heptafluoro-propane	2	22
Benzene		37			
Furan	3	37	1,1,1,3,3,3-Hexafluoro-propane	2	22
	2	36			
2-Methylbenzofuran	3	36	*m*-Carborane	1 or 7	22
3-Methylbenzofuran	2	35	Ethyl fluoroacetate	α	22
2-Methylbenzothiophen	3	36	t-Butyl methyl ketone	$COCH_3$	21
3-Methylbenzothiophen	2	35	Trifluoroethylene		20
Toluene	α	35	Ethyl chlorofluoroacetate	α	20
Thiophen	2	35	Phenylacetylene		19
Selenophen	2	35	*o*-Carborane	1 or 2	18
1-Acetylindole	3	34	Cyclopentadiene	CH_2	16
1-Acetyl-3-methylindole	2	33	Chloroform		15
3-Acetyl-1-methylindole	2	32	Ethyl ββ-trifluoropropionate	α	15
p-Carborane	1 or 12	32	Ethyl αββ-tetrafluoro-propionate	α	14
Pentachlorobenzene		31			
Vinyl chloride	2	31	Ethyl bistrifluoromethyl-acetate	α	13
			Hydrogen cyanide		12
			Bromoform		9
			Tristrifluoromethyl methane		7

The following CH acids were chosen for the experimental determination of the constant ρ (Eqn. 19)—(i) hydrogen cyanide, with pK_a = 12 determined by potentiometric titration in dimethylformamide, (ii) phenylacetylene, cyclopentadiene, toluene, and benzene, whose acidities were known on the MSAD scale, and (iii) methyl acetate, whose pK_a was taken to be 24 [104]—and a calibration graph was drawn through these points. Knowing the values of αn_a and $E_{\frac{1}{2}}$ for other organomercury compounds, we can hence determine the pK_a values for other CH acids. The graph in Fig. 5 shows that a correlation actually exists between values of $\alpha n_a E_{\frac{1}{2}}$ for R_2Hg and the pK_a of the corresponding acids RH.

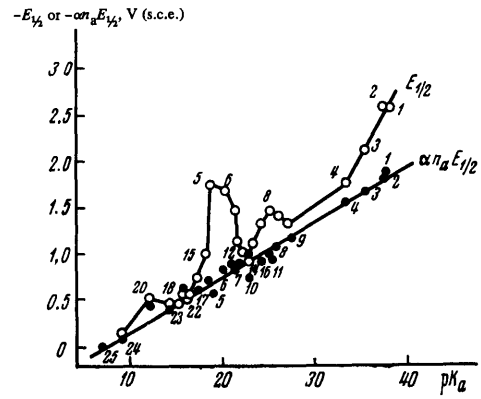


Figure 5. Correlation of parameters of polarographic reduction of organomercury compounds with acidity of corresponding CH acids. Numbering of points corresponds to that of compounds in Table 1 of Ref. 93.

It is important to note that the half-wave potentials do not correlate with the acidity. The reason is that they do not have the same physical significance in an irreversible electrochemical process as in reversible reduction: i.e. the value of $E_{\frac{1}{2}}$ does not directly represent the redox properties of the substance that is reduced irreversibly.

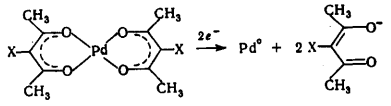
The polarographic method enabled a very wide range of variation in acidity to be investigated. It can be used to determine the acidity of compounds containing groups sensitive to the action of bases and, what is very important, the relative stability of isomeric carbanions differing in the position of their charge. The main experimental difficulty (usually easily overcome) is the need to prepare isomeric mercury derivatives of the CH acids.

The correlation of $\alpha n_a E_{\frac{1}{2}}$ with pK_a is valid only when the carbon–mercury bond alone is broken in the transition state, and no subsequent processes stabilising the resulting carbanion influence the potential. This requirement may not always be made for compounds towards the end of Table 14, since their reduction is in considerable measure reversible: e.g.

$$(CBr_3)_2Hg \overset{2e^-}{\rightleftharpoons} Hg + 2CBr_3^- \xrightarrow[\text{potential}]{\text{influences}} 2\,CBr_3 + 2Br^-.$$

If the proton affinity of carbanions is assumed to be linearly related to their affinity not only for the mercury cation but also for cations of other metals, similar correlations between cathodic reduction parameters and pK_a values should be observed for many other organometallic compounds. We have examined published data[108,109], and found that Eqn. (19) holds for acetylacetonate complexes of

palladium and acidopenta-amminecobalt complexes, which are reduced according to the schemes



$$[Co(NH_3)_5X]^{n+} \xrightarrow{e^-} [Co(NH_3)_5]^{n+} + X^-$$

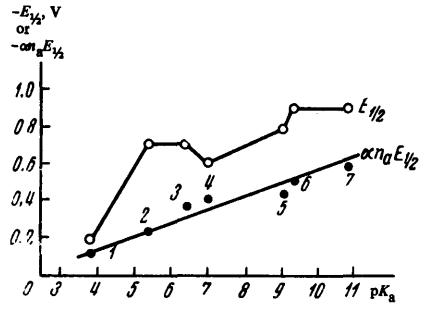


Figure 6. Dependence of $\alpha n_a E_{\frac{1}{2}}$ on pK_a of substituted acetylacetones for acetylacetonate complexes of palladium (substituent X): 1) CN; 2) $NHCOCH_3$; 3) $COOC_2H_5$; 4) Br; 5) H; 6) C_6H_5; 7) CH_3.

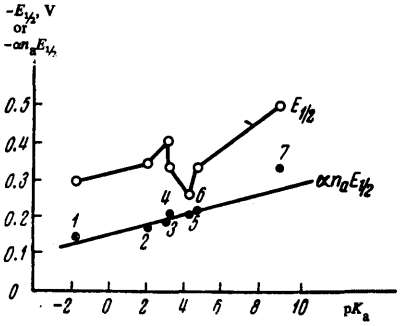


Figure 7. Dependence of $\alpha n_a E_{\frac{1}{2}}$ on pK_a of HX for reduction of $[CoX(NH_3)_5]$ where X is: 1) H_2O; 2) HSO_4^-; 3) F^-; 4) NO_2; 5) fumarate; 6) CH_3COO^-; 7) NH_3.

Figs. 6 and 7 show that the product $\alpha n_a E_{\frac{1}{2}}$ for the palladium complexes correlates well with the pK_a values of the corresponding pentane-2,4-diones, and that for the cobalt complexes with the pK_a values of the acids HX. As with the organomercury compounds, a linear relation is not observed between pK_a and $E_{\frac{1}{2}}$ (Figs. 6 and 7). With reversibly reducible cobalt complexes containing a cobalt–carbon σ-bond, however, good correlations are observed between the half-wave potential of the first polarographic wave and the pK_a values of the corresponding carbanions[110]. Graphs illustrating this relation are given in Figs. 8 and 9.

5. Breslow's Electrochemical Method

An interesting electrochemical method for determining the acidity of hydrocarbons for which direct measurement of pK_a is impossible was suggested by Breslow et al.[111-113]. It involved indirect determination of equilibrium acidity on the basis of the series of reversible reactions

$$R{-}H \overset{1}{\rightleftharpoons} R{-}OH \overset{2}{\rightleftharpoons} R^+ \overset{3}{\rightleftharpoons} R\cdot \overset{4}{\rightleftharpoons} R^-.$$

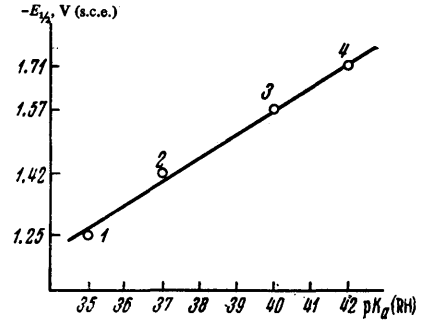


Figure 8. Dependence of half-wave potential for reduction of the complexes [CoR salen dmf] complexes[109] (first wave) on pK_a of RH on MSAD scale for R: 1) $C_6H_5CH_2$; 2) C_6H_5; 3) CH_3; 4) C_2H_5.

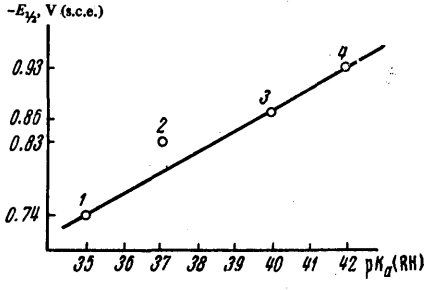


Figure 9. Dependence of half-wave potential for reduction of [CoR(DO)(DOH)pndmf] [109] on pK_a(RH). Numbering as in Fig. 8.

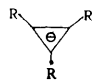
Breslow's method is applicable to hydrocarbons which yield relatively stable carbonium ions and relatively unstable carbanions. In this case it is easy to determine thermodynamic parameters for stages *3* and *4* by some electrochemical method, e.g. by measuring the redox potentials for the reduction in stages of the carbonium ion to the carbanion. The thermodynamic parameters for stage *2* are Deno's pK_{R^+} values[114], which characterise the equilibrium

$$R{-}OH + H^+ \overset{K_{R^+}}{\rightleftharpoons} R^+ + H_2O$$

between the alcohol and the carbonium ion. It is difficult to obtain thermodynamic parameters for stage *1*, but it was suggested that the difference between the heats of formation of hydrocarbon and alcohol was roughly constant for a series of related compounds.

Breslow et al. took $pK_a = 33$ on the McEwen scale for triphenylmethane as basis, and determined the thermodynamic acidity of several substituted triphenylmethanes,

as well as cycloheptatriene and substituted cyclopropenes (Table 15). The high pK_a values for substituted cyclopropenes are explained by the instability (anti-aromaticity) of the corresponding anion



unstable

Breslow's method is primarily valuable because such a low acidity is difficult to investigate by other methods.

Table 15. Breslow acidity scale for CH acids[111-114].

pp'p''-Trisubstituted triphenylmethane	pK_a ±2,0	Compound	pK_a
Trichloro	32.3	Cycloheptatriene	36±3
Monomethoxy	33.1	Triphenylcyclopropene	51±4
Trimethoxy	33.4	Trimethylcyclopropene	62±5
Trisdimethylamino	34.7	Tri-n-propylcyclopropene	64±5
Trimethyl	33.6	Tri-t-butylcyclopropene	65±5
Tri-isopropyl	36.2		
Tri-t-butyl	35,2		

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In this Review we have been considering only papers reporting the determination of the equilibrium acidity of a *series* of CH acids by various methods, i.e. in which scales of relative acidity have been set up. There are also many isolated data on the acidity of individual CH acids, determined under various conditions (e.g. in an alkali-metal alkoxide—alcohol system) or estimated indirectly. These results, which undoubtedly merit attention, have been excluded from the present paper to avoid increasing its length.

It is now possible to determine the acidity of CH acids in aprotic solvents up to values of $pK_a \simeq 30$. The acidity of weaker acids (alkenes, arenes, alkanes, etc.) is assessed by indirect methods, since no direct methods are available. The acidity of these compounds is evidently less than that predicted by Cram's MSAD scale. The main problem of future research will be to compile a *quantitative* scale of acidities in the gas phase and to work out methods for calculating theoretically the empirical constants occurring in the equations relating pK_a values with other thermodynamic or kinetic parameters.

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The Electronic Nature of Fluorine-containing Substituents

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The available literature data up to 1973 on the electronic effects of fluorine-containing substituents are considered and discussed in the review.
The bibliography includes 143 references.

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I. INTRODUCTION

The chemistry of organofluorine compounds is developing very vigorously. Novel methods of synthesis are being devised, new reactions and new types of organofluorine compounds are being discovered, and relations are being established between their structures and properties[1,2]. The quantitative characteristics of the electronic effects of 80 fluorine-containing substituents were determined in recent years and the results of a gradual substitution of hydrogen atoms by fluorine in alkyl groups demonstrated, the positions of new fluorine-containing groups in the series of thoroughly investigated substituents were established, and substituents with unique properties (the most pronounced electron-accepting properties among all known compounds) were discovered. The results are of great interest for theoretical organic chemistry. Substituents such as the fluorine atom and the CF_3 group are introduced into organic molecules as frequently as other substituents which do not contain fluorine. Since convenient preparative methods have been developed recently for the synthesis of compounds containing various perfluoroalkyl [CF_3O, CF_3S, CF_3SO_2, and $N(CF_3)_2$] and other similar groups, there is no doubt that these substituents too will soon become commonplace.

Since organic compounds with fluorine-containing substituents are finding increasing application as medicinal preparations, pesticides, dyes, and monomers for thermostable polymers, a review of the available data on the electronic effects of fluorine-containing groups may be useful for the specific synthesis of substances with valuable properties.

The electronic nature of substituents was characterised quantitatively for the first time by Hammett[3,4] in terms of σ_m and σ_p constants. Subsequently the latter were resolved by Taft and Lewis[5-9] into components reflecting the inductive (σ_I) and resonance (σ_R) effects. In the presence of direct polar conjugation between the substituents and the reaction centre, anomalously high σ constants are observed. Therefore one distinguishes σ_p^0 and σ_R^0 constants without taking into account direct polar conjugation from σ constants when such conjugation is taken into account (σ_p^- and σ_R^- for electron-accepting substituents and σ_p^+ and σ_R^+ for electron-donating substituents).[10]

In order to determine the σ constants of fluorine-containing substituents, the following methods are most widely used: ^{19}F NMR on the basis of the chemical shifts δ^F of the fluorine atoms in *meta*- and *para*-substituted fluorobenzenes relative to fluorobenzene[11]; the determination of σ constants from the dissociation constants of *meta*- and *para*-substituted benzoic acids[3,6,12]; the measurement of pK_a for anilinium[6,13] or dimethylanilinium ions[14]; the determination of the dissociation constants of phenols[6,15].

Dewar and Grisdale[16,17] and Swain and Lupton[18] developed new methods for the resolution of σ constants into inductive and resonance components—F and M, and F and R respectively. The electronic nature of fluorine-containing substituents has been investigated also by other correlations between σ constants and absorption band shifts of azo-dyes or passing from a neutral to an acid medium[19], the pK_a of cyanine dyes[20,21], and the absorption intensity in the infrared spectra of monosubstituted benzenes[22,23]. Methods based on the measurement of molecular dipole moments are also used[24]. The determination of interaction dipole moments (μ_{int}), which reflect the direct polar conjugation between the substituent and the reaction centre and are correlated with the σ^- and σ^+ constants[10,24,25], is particularly valuable.

The electronic effects of fluorine-containing substituents can be estimated from their directing influence in electrophilic or nucleophilic substitution reactions involving the aromatic ring. Correlations have been discovered between the reaction rate constants and the σ^+ or σ^- constants[26,27].

The most detailed data on the applications of various σ constants are quoted in a series of monographs and reviews[3,4,10,28-30]. This review deals with published data on the electronic effects of fluorine-containing substituents and a comparison is made with the electronic influence of the analogous substituents without fluorine.

II. FLUORINE AND OTHER HALOGENS

Fluorine is the most electronegative element. The C–F bond is the most polar among bonds between carbon and halogens[31,32]. In aliphatic compounds the fluorine atom exhibits a powerful electron-accepting inductive effect. This can be inferred, for example, from the pK_a values for halogenoacetic acids[33] and the molecular diagram for methyl fluoride[34]:

$$\begin{matrix} 0.00 + 0.187 - 0.187. \\ H_3C - F \end{matrix}$$

Halogen atoms linked to an unsaturated carbon atom or an aromatic ring exhibit an electron-accepting inductive effect ($\sigma_I > 0$) and an electron-donating conjugation† effect ($\sigma_R < 0$), decreasing in the sequence F > Cl > Br > I (Table 1). Among the halogens, the fluorine atom has the smallest covalent radius[32], close to that of the carbon atom, which results in conditions for maximum overlapping of the *p* orbitals. Therefore despite its high electronegativity, the fluorine atom exhibits the most pronounced electron-donating conjugation effect among all the halogens.

Table 1. σ constants of the halogens*.

Substituent	σ_m^{12} B	σ_p^{12} B	$\sigma_p^{0\,35}$	$\sigma_p^{+\,36}$	σ_I B[11]	σ_I A[35]	σ_I F[10]	$\sigma_R^{0\,11}$ B	$\sigma_R^{0\,11}$ F	σ_R^{10} B
F	0.34	0.06	0.17	−0.07	0.52	0.55	0.52	−0.35	−0.32	−0.46
Cl	0.37	0.23	0.27	0.11	0.47	0.43	0.40	−0.20	−0.18	−0.24
Br	0.39	0.23	0.26	0.15	0.45	0.42	0.44	−0.19	−0.16	−0.22
I	0.35	0.28[4]	0.27	0.13	0.39	0.34	0.44	−0.12	−0.14	−0.13

*In this and subsequent tables the methods of determination of σ constants are indicated by letters: B—from the pK_a for benzoic acids; A—from the pK_a for anilinium ions; DA—from the pK_a for dimethylanilinium ions; F—from the δF chemical shifts (^{19}F NMR); P—from the pK_a of phenols; i.r.—from infrared spectra; Dy—from $\Delta\lambda$ for azo-dyes; C—from the pK_a for cyanine dyes.

The overall electronic effect of fluorine, characterised by the σ_p constant, is the smallest among all the halogens, since its large conjugation effect to a considerable extent neutralises the inductive effect. The σ_R^0 constant for fluorine in *p*-difluorobenzene, determined by ^{19}F NMR, is smaller than σ_R found from pK_a for *p*-fluorobenzoic acid in which the fluorine atom is involved in direct polar conjugation with the COOH group (−0.32 and −0.46 respectively). As a result the σ_p constant for fluorine is smaller than σ_p^0.

Since the σ_p constant for fluorine is close to zero, the acid-base properties of benzoic acid, phenol, and aniline hardly change when the fluorine atom is introduced into the *para*-position relative to the functional group. The remaining halogens increase the acid properties and reduce the basic properties to a much greater extent than fluorine[37].

† Usually referred to as the resonance effect in English (Ed. of Translation).

The σ_p^+ constants for halogen atoms are much smaller than σ_m, which is usually observed for *ortho*, *para*-directing substituents. Indeed in electrophilic substitution reactions the halogens behave as substituents of the first kind with predominantly *para*-directing properties, particularly in the case of fluorine. In nitration reactions fluorine deactivates the benzene ring but to a much smaller extent than chlorine and bromine[38].

The electrophilic constant σ_p^+ of the fluorine atom is negative, in contrast to the other halogens. Accordingly, fluorobenzene is chlorinated much faster than benzene. The relative rates of chlorination of halogenobenzenes and benzene increase in the sequence F > H > Cl > Br (6.3, 1.0, 0.4, and 0.25 respectively).[38]

The distribution of electrons in vinyl fluoride and fluorobenzene, calculated by the quantum-chemical method taking into account σ and π electrons, confirmed that the inductive effect of the fluorine atoms makes it a powerful electron acceptor and the conjugation effect makes it a powerful electron donor. The overall charge of the fluorine atom in fluorobenzene is negative[39]. Fluoro-, chloro-, bromo-, and iodo-benzenes have dipole moments of 1.47, 1.59, 1.57, and 1.40 D respectively with the negative pole at the halogen atom[24,40].

Many instances where the fluorine atom exhibits not only an inductive effect but also a conjugation effect have been observed in studies on the reactivities of fluoro-olefins and described in reviews[41–43]. An interesting case of the electron-donating effect of fluorine was observed in cyanine dyes with fluorine atoms in the polymethine chain[44]. It was found that, as a powerful electron-donating substituent, fluorine affects the colour of the dyes in a manner similar to that, for example, of the methoxy-group.

Thus, in considering the influence of fluorine atoms on the properties of organic compounds, one must take into account the unusual behaviour of fluorine, related to its dual electronic nature involving a powerful electron-accepting inductive effect and an electron-donating conjugation effect.

III. FLUOROALKYL GROUPS (R_F)

Among the fluoroalkyl groups, the CF_3 group is most frequently introduced as a substituent. The σ constants of this group have been determined by various methods. Their values together with the σ constants of other fluoroalkyl groups are listed in Table 2.

The trifluoromethyl group is a fairly powerful electron-accepting substituent both as regards the inductive and conjugation effects. A number of studies have been made on its unusual properties[14,45,55,56]. The inductive effect plays the main role in its electronic influence. It is somewhat smaller for the CF_3 group than for the fluorine atom. Thus the dissociation constant of trifluoromethylacetic acid is smaller by a factor of 2.2 than that of fluoroacetic acid[57].

The conjugation effects of the CF_3 group and the fluorine atom act in the opposite directions. The electrophilic constant $\sigma_m^+ = 0.52$ of the CF_3 group is smaller than $\sigma_p^+ = 0.61$.[36] In conformity with these data, trifluoromethylbenzene enters into electrophilic substitution reactions with greater difficulty than benzene and its *meta*-position is involved preferentially. Thus the nitration of trifluoromethylbenzene results in the formation of 100% of the *m*-nitro-isomer[58], while chlorination gives 80.2% of the *m*-isomer, 15.7% of the *o*-isomer, and 4.1% of the *p*-isomer[59].

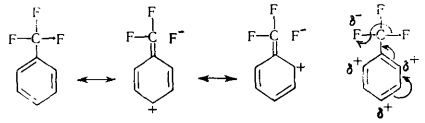
Table 2. σ constants for fluoroalkyl groups.

Substituent	σ_m			σ_p			σ_I			σ_R		
	B	A	F	B	A	F	B	A	F	B	A	F
CH_2F			0.12			0.11			0.13[47,48,a]			−0.02[47–49,b]
CHF_2			0.29			0.32			0.26[47,48,c]			0.06[47–50]
CF_3 *	0.43[12,d]	0.49[14,c]	0.44[14]	0.54[12,f]	0.62[14]	0.49[14]	0.41[11,g]	0.44[14]	0.39[14,3]	0.13[46,i]	0.18[14]	0.10[14]
CH_2CF_3 [2]		0.16	0.12		0.14	0.09			0.14			−0.05
CF_2CF_3 [14]		0.52[j]	0.47		0.69[j]	0.52			0.41			0.11
$(CF_2)_3CF_3$ [14]		0.55[j]	0.47		0.73[j]	0.52			0.39			0.11
$CF(CF_3)_2$ [14]	0.37	0.52	0.50	0.53	0.68	0.52	0,25	0.48	0.48	0.26	0.17	0.04
$C(CF_3)_3$ [51]	0.35	0.39	0.55	0.52	0.71	0.55	0,27		0.55	0.26		0.00
$C(CF_3)_2OH$ [14]		0.35	0.29		0.48	0.30		0.31	0.28		0.15	0.02
$\overline{CF(CF_2)_2CF_2}$ [2]			0.48			0.53			0.45			0.08
$\overline{C(OH)CF_2CF_2CF_2}$ [2]			0.36			0.37			0.35			0.02
m, p-CF_2OCF_2 [52]				0.81								
$CF_2CF_2C_6H_4F$-p [53,54]			0.34			0.39			0.29			0.10

Other data: [a]0.12;[49,50] [b]−0.01;[50] [c]0.29;[49,50] [d]0.41 [45] and 0.42;[14] [e]0.41;[45] [f]0.53 [12,14] and 0.55;[4] [g]0.33;[14] [h]0.41;[11] [i]0.18 [14] and 0.11 (i.r.)[23]; [j](DA).
*$\sigma_p^+ = 0.61$.[36]

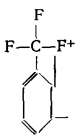
The following postulates have been used to account for the electronic nature of the trifluoromethyl group and in particular its electron-accepting conjugation effect.

1. The CF_3 group is conjugated with the aromatic ring—a negative hyperconjugation effect[45] (in contrast to the positive hyperconjugation effect of the methyl group, which acts in the opposite direction[60]). This effect can be represented by a series of limiting structures with an unbound fluoride anion or by curving arrows:



2. The trifluoromethyl group exhibits a π-inductive effect (I_π)—it withdraws electrons from the adjacent ring carbon atom at which a partial positive charge arises and withdraws electrons from the *ortho*- and *para*-positions via a resonance mechanism[14,60]:

3. The *p* electrons of the fluorine atoms of the CF_3 group interact with the π electrons of the benzene ring in such a way that the electron density in the *meta*-position is enhanced—*p*-π interaction[14]. Many experimental facts and also quantum-mechanical calculations[55,56], carried out taking into account all the valence electrons in the atom, have shown that not only σ electrons but also ring π electrons are transferred to the CF_3 group in the trifluoromethylbenzene molecule. This confirms the hypothesis of a significant role of the hyperconjugation of the CF_3 group with the aromatic ring.



$+0.0508\,\sigma - 0.0508\,\delta$
$+0.0134\,\pi - 0.0134\,\pi$
$C_6H_5 - CF_3$

Negative hyperconjugation is a consequence of the overlapping of the *p* orbital of the adjacent carbon atom of the aromatic ring and the CF_3 group orbital comprising the orbitals of the fluorine atoms forming σ bonds. As a result of the high electronegativity of the fluorine atom, the hyperconjugation effect leads to a decrease of the π electron density in the aromatic ring and its increase at the fluorine atoms of the CF_3 group. When electron-donating substituents are introduced in the *para*-position of trifluoromethylbenzene, the electron shift to the CF_3 group increases owing to direct polar conjugation. This is confirmed, for example, by calculated data[56] for the distribution of π electrons in *p*-fluoro(trifluoromethyl)benzene in relation to the analogous values for fluorobenzene and trifluoromethylbenzene:

$$\underset{F-\ C_6H_5}{+0.0489\,\pi - 0.0489\,\pi} \quad \underset{p\text{-}F-\!-\!C_6H_4-\!-\!CF_3}{+0.0522\pi - 0.0368\,\pi - 0.0154\,\pi} \quad \underset{C_6H_5-CF_3}{+0.0134\,\pi - 0.0134\,\pi}\ .$$

In the *p*-fluoro(trifluoromethyl)benzene molecule the π electron density at the CF_3 group is higher than in the trifluoromethylbenzene molecule, while at the fluorine atom it is lower than in fluorobenzene, i.e. direct polar conjugation results in a transfer of electrons from the fluorine atom to the trifluoromethyl group.

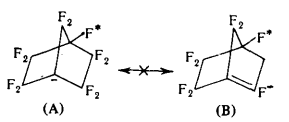
Direct polar conjugation of the CF_3 group with powerful electron-donating substituents (NH_2, NMe_2, O^-) was observed in a study of the dipole moments and chemical properties of *para*-substituted trifluoromethylbenzene. For example, *p*-amino(trifluoromethyl)benzene has μ_{int} = 0.49 D.[61] As a result of direct polar conjugation, *o*- and *p*-hydroxy- and *o*- and *p*-amino-(trifluoromethyl)benzenes readily undergo alkaline hydrolysis, in contrast to the *meta*-isomers[62,63]. For example, this has been used to synthesise 4-trifluoromethylanthranilic acid (a valuable intermediate) from 2,5-di(trifluoromethyl)aniline. In the alkaline hydrolysis of the latter the CF_3 group in the *ortho*-position relative to the amino-group is converted into a carboxy-group, while the substituents in the *meta*-position remain unchanged[64,65].

The high σ constants determined from the pK_a of substituted anilines (σ_p^-), compared with the values found by other methods, have been explained by direct polar conjugation (Table 2).

Andreades[66] investigated the base-catalysed exchange of hydrogen for deuterium in monohydrofluorocarbons: $R_FH + CH_3OD \rightleftharpoons R_FD + CH_3OH$. This reaction proceeds via a stage involving the formation of a carbanion and the

rate of exchange depends on its stability. Comparison of the deuteration rate constants showed that the relative reactivity increases in the series $R_F = CF_3 < CF_3(CF_2)_5CF_2 < (CF_3)_2CF < (CF_3)_3C$, the corresponding values being $1, 6, 2 \times 10^5$, and 10^9. The delocalisation of the charge in the corresponding anions can be described by 0, 2, 6, and 9 resonance structures, the stability of the carbanions and the rate of deuterium exchange increasing in the same sequence. This parallel variation is evidence in support of the hyperconjugation effect.

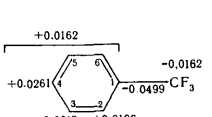
According to Streitwieser and Holtz [67,68] the following observation constitutes evidence against a significant role of negative hyperconjugation in the electronic effect of the CF_3 group. The rate of exchange of protons for the corresponding tritium species in 1*H*-undecafluorobicyclo[2,2,1]heptane is higher by a factor of five than for $(CF_3)_3CH$. Moreover the carbanion of the latter compound is stabilised by nine resonance structures, while the carbanion (A) is not stabilised by resonance in the authors' view, since, according to Bredt's rule, a double bond cannot be located at the bridgehead, i.e. structure (B) is impossible.



(A) (B)

However, these arguments are insufficient for the complete rejection of a contribution by hyperconjugation, since the involvement of the CF_3 group in conjugation does not require a change in the hybridisation of its carbon atom from sp^3 to sp^2 and its hyperconjugation effect is not described exactly by the resonance theory in terms of limiting structures with an unbound fluorine atom and a C=C double bond. As mentioned above, the hyperconjugation of the CF_3 group is due to the overlapping of the *p* orbitals of the adjacent carbon atom with the orbitals of the fluorine atoms of this group without a change in its steric configuration. Thus hyperconjugation in the carbanion (A) can be achieved also without the involvement of (B) type structures. Apart from this, the field effect of the fluorine atom (F*) at the bridgehead can have an influence on the stabilisation of the carbanion (A). [50]

The trifluoromethyl group exerts a powerful electron-accepting inductive effect on the aromatic ring, which is transmitted both via the nearest σ bonds and through space in the form of the field effect. This effect leads to the polarisation not only of σ electrons but also of π electrons, i.e. results in a I_π effect. The influence of the latter is indicated by the calculated π electron distribution in the trifluoromethylbenzene molecule [50]:



According to these data, a negative charge (−0.0499) is concentrated on carbon atom 1, exceeding the charge of the CF_3 group (−0.0162). Thus polarisation of the ring π electrons under the influence of the inductive effect of the CF_3 group is evidence for the presence of an I_π effect.

However, there are also objections to a significant role of the I_π effect [49,71]. They are based on the observation that groups such as $C(CN)_3$ and ICl_2, which have very high inductive effects ($\sigma_I = 0.98$ [49] and 1.3 [71]) do not exhibit a conjugation effect ($\sigma_R = 0.01$ [49] and 0.0 [71] respectively). The $C(CF_3)_3$ group behaves similarly (Table 2). The I_π effect should increase with the inductive effect of the substituents on the ring π electrons and should lead to an increase of the σ_R. However, this is not observed. The I_π effect probably does not play a significant role in the electronic influence of perfluoroalkyl groups.

In the study of the hyperconjugation effect of fluoroalkyl groups, it is interesting to compare the σ constants of the substituents CF_3, CF_2CF_3, $CF(CF_3)_2$, and $C(CF_3)_3$ in which the number of fluorine atoms capable of being involved in conjugation decreases steadily. All these groups are fairly powerful electron-accepting substituents with positive σ_m and σ_p constants.

Comparison of the σ_I and σ_R constants of the above perfluoroalkyl substituents obtained from ^{19}F NMR data (Table 2) shows that the replacement of fluorine atoms in the CF_3 group by trifluoromethyl substituents leads to a gradual increase of the σ_I constant and a decrease of the conjugation constant σ_R. The conjugation constant for the $C(CF_3)_3$ group is zero [51]. These findings confirm the hypothesis of an effect of the hyperconjugation of the fluorine atoms in the trifluoromethyl group with the aromatic ring, which decreases as CF_3 groups accumulate at a single carbon atom.

Despite the fact that the inductive effect of the fluorine atom is greater than that of the trifluoromethyl group, the σ_I constants increase on replacement of the fluorine atoms in the CF_3 group by trifluoromethyl substituents. This can probably be explained by the fact that the inductive effect is transmitted not only via σ bonds but also through space—the field effect *F*. The latter depends on the distance *r*, the dipole moments μ of the bonds in the substituent, the angles θ between the directions of the moments and the lines joining the centres of the dipoles to the reaction centre, and the dielectric constant *D* of the solvent [69,70]: $F = \mu \cos\theta / Dr^2$.

Sheppard explained a similar increase of the σ constant on passing from $CN(\sigma_I = 0.47)$ to the $C(CN)_3$ group ($\sigma_I = 0.98$) also by an increase of the field effect [49,71].

Since the inductive effect plays a dominant role in the electronic behaviour of perfluoroalkyl substituents, its increase according to ^{19}F NMR data in the series $CF_3 < CF_2CF_3 < CF(CF_3)_2 < C(CF_3)_3$ leads to an increase of the constants σ_m and σ_p in the same sequence despite the decrease of the σ_R. The constants σ_p obtained from the ^{19}F NMR data and the pK_a for the acids are virtually identical.

The σ_m and σ_I constants for the $CF(CF_3)_2$ and $C(CF_3)_3$ groups obtained from the same data differ markedly. The field effect of the $CF(CF_3)_2$ and $C(CF_3)_3$ substituents is greater than that of the CF_3 group and therefore their electronic influence depends to a greater extent on the possible operation of the field effect. In the *para*-position it is transmitted through space in the ring with its low dielectric constant and in the *meta*-position the effect is transmitted via the solvent and greatly depends on its polarity. It decreases with increase of the polarity. The acid dissociation constants were determined in a highly polar solvent—aqueous alcohol. This probably explains why the $CF(CF_3)_2$ and $C(CF_3)_3$ groups in the *meta*-position have a weaker electron-accepting influence than the CF_3 group.

In a series of *para*-substituted derivatives, the decrease of the field effect of the substituents under the influence of the solvent does not occur and therefore the strengths of the *p*-CF_3-, *p*-$CF(CF_3)_2$-, and *p*-$C(CF_3)_3$-benzoic acids are approximately the same [14,51]. The fact that *m*-(perfluoro-t-butyl)aniline is a stronger base and its *para*-isomer a

weaker base than the corresponding trifluoromethylanilines can be explained by a similar field effect[51]. For the same reason, the σ_p constants determined from the pK_a for the anilinium ions (σ_p^-) increase on gradual substitution of the fluorine atoms in the CF_3 group by trifluoromethyl groups.

Examination of the constants $\sigma_R^- = \sigma_p^- - \sigma_I$ shows that, when CF_3 groups accumulate at the same carbon atom, there is a tendency towards a decrease of direct polar conjugation. A similar phenomenon was observed in the study of the dipole moments of aromatic compounds with polyfluoroalkyl substituents. The dipole moments of the compounds C_6H_5X, where $X = CF_3$, C_2F_5, $CF(CF_3)_2$, and $C(CF_3)_3$, are very close (2.60[45], 2.73[14], 2.68[14], and 2.72 D[51]). The values of μ_{int} for *p*-amino(trifluoromethyl)benzene and *p*-amino(perfluoro-t-butyl)benzene (0.42[45] and 0.30 D[51]) show that the direct polar conjugation between the CF_3 and NH_2 groups is somewhat more pronounced than between $C(CF_3)_3$ and NH_2.

Like the CF_3 group, all the perfluoroalkyl groups are *meta*-directing in electrophilic substitution reactions (nitration, bromination)[14,51].

In order to account for the greater deactivation of the *para*-position compared with the *meta*-position by the CF_3, C_2F_5, and $CF(CF_3)_2$ substituents, for which $\sigma_m < \sigma_p$, Sheppard[14] put forward the hypothesis of p-π interaction of the p electrons of the fluorine atoms of the perfluoroalkyl groups with the π electrons of the aromatic ring. Such interaction results in an electron shift, which partially compensates the powerful inductive effect of the substituents in the *meta*-position, while the *para*-position is greatly deactivated.

A number of objections have been made to the hypothesis of p-π interaction. Dewar[72] noted that the p-π interaction has no chemical analogies and that a shift of π electrons to the *meta*-position as a result of a conjugation effect is unlikely. Stock and coworkers[73], Smith and Menger[74], and Holtz[68] failed to observe such p-π conjugation in model compounds.

We established[51] that the $C(CF_3)_3$ group does not exhibit a conjugation effect although in the presence of p-π interactions the nine fluorine atoms in the β-position should be equivalent to the three fluorine atoms of the CF_3 group, according to Sheppard's hypothesis, and should lead to similar values of the σ_R constants of these substituents. Theoretical calculations of the distribution of electrons and of bond orders in the trifluoromethylbenzene molecule also failed to confirm the hypothesis of $p - \pi$ interaction[50]. Thus the hypothesis has not been confirmed by theoretical and experimental studies[30,50,68].

The results of studies on the electronic nature of trifluoroalkyl groups discussed above lead to the conclusion that the electron-accepting inductive effect of these substituents, which is transmitted both via σ bonds and through space (field effect) is most important in their electronic influence. The conjugation effect of these groups is small and is mainly caused by hyperconjugation.

On gradual substitution of hydrogen atoms in the methyl group by fluorine, the electron-accepting properties of the substituents become more pronounced—the σ_m, σ_p, σ_I, and σ_R constants increase and their sign changes from negative to positive (Tables 2 and 3).

When fluorine atoms are introduced into the CH_3 group, the σ_I constant does not increase in proportion to their number. The "saturation effect" is particularly marked for chloro-, bromo-, and iodo-derivatives. As a result of this effect, the σ_I constants of the $CHCl_2$ and CCl_3 groups and of the $CHBr_2$ and CBr_3 groups hardly differ. Another anomaly is that the σ_I constants of the CH_2X and CHX_2 groups do not decrease in the sequence X = F, Cl, Br, and I, although the electronegativity of the halogens decreases on passing from fluorine to iodine. These anomalies may be related to the different field effects of the CH_2X, CHX_2, and CX_3 groups. When X = Cl, Br, and I, the CH_2X and CHX_2 groups cannot rotate freely about the bond with the aromatic ring owing to steric hindrance, in contrast to the analogous fluorine-containing substituents, and occupy fixed positions. The angle θ (see above) between the C–X bond and the line joining the centre of this bond to the fluorine atom in the *meta*-position (from the chemical shifts of which the σ_I constants are determined) will be smaller than the average statistical angle for freely rotating fluorine-containing groups.

Table 3. σ constants for halogenoalkyl groups[47,48].

Substituent	σ_I	σ_R	Substituent	σ_I	σ_R	Substituent	σ_I	σ_R
CH_3[11]	−0.08	−0.15						
CH_2F[a]	0.13	−0.02	CHF_2[a]	0.26	0.06	CF_3	0.39	0.10
CH_2Cl	0.14[11,b]	−0.03[11, 50, c]	$CHCl_2$	0.29[d]	0.02[49, 50, e]	CCl_3	0.29[f]	0.02[g]
CH_2Br	0.14[h]	−0.03[i]	$CHBr_2$	0.29[j]	0.02[49, k]	CBr_3	0.25[l]	0.02[n]
CH_2I	0.14[n]	−0.04	CHI_2	0.26	0.00	CI_3	—	—
CH_2CF_3[a]	0.14	−0.05	$CH(CF_3)_2$	—	—	$C(CF_3)_3$[a]	0.55	0.00
CH_2CN[49]	0.26	−0.08	$CH(CN)_2$[49]	0.55	−0.03	$C(CN)_3$[49]	0.98	0.01

Other data: [2]Table 2; [b]0.15,[50,55] 0.16,[49] and 0.17;[10,11] [c]0.04;[49] [d]0.28,[10] 0.30,[49] and 0.31;[50] [e]0.04;[10] [f]0.30[49] and 0.31;[50] [g]0.03;[49,50] [h]0.16[10,49,50] and 0.18;[75] [i]−0.02;[49,50] [j]0.26[50] and 0.30;[49] [k]0.03;[50] [l]0.26;[49,50] [m]0.03;[49,50] [n]0.16.[75]

The field effect of the CH_2X and CHX_2 substituents, where X = Cl, Br, and I, depends on $\cos\theta$, increases for this reason, and leads to an increase of the σ_I constants.

The accumulation of the large chlorine and bromine atoms at the same carbon atom in the CCl_3 and CBr_3 groups leads to an increase of the bond angles or and hence to an increase of the angle θ and a decrease of the field effect. This may be the reason for the appearance of the "saturation effect".

The angle θ in the $C(CF_3)_3$ substituent must be smaller than for CBr_3 and for the $C(CN)_3$ group θ should be smaller still, the steric hindrance to the rotation of this group is low and the valence angles apparently do not change, so that saturation is not observed for the $C(CN)_3$ group and the latter exhibits a very high inductive effect.

The conjugation constants for halogenoalkyl substituents are small. In terms of its conjugation effect, the CH_2F group is still not an electron donor and its σ_R constant is negative, while the CHF_2 and CF_3 substituents are electron acceptors on the basis of this effect.

On passing from fluorine to iodine in the series of substituents CH_2X, the electron-donating conjugation effect increases slightly, while the electron-accepting effect of the CHX_2 and CX_3 groups decreases.

The CH_2F and CH_2Cl groups are very similar as regards their electronic properties. Their directing effect in electrophilic substitution reactions is the same—they are

predominantly *ortho*, *para*-directing substituents. In the nitration of benzyl fluoride the ratios of the *p*-, *m*-, and *o*-isomers correspond to 54, 28, and 18%,[76] while the corresponding proportions for benzyl chloride are 52.5, 32, and 15%.[77] The directing effects of other partly fluorinated alkyl groups in electrophilic substitution reactions have not been investigated.

IV. PERFLUOROACYL GROUPS (COR_F)

The σ constants of the $C(=O)F$, $COCF_3$, and COC_3F_7[2] groups have been determined by ^{19}F NMR (Table 4). The $COCF_3$ and COC_3F_7 groups are much more powerful electron-accepting substituents, in terms of both their inductive and conjugation effects, than the analogous non-fluorinated acyl groups. In terms of the σ_p constants, they resemble the nitro-group ($\sigma_p = 0.78$)[10]. This is because, under the influence of the perfluoroalkyl substituents at the carbon atom of the carbonyl group, the positive charge increases appreciably and the inductive effect and capacity of the carbonyl group of the perfluoroacyl substituents become much more marked. The latter should also exhibit the effect of direct polar conjugation with electron-donating groups. It can be estimated from the σ_p^- constants. We calculated it from the correlation equation of Swain and Lupton[18]. σ_p^- for the $COCF_3$ group was found to be 1.22 (the corresponding values for the O_2 and $COCH_3$ groups are 1.27 and 0.8).[10]

Table 4. σ constants of perfluoroacyl groups.

Substituent	σ_m	σ_p	σ_I	σ_R
COF[2,11]	0.55	0,70	0,39	0,31
$COCF_3$[2,14]	0.63	0.80	0.47[a]	0.33
COC_3F_7[b]	0.63	0,79	0.46	0.33
COH[10,B]	0.43	0.52	0,25	0.27
COCl[10,B]	0.53	0.69	0,38	0.31
$COOC_2H_5$[10,C]	0,20	0.30	0.11	0.19
$COCH_3$[10,C]	0.28	0.38	0.18	0.20

Other data: [a]0.45;[11] [b]calculated from δ_m^F and δ_p^F (Sheppard[14]) data; [c](F).

In electrophilic substitution reactions, for example in nitration, the $COCF_3$ group exhibits predominantly a *meta*-directing effect[78].

The substitution of the hydrogen atom in the aldehyde group by fluorine leads to an increase of the electron-accepting inductive effect and of the conjugation effect. However, the fluoroformyl group has smaller σ constants than the $COCF_3$ group. This is because the fluorine atom exhibits, apart from a powerful electron-accepting inductive effect, an electron-donating conjugation effect. The latter is much smaller than for the ethoxy-group in the $COOC_2H_5$ substituent. For this reason, the COF group is a stronger electron-accepting substituent than $COOC_2H_5$. The constant σ_p^- for the COF group is also somewhat smaller than for $COOC_2H_5$, amounting to 1.09.

V. NITROGEN- AND PHOSPHORUS-CONTAINING SUBSTITUENTS (N – R_F, P – R_F)

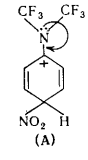
The electronic properties of the substituents in which the CF_3, COF, $COCF_3$, and SO_2CF_3 groups are linked to the nitrogen atom have been investigated (Table 5). The replacement of the methyl by trifluoromethyl in the dimethylamino-group converts this powerful electron-donor into an electron-acceptor, whose σ_m and σ_p constants are close to those of the trifluoromethyl group. However, the inductive effect contributes most to the electronic influence of the $N(CF_3)_2$ group. Its conjugation effect is close to zero owing to the withdrawal of the free electron pairs of the nitrogen atom by the trifluoromethyl groups. For the same reason, di(trifluoromethyl)aniline and its derivatives do not exhibit basic properties and do not form salts with acids[79,82].

Table 5. σ constants for nitrogen-containing substituents (^{19}F NMR method).

Substituent	σ_m^a	σ_p^a	σ_I	σ_R
NH_2[10]	−0.23	−0,47	0.01	−0,48
$N(CH_3)_2$[10]	−0.17	−0,44	0,10	−0,54
$N(CF_3)_2$[2,79,b]	0,49	0.50	0,49	0,01[c]
$NHCOCH_3$[80]	0.17	0.05	0.28	−0.23
$NHCOCF_3$[80]	0.37[d]	0.27[d,e]	0.46[f]	−0.19[f]
$NHSO_2CH_3$[80]	0.32	0.21	0,42	−0.21
$NHSO_2CF_3$[80]	0.44	0.39	0.49	−0.10
$N(CH_3)COCH_3$[80]	0.31	0.26	0.36	−0.10
$N(CH_3)COCF_3$[80]	0.41	0.39	0,43	−0.04
$N(CH_3)SO_2CH_3$[80]	0.29	0,24	0.34	−0.10
$N(CH_3)SO_2CF_3$[80]	0.46	0.44	0.48	−0.04
$N(COCH_3)_2$[80]	0.35	0.33	0.37	−0,04
$N(SO_2CH_3)_2$[80]	0,47	0.49	0,45	0.04
$N(SO_2CF_3)_2$[80]	0.75	0,80	0.70	0.10
$N(CF_3)COF$[79]	0.56	0,56	0,56	0.00
$N(COF)_2$[79]	0.58	0,57	0.58	−0.01
$N{=}C(CF_3)_2$[2]	0.29	0.23	0.35	−0.12
$N{=}N{-}CF_3$[80]	0.56	0.68[g]	0,44	0.24
$N{=}N{-}C_6H_5$[10]	0.23	0.27	0.19	0.08

Other data: [a]calculated from σ_I and σ_R; [b]$\sigma_m = 0.40$, $\sigma_p = 0.53$, $\sigma_I = 0.29$, $\sigma_R = 0.23$ (B),[14] $\sigma_m = 0.47$, $\sigma_p = 0.53$, $\sigma_I = 0.44$, and $\sigma_R = 0.06$ (A)[14]; [c]0.13 (i.r.)[23]; [d]$\sigma_m = 0.30$ and $\sigma_p = 0.12$ (B)[81]; [e]0.13 (C)[21]; [f]$\sigma_I = 0.38$ and $\sigma_R = -0.15$;[10] [g]0.74 (C)[21].

However, in electrophilic substitution reactions the $N(CF_3)_2$ group still behaves as an *ortho*, *para*-directing substituent. In the nitration of di(trifluoromethyl)aniline the proportions of the *para*-, *ortho*-, and *meta*-isomers are 92.4, 5.6, and 1.9%, while in the bromination reaction the corresponding proportions are 94.9, 0.3, and 1.7%.[79] Under the influence of electrophilic agents, the free electron pair at the nitrogen atom is probably nevertheless involved in conjugation and stabilises the transition state (A):



(A)

We estimated by two methods the constants σ_p^+ and σ_R^+, which determine the directing effect of the substituents

in electrophilic substitution reactions. The constants $\sigma_p^+ = 0.42$ and $\sigma_R^+ = 0.07$ were calculated for the $N(CF_3)_2$ group by the equation of Swain and Lupton[18].

The constant σ_R^+ was determined by another method, using the correlation equation $\mu_{int} = 1.10\ (\sigma_R - \sigma_R^+)$ derived by the present authors, for the compounds *p*-$XC_6H_4NO_2$, where X = NMe_2, NH_2, OH, Br, or SCH_3.[24] The dipole moments of *p*-$NO_2C_6H_4N(CF_3)_2$ and $C_6H_5N(CF_3)_2$ are 1.80 and 2.69 D,[79] $\mu_{int} = 0.40$ D, $\sigma_R^+ = 0.13$, and $\sigma_p^+ = 0.36$. The two methods yielded similar negative values of σ_R, and $\sigma_p^+ < \sigma_m$. Consequently the $N(CF_3)_2$ group should be *ortho*, *para*-directing, in agreement with experimental data.

The replacement of the hydrogen atom in the amino-group by $COCH_3$, SO_2CH_3, $COCF_3$, and SO_2CF_3 groups leads to an increase of the electron-accepting inductive effect and a decrease of the conjugation effect. However, the latter still retains its electron-donating character. Thus, even the $NHSO_2CF_3$ group is *ortho*, *para*-directing[83]. A change in the sign of the constant σ_R is observed only when two methane- or trifluoromethane-sulphonyl groups are introduced at the nitrogen atom. The σ_m and σ_p constants of the $N(SO_2CF_3)_2$ substituent resemble those of the nitro-group. Nitration of di(trifluoromethylsulphonyl)aniline yields a mixture of *meta*- and *para*-nitro-isomers in proportions of 8 : 1.[83] The $N(SO_2CH_2)_2$ group is predominantly *ortho*, *para*-directing[84].

The electrophilic constants σ_R^+ and σ_p^+ of the $N(SO_2CF_3)_2$ group, calculated by the method of Swain and Lupton[18], are 0.04 and 0.74. The positive value of the σ_R^+ constant indicates a *meta*-directing effect of this substituent. Thus the directing effect of the amino-group in electrophilic substitution reactions involving an aromatic ring was altered for the first time only by introducing at the nitrogen atom two powerful electron-accepting CF_3SO_2 groups[83].

There are linear relations[21,80] between the σ_p and σ_I constants of the NHR group on the one hand and the corresponding constants of the substituents R, where R = $COCF_3$, SO_2CF_3, and other acyl groups, on the other; they are expressed by the equations

$$\sigma_p(NHR) = 0.49\,\sigma_p(R) - 0.13 \text{ and } \sigma_I(NHR) = 0.38\,\sigma_I(R) - 0.23.$$

It is interesting to note that the $N(CH_3)R$ groups, where R = $COCH_3$, SO_2CH_3, or SO_2CF_3, are weaker electron donors in terms of their conjugation effects than the corresponding NHR groups, although the introduction of the electron-donating methyl group in place of a hydrogen atom should have resulted in the opposite effect[80]. The explanation is probably that the $N\begin{smallmatrix}CH_3\\R\end{smallmatrix}$ groups are displaced from the plane of the benzene ring owing to steric hindrance, which reduces the degree of conjugation between the free electron pair at the nitrogen atom and the ring π electrons.

The $N(CF_3)COF$ and $N(COF)_2$ substituents are somewhat stronger electron acceptors than $N(CF_3)_2$ due to the greater contribution of the inductive component. The trifluoromethylazo-group $-N{=}N{-}CF_3$ is a powerful electron-accepting substituent, approaching in this respect the nitro-group and greatly superior in its electron-accepting influence to the $-N{=}NC_6H_5$ group. In terms of its conjugation effect, the $-N{=}C(CF_3)_2$ substituent is an electron donor. This group is probably not located in the plane of the benzene ring and the free electron pair at the nitrogen atom is involved in conjugation with the aromatic ring.

The phosphorus-containing groups $P(CH_3)_2$ and $P(CF_3)_2$ are less effective electron-accepting substituents than their nitrogen-containing analogues. The inductive effects of the corresponding substituents are close and the conjugation effects of the phosphorus-containing groups indicate more pronounced electron-accepting properties than those of the nitrogen-containing groups (Tables 5 and 6). The σ_I and σ_R constants of the $P(CF_3)_2$ group virtually correspond to those of the nitro-group.

Table 6. σ constants for fluorine-containing substituents.

Substituent	σ_m^a	σ_p^a	σ_I	σ_R
$P(CH_3)_2$ [85]	0.05	0.03	0.08	−0.05
$P(CF_3)_2$ [85]	0.60	0.69	0.50	0.19
$P(CF_3)(C_6H_4F)$[b]	0.44	0.47	0.41	0.06

[a]calculated from σ_I and σ_R (F) data; [b]σ_I and σ_R calculated from δ_m^F and δ_p^F.[85]

The involvement of the free *d* orbitals of the phosphorus atom in conjugation with the π electrons of the aromatic ring is characteristic of phosphorus-containing substituents. The presence of electron-accepting groups at the phosphorus atom, such as CF_3, leads to a decrease of the size and diffuseness at the *d* orbitals, which makes their overlapping with the π electron cloud of the ring more effective and increases the electron-accepting character of the conjugation of the substituent. The replacement of one of the CF_3 groups by an aromatic ring with more marked electron-donating properties makes the conjugation effect of the $P(CF_3)(C_6H_4F)$ group much weaker than for $P(CF_3)_2$. Linear relations have been found for substituents of the type PX_3, where X = F, CF_3, CN, and other groups, whereby the constants of the substituents PX_2 can be calculated from the values of σ_I and σ_R for X:[85]

$$\sigma_I(PX_2) = 0.78\,\sigma_I(X) + 0.47\,\sigma_R(X) + 0.15;\quad \sigma_R(PX_2) = 0.44\,\sigma_I(X) + 0.08\,\sigma_R(X) - 0.03.$$

VI. OXYGEN-CONTAINING GROUPS (O–R_F)

The σ constants of fluorinated oxygen-containing groups are listed in Table 7. The replacement of three hydrogen atoms in the OCH_3 group by fluorine atoms greatly increases its electron-accepting inductive effect and decreases the electron-donating conjugation effect. However, the σ_R constant of the OCF_3 group is still negative, in contrast to all the known substituents of the type $X(CF_3)_n$. All the σ constants of the OCF_3 group resemble most closely those of the chlorine atom. Like the latter, the OCH_3 group is an *ortho*, *para*-directing substituent[97,98], but in the nitration and bromination of phenyl trifluoromethyl ether only the *para*-isomers are formed in yields of 91 and 82% respectively[99,100].

The *para*-directing influence of the trifluoromethoxy-group can be accounted for by the stabilisation of the transition state by the electron-donating conjugation effect of this group. The *ortho*-position relative to the OCF_3 group is deactivated, as in fluorobenzene, by the powerful electron-accepting inductive effect. The σ_I constant of the OCF_3 group is closer to that of fluorine than chlorine.

Table 7. σ constants for oxygen-containing groups.

Substituent	σ_m			σ_p			σ_I			σ_R		
	B	A	F*	B	A	F*	B	A	F	B	A	F
OCH_3 [10]	0.12		0.08	−0.27	−0.27	−0.14	0.30 [86]		0.25	−0.57 [86]		−0.43
OCH_2F [a]			0.20			0.02			0.37			0.35
$OCHF_2$	0.31 [86]		0.33	0.18 [86]	0.11 [88]	0.21	0.44 [86]		0.45 [87,89]	−0.24 [86]		−0.24 [89, b, c]
OCF_3 [52–54, 10, d]	0.35[e]	0.47 [90]	0.46	0.32[f]	0.27 [90, g]	0.37	0.40	0.50 [90]	0.55	−0.07 [i]	−0.23 [90]	−0.18 [j]
OCH_2Cl [87]			0.25			0.08			0.41			−0.33
$OCHCl_2$ [87]			0.38			0.26			0.49			−0.23
$OCCl_3$ [87]			0.43			0.34			0.51			−0.17
OCF_2CF_3 [90, k]		0.48			0.28			0.52				
OCF_2CHF_2 [90]	0.34	0.43		0.25	0.21		0.39	0.45		−0.14	−0.25	
OCF_2CHFCl [91]	0.35			0.28			0.42			−0.12	−0.25	
$OCOCH_3$ [10]	0.39		0.17	0.31		0.06			0.27			−0.21
$OCOCF_3$ [92]			0.56			0.46			0.65			−0.19
OSO_2CF_3 [93, 94]	0.56		0.80	0.53	0.49 [88]	0.90	0.58		0.70	−0.05		0.20
OSF_5 [2, 95]				0.44								
[52]				0.36[l]								

*Calculated from σ_I and σ_R data.

Other data: [a]approximate values, σ_R = −0.31 (i.r.)[87]; [b]−0.27;[87] [c]−0.23 (i.r.)[87]; [d]σ_m = 0.40, σ_p = 0.26, σ_I = 0.36, and σ_R = −0.15(P)[10]; [e]0.38;[2,14] [f]0.35;[2,14,19] [g]0.25;[88] [i]−0.04[2] and −0.17;[11] [j]−0.19[87] and −0.25 (i.r.)[22,23]; [k]σ_m = 0.43, σ_p = 0.21, σ_I = 0.42, and σ_R = −0.17(ρ);[90] [l]0.21(Dy).[96]

On gradual substitution of the hydrogen atoms in the OCH_3 group by fluorine, the σ_I constants increase regularly approximately by 0.1 and the absolute values of the σ_R constants decrease on average by 0.08 (according to ^{19}F NMR). The saturation effect is hardly observed. The inductive effects for analogous chlorinated groups also increase on accumulation of chlorine atoms, but a marked saturation effect is shown. Compounds containing the OCH_2F substituent have not so far been obtained but its σ constants have been calculated (Table 7).

Like OCF_3, the $OCHF_2$ group is an *ortho*, *para*-directing substituent[101]. However, since the inductive effect of the $OCHF_2$ group is smaller, the *ortho*-position in the difluoromethylphenyl ether molecule is less deactivated in relation to electrophilic substitution reactions than in phenyl trifluoromethyl ether, but is nevertheless more deactivated than in anisole. Thus nitration of anisole yields a mixture of *ortho*- and *para*-isomers in proportions of 1 : 2,[102] nitration of difluoromethylphenyl ether gives the corresponding proportion of 1 : 2.6,[101] while phenyl trifluoromethyl ether is nitrated only in the *para*-position.

Methoxy- and fluoromethoxy-groups are irregular substituents[24]. The methoxy-group has a group moment of 1.28 D[41] and an angle $\theta = 72°$,[41] the substituent constituting the positive end of the dipole. The fluorinated groups $OCHF_2$ and OCF_3 have group moments of 2.46[103] and 2.27 D[104] (2.36 D[90]) and angles θ of 137°30′[103] and 154°[104] (160°[24]). When the hydrogen atoms are replaced by fluorine in the methoxy-group, the angle gradually increases, the direction of the group moment approaches the direction of the C_{aryl}–O bond, and the substituent becomes the negative end of the dipole.

The conjugation effect of the OCH_3, OCH_2F, $OCHF_2$, and OCF_3 substituents depends on whether they are located in the plane of the aromatic ring or whether they are displaced from it under the influence of their steric interaction with the hydrogen atoms in the *ortho*-positions. It has been shown by quantum-mechanical calculations[87] that the π electron density in the *para*-position of the benzene ring depends on the angle between the planes of the benzene ring and C_{aryl}–OR. For the OCH_3, OCH_2F, $OCHF_2$, and OCF_3 substituents, these angles are 18°, 56°, 90°, and 90° respectively. With increase of the angle, the electron-donating properties of the substituents diminish, but still persist even when the angle is 90°.

The OCF_2CF_3, OCF_2CHF_2, and OCF_2CHFCl substituents have σ constants close to those of the OCF_3 group. The trifluoroacetoxy-group exhibits a more powerful electron-accepting inductive effect than the $OCOCH_3$ substituent and even OCF_3, while they all have virtually identical electron-donating conjugation effects.

As was to be expected, among all the known groups OR the OSO_2CF_3 group is the most powerful electron acceptor[84,93] and has the highest σ_I constant. Nevertheless in electrophilic substitution reactions the group is an *ortho*, *para*-directing substituent[93]. The OSF_5 group behaves similarly[95].

VII. SULPHUR- AND SELENIUM-CONTAINING GROUPS (S–R_F, Se–R_F)

According to ^{19}F NMR data, on passing from the methoxy- to the methylthio-group, the electron-accepting inductive effect diminishes by a factor of two, while the electron-donating conjugation effect decreases approximately by a factor of three (Tables 7 and 8). The methylthio-group exhibits inductive and conjugation effects which are almost of the same magnitude but have the opposite signs. The introduction of three fluorine atoms sharply enhances the electron-accepting properties of the methylthio-group. The inductive effect increases appreciably, being only slightly inferior to that of the ECF_3 group, while the conjugation effect of the trifluoromethylthio-group changes direction and becomes an electron-accepting effect, in contrast to that of the oxygen analogue. As a result, the σ_m constants of the OCF_3 and SCF_3 groups are very close and the σ_p constant of the SCF_3 group shows that it is a much more powerful electron-accepting substituent than OCF_3.

Successive substitution of the hydrogen atoms of the SCH_3 group by fluorine results in a gradual increase of the electron accepting inductive effect, while the conjugation effect changes from electron-donating for the SCH_3 and

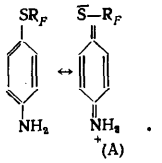
Table 8. σ constants for sulphur- and selenium-containing substituents.

Substituent	σ_m			σ_p			σ_I			σ_R		
	B	A	F*	B	A	F*	B	A	F	B	A	F
SCH_3 [86,89]	0.15		0.05	0.00		−0.03	0.19		0.13	−0.19		−0.16
SCH_2F [89]			0.23			0.20			0.27			−0.07
$SCHF_2$ [86,89]	0.33		0.34	0.36[a]	0.48 [88]	0.35	0.31		0.33	0.07		0.02
SCF_3 [10,52—54,b]	0.36 [105,c]	0.46 [90]	0.53	0.46[a]	0.64 [90, e]	0.56	0.30[f]	0.40 [90]	0.44[g]	0.17	0.22 [90]	0.16[i]
SCF_2CF_2H [90]	0.38[k]	0.42		0.47[j]	0.61		0.29	0.37		0.20	0.21	
$SOCH_3$ [10]	0.52		0.49	0.49		0.49	0.52		0.49			0.00
$SOCHF_2$ [89, j]			0.70		0.93 [88]	0.76			0.65			0.11
$SOCF_3$ [19, 53, 54, 88]	0.63	0.76 [2]	0.74	0.69	1.05[m]	0.80	0.60	0.70 [2]	0.67	0.11	0.32 [2]	0.13
SOF [107]			0.74			0.83			0.66			0.17
SOCl [107]			0.75			0.82			0.68			0.14
SO_2CH_3 [10,89]	0.60	0.66 [88]	0.56	0.72	1.09 [88]	0.64	0.62 [90]		0.48	0.16 [90]	0.51 [90]	0.16
SO_2CH_2F [89]			0.66		1.17 [88]	0.77			0.55			0.22
SO_2CHF_2 [86,89, n]	0.75	0.87 [88]	0.73	0.86	1.44 [88]	0.87	0.70[o]		0.59	0.19		0.28
SO_2CF_3 [52—54, p]	0.76	0.98 [88]	0.88[r]	0.96	1.63 [88]	1.04[s]	0.64[t]	0.84 [90]	0.73 [89, u]	0.32[v]	0.73 [90]	0.31 [89]
$SO_2CF_2CHF_2$				1.01[w]								
SO_2CF_2CHFCl				0.98[w]								
$SO_2CF_2CHFCF_3$				1.03[w]								
SO_2F [2]	0.98	0.99	0.88	1.08	1.54	1.01	0.88	0.87	0.75	0.21	0.59	0.26
SO_2Cl [10]			0.92			1.04			0.80			0.24
CH_2SCF_3 [108]	0.12		0.15	0.15		0.12	0.11		0.19[x]	0.04		−0.07[y]
$CH(SCF_3)_2$ [47]			0.44			0.43			0.44			0.01[z]
$C(SCF_3)_3$ [47]			0.50			0.52			0.49			0.03[aa]
CH_2SOCF_3 [108]			0.25			0.24			0.26			−0.02
$CH_2SO_2CF_3$ [108]	0.29		0.29	0.31		0.31	0.28		0.28	0.03		0.03
$SeCF_3$ [109]	0.32		0.44	0.38[bb]	0.53 [88]	0.46	0.28		0.42	0.10		0.04
$SeOCF_3$ [111]			0.81			0.86[cc]			0.76			0.10
SeO_2CF_3 [111]			1.08			1.21			0.96			0.25

*Calculated from σ_I and σ_R.

Other data: [a]0.34;[105] [b]σ_m = 0.43, σ_p = 0.57, σ_I = 0.39, and σ_R = 0.14(P)[90]; [c]0.37 [106] and 0.40;[90] [d]0.42 [106] and 0.50;[90,105] [e]0.91;[88] [f]0.31;[90] [g]0.42;[2,71] [i]0.00 (i.r.)[22,23]; [j]σ_m = 0.54 and σ_p = 0.58;[105] [k]0.39;[106] [l]0.45;[106] [m]10.7;[2] [n]σ_m = 0.76 and σ_p = 0.84(B)[105]; [o]0.65;[86] [p]σ_m = 0.92, σ_p = 1.36, σ_I = 0.84, and σ_R = 0.49(P)[90]; σ_m = 0.76 and σ_p = 0.93(Dy)[19]; [r]0.90;[2] [s]1.06;[2] [t]0.62;[2] [u]0.75 [2] and 0.78;[107] [v]0.22;[2] [w]method (C); [x]0.21;[49] [y]−0.06;[49] [z]0.00;[49] [aa]0.04;[49] [bb]0.38(Dy)[110]; [cc]0.63(Dy)[110].

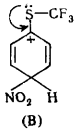
SCH_2F groups to electron-accepting for the $SCHF_2$ and SCF_3 substituents. The interaction of a sulphur atom with the aromatic ring is of a dual nature: it is an electron-donating $(3p - 2p)\pi$ interaction with charge transfer to the ring and an electron-accepting $(3d - 2p)\pi$ interaction with charge transfer from the ring to the vacant *d* orbitals of the sulphur atom. Electron-accepting substituents at the sulphur atom tend to increase the interaction involving the *d* orbitals of sulphur. The electron-accepting $(3d - 2p)\pi$ conjugation occurs when the *para*-position relative to the fluoroalkylthio-group contains electron-donating substituents, for example the amino-group.



As fluorine atoms accumulate in the methylthio-group, the $(3d - 2p)\pi$ conjugation becomes more marked and the contribution of the resonance structure (A) gradually increases, as can be seen from the increase of μ_{int} in the series of substituents $SCH_3 < SCHF_2 < SCF_3$ (0.27, 0.46, and 0.68 D)[103,104]. The group moments and the angles θ between the direction of the dipole moment and the Caryl–S bond of the above substituents also gradually increase (μ = 1.34[104], 2.48,[103] and 2.50 D[104]; θ = 77.5°,[24] 137°,[103] and 156°[24,104]). The change in the angle θ shows that the electrons in the SCH_3 group are displaced to the benzene ring ($\theta < 90°$), while in fluorinated groups the opposite shift obtains.

The electron-donating $(3p - 2p)\pi$ conjugation decreases on accumulation of fluorine atoms in the methylthio-group. This is evident from a comparison of the μ_{int} for the corresponding *p*-nitro-derivatives, which diminishes on passing from SCH_3 to $SCHF_2$ and SCF_3 (θ_{int} = 0.78, 0.48, and 0.21 D respectively).[103,104]

In electrophilic substitution of an aromatic ring, the SCF_3 group is *ortho*, *para*-directing. Thus nitration of phenyl trifluoromethyl sulphide results in the formation of 65% of the *p*-nitro-isomer and 35% of the *o*-nitro-isomer[112]. This is probably due to the stabilisation of the transition state (B) by $(3p - 2p)\pi$ conjugation with the electron pair of the sulphur atom:



(B)

An approximate estimate of the electrophilic conjugation constant σ_R^+ of the SCF_3 group from data for μ_{int} for the interaction with a nitro-group (see above) yields 0.09. The negative value of the constant is also consistent with the *ortho*, *para*-directing influence of the substituent. The electronic influence of the SCF_2CF_2H group hardly differs from that of the SCF_3 group.

When the SCF_3 group is converted into $SOCF_3$ and SO_2CF_3, there is a marked enhancement of the electron-accepting properties of the substituent. We have established[52,113] that the CF_3SO_2 group is one of the most powerful electron acceptors. The σ constants of this substituent greatly exceed those of the nitro-group. The strength of the $SOCF_3$ group is close to that of the nitro-group.

In contrast to SCF_3, the $SOCF_3$ and SO_2CF_3 groups are *meta*-directing. Nitration of phenyl trifluoromethyl sulphoxide yields 90% of the *m*-nitro-isomer and only 5% of the *p*-nitro-isomer[114] and nitration of phenyl trifluoromethyl sulphone results in the formation of the *m*-nitro-isomer alone[113].

When the hydrogen atoms in the $SOCH_3$ and SO_2CH_3 groups are replaced successively by fluorine, the inductive and conjugation effects gradually increase. The σ constants of the SO_2CH_2F group correspond to those of the nitro-group and the constants of the SO_2CHF_2 group are actually higher.

More marked electron-accepting properties of the SO_2CF_3 and SO_2CHF_2 substituents compared with those of the nitro-group are observed also in nucleophilic substitution reactions involving the aromatic ring. Thus the introduction of the SO_2CF_3 group in place of the nitro-group in the 4-position of 1-halogeno-2,4-dinitrobenzenes increases the rate of substitution of fluorine and chlorine in the reactions with aniline by a factor of 10 and 40 respectively[115].

When *p*-nitrophenyl trifluoromethyl and *p*-nitrophenyl difluoromethyl sulphones react with sodium alkoxides, the weaker electron-accepting substituent (the nitro-group) is preferentially substituted by the alkoxy-group[116-118]. In *p*-nitrophenyl trifluoromethyl sulphoxide the weaker electron-accepting $SOCF_3$ group is replaced.

The group moments of the SCF_3, $SOCF_3$, and SO_2CF_3 substituents gradually increase and are 2.50, 3.88, and 4.32 D, while the angles θ are 156°, 143°, and 167°.[104] The angles θ increase in the series of substituents SO_2CH_3, SO_2CH_2F, SO_2CHF_2, and SO_2CF_3: 117°,[24] 136°,[113] 152°,[103] and 167°,[104] while the group moment passes through a minimum: 4.73,[24] 4.04,[119] 4.08,[103] and 4.32 D.[104] The vibration frequencies (ν_{as}) of the SO bond[120] gradually increase in the above series of substituents: 1334, 1342, 1358, and 1380 cm^{-1}.

The σ_I constants for the SCF_3, $SOCF_3$, and SO_2CF_3 groups were also determined from the pK_a data for the corresponding substituted acetic acids and the σ_p constants were determined from the pK_a for the phenylacetic acid derivatives[108]. These results are close to the values of σ_I and σ_p constants obtained by ^{19}F NMR. It was found that trifluoromethylthioacetic acid is approximately 65 times, trifluoromethylsulphoxyacetic acid is 500 times, and trifluoromethylsulphonylacetic acid is 750 times stronger than acetic acid[108]. The last acid is the strongest of all known monosubstituted acetic acids.

The σ constants determined by different methods for powerful electron-accepting substituents, for example SO_2CHF_2 and SO_2CF_3, show differences. This is probably due to a contribution by the direct polar conjugation between these substituents and the reaction centre (the fluorine atom and the hydroxy- and amino-groups). The σ_R constants of the SCF_3, $SOCF_3$, and SO_2CF_3 groups determined by ^{19}F NMR include a definite contribution by polar conjugation as for other powerful electron-accepting substituents. Correlations whereby it is possible to determine the constants σ_R^0 free of the contribution by direct polar conjugation have been found by comparing the σH, $\sigma^{13}C$, and σF chemical shifts[121]. The σ_R^0 constants of the SCF_3, $SOCF_3$, and SO_2CF_3 groups are 0.01, 0.09, and 0.20; they are appreciably smaller than the σ_R = 0.06, 0.13, and 0.31 found by ^{19}F NMR.

The basicity of the anilines *p*-$NH_2C_6H_4SO_2R$ decreases markedly as fluorine atoms accumulate in the substituents. Thus pK_a = 1.48, 1.28, 0.51, and −0.02 for R = CH_3, CH_2F, CHF_2, and CF_3.[88] *p*-Trifluoromethylsulphonylaniline is the weakest base among all the known *p*-substituted anilines.

The enhancement of the electron-accepting influence of the substituents with increase of the number of fluorine atoms in the OCH_3, SCH_3, $SOCH_3$, and SO_2CH_3 groups is clearly shown in the ESR spectra of the radical-anions obtained by the reduction of the corresponding substituted nitrobenzenes. The splitting constants a_N for the nitrogen atoms of the nitro-groups and the reduction half-wave potentials $E_{1/2}$ decrease steadily as the electron-accepting properties of the substituent become more pronounced[122].

Transmission of the electronic effects of substituents in an aromatic ring to the OCF_3, SCF_3, and SO_2CF_3 groups was observed by ^{19}F NMR from the change in the chemical shifts of the fluorine atoms in these groups. It was found that the electronic influence is transmitted most effectively via the sulphur atom and with greater difficulty via the oxygen atom of the SO_2 group[123]. A similar behaviour was observed in a study of the shifts of the C–F stretching vibration frequencies in the infrared spectra of compounds of the type $XC_6H_4OCF_3$, $XC_6H_4SCF_3$, and $XC_6H_4SO_2CF_3$.[124,125]

When one hydrogen atom in the methyl group is replaced by the SCF_3, $SOCF_3$, or SO_2CF_3 groups, the inductive effect becomes of the electron-accepting type and the conjugation effect changes sign only for the $CH_2SO_2CF_3$ group. As the SCF_3 groups accumulate at the carbon atom, the inductive effect becomes increasingly of the electron-accepting type and a saturation effect is observed, as for chloro- or bromo-methyl groups. The conjugation effect becomes of the electron-accepting type only for the $C(SCF_3)_3$ group.

The SOF and SO_2F substituents have σ constants close to those for the SOCl and SO_2Cl groups. The SO_2F group is a much more effective electron-accepting substituent than SOF. The latter hardly differs in the values of the σ constants from the $SOCF_3$ group. The SO_2F substituent has a σ_I constant close to that of the SO_2CF_3 group, but its σ_R constant is somewhat smaller, probably owing to the electron-donating conjugation effect of the fluorine atom.

The electron-accepting inductive effect decreases in the series of substituents with Group VI elements $OCF_3 > SCF_3 > SeCF_3$, the values for the last two being very close, as for the corresponding methyl derivatives[109]. In contrast to the trifluoromethoxy-group, which exhibits an electron-donating conjugation effect, the SCF_3 and $SeCF_3$ groups have positive σ_R constants owing to the involvement in conjugation of the vacant *d* orbitals of the sulphur and selenium atoms. The more diffuse 4*d* orbitals of selenium show a smaller tendency towards $(p-d)\pi$ conjugation than the 3*d* orbitals of the sulphur atom and therefore the $SeCF_3$ groups exhibit a weaker electron-accepting conjugation effect than SCF_3. A similar phenomenon was observed on comparing the SCH_3 and $SeCH_3$ substituents[109]. The dipole moment of the interaction between $SeCF_3$ and the amino-group in the *para*-position (μ_{int} = 0.43 D)[126] is somewhat smaller for the same reason than that for the interaction between SCF_3 and NH_2 groups (μ_{int} = 0.68 D)[104].

Owing to the smaller tendency of the selenium atom towards $(4p-2p)\pi$ conjugation, the $SeCF_3$ substituent does not show electron-donating properties, in contrast to the

SCF_3 group, even when a nitro-group is present in the *para*-position (μ_{int} = 0.01 D)[126]. The group moment of the $SeCF_3$ substituent is 2.48 D (2.50 D for SCF_3) and its vector forms an angle $\theta = 140°$ with the C_{aryl}–Se bond[116] ($\theta = 156°$ for SCF_3).

Thus the SCF_3 and $SeCF_3$ substituents with bivalent sulphur and selenium have similar electronic properties; the substituents containing atoms of these elements in the quadrivalent ($SOCF_3$ and $SeOCF_3$) and hexavalent (SO_2CF_3 and SeO_2CF_3) states differ more markedly.

The $SeOCF_3$ and SeO_2CF_3 substituents have higher σ_I constants and somewhat lower σ_R constants than the corresponding sulphur-containing groups. This is probably due to the greater contribution of polar structures of the type $CF_3Se^+(=O)-O^-$, which results in a high positive charge on the selenium atom and a decrease of the multiplicity of the Se–O bond. The study of the dipole moments confirms this hypothesis. The group moments of the $SeOCF_3$ (4.13 D)[127] and SeO_2CF_3 (5.37 D)[127] substituents are higher than for the sulphur-containing groups (3.88 and 4.32 D respectively), while the μ_{int} for interaction with electron-donating substituents are lower. For example, μ_{int} is 0.97 D for *p*-$NH_2C_6H_4SeOCF_3$,[127] 1.11 D for the sulphur analogue[104], 0.18 D for *p*-$CH_3C_6H_4SeO_2CF_3$,[127] and 0.78 D for the analogous sulphone[104].

As for the SCF_3 and $SeCF_3$ groups, the angles θ in the $SeOCF_3$ and SeO_2CF_3 substituents (128° and 151°)[127] are smaller by approximately 15° than for the sulphur-containing groups. The electron-accepting influence of the $SeOCF_3$ and SeO_2CF_3 substituents, characterised by the σ_m and σ_p constants, is much greater than that of the analogous $SOCF_3$ and SO_2CF_3 groups. In terms of its inductive effect, SeO_2CF_3 is an even more powerful electron acceptor than the SO_2CN and $N^+(CH_3)_3$ groups (σ_I = 0.94[107] and 0.93[10] respectively).

VIII. UNSATURATED FLUORINATED GROUPS

The vinyl group has σ constants close to zero. On replacement of a hydrogen atom in such groups by CF_3 and SO_2CF_3, unsaturated groups are formed with electron-accepting properties, albeit considerably weakened by the introduction of the vinylene group (Table 9). The inductive effect decreases particularly markedly.

A correlation has been found between the σ_I constants of the CH=CHX and X substituents[10]: σ_I (*trans*-CH=CHX) = 0.01 + 0.41 σ_I(X). The decay of the inductive effect transmitted via the vinyl group is smaller by a factor of approximately two than via two methylene groups. This suggests that the inductive effect is transmitted not only via σ bonds but also via π bonds. In these unsaturated systems the I_π effect probably plays a certain role.

The σ_R constants of the CH=CHX and X groups are also linearly related: σ_R (*trans*-CH=CHX) = −0.03 − 0.96 σ_R(X). Comparison of the coefficients of σ_I(X) and σ_R(X) shows that the conjugation effect is more effectively transmitted via the vinyl unit than the inductive effect.

In the *cis*-isomer of the group $CH=CHCF_3$ the σ_I and σ_R constants are smaller than for the *trans*-isomer. This is probably because, owing to steric hindrance, the CH = $CHCF_3$ group in the *cis*-isomer is partly displaced from the plane of the benzene ring.

The σ_m and σ_p constants of the CH = $CHSO_2CF_3$ group resemble those of the CF_3 group. The ethynyl group is a more powerful electron acceptor than the vinyl group and the replacement of its hydrogen atom by a CF_3 group leads to the substituent $C{\equiv}CCF_3$ with more powerful electron-accepting properties than those of the $CH=CHCF_3$ group. The *trans*-$CF=CF-CF_3$ group has the same σ constants as the $C{\equiv}C-CF_3$ group. Thus the replacement of hydrogen atoms in the substituent $CH=CHCF_3$ by fluorine atoms is equivalent to the conversion of a double bond into a triple bond. The σ constants of the $CF=CFCF_3$ and $C{\equiv}CCF_3$ substituents are very close to those of the CF_3 group.

Table 9. σ constants for unsaturated fluorinated substituents.

Substituent	σ_m		σ_p		σ_I		σ_R	
	B	F*	B	F*	B	F	B	F
$CH=CH_2$ [10]		0.00		−0.02	0.05[11]	0.01		−0.03
CF_3 [10]	0.43	0.44	0.54	0.49	0.41	0.38	0.13	0.10
$CH=CH-CF_3$-*trans* [10, 53, 54]	0.22[a]	0.23	0.20[b]	0.27	0.23[c]	0.19[d]	−0.03[e]	0.08[f]
$CH=CH-CF_3$-*cis* [2,71]	0.16	0.15	0.29	0.17	0.14	0.12	0.14	0.05
SO_2CF_3 [10]	0.76	0.88	0.96	1.04	0.64	0.73	0.32	0.31
$CH=CH-SO_2CF_3$-*trans* [10, 53, 54, g]		0.44		0.56		0.31		0.25
$CH=CH-NO_2$ [10, 11]	0.34	0.41	0.26	0.39	0.38	0.24		0.15
$CF=CF-CF_3$-*trans* [10, 53, 54, i]		0.37		0.44		0.30		0.14
$C{\equiv}CH$ [10]		0.12	0.28	0.16		0.08		0.08
$C{\equiv}C-CF_3$ [10, 53, 54]	0.41	0.39	0.51	0.47	0.35	0.31	0.17	0.16
C_6H_5 [10, 11]	0.06	0.04	−0.01	−0.01	0.10	0.08	−0.10	−0.09
C_6F_5 [129, i]	−0.12	0.26	−0.03	0.27		0.25		0.02
C_6Cl_5 [129]		0.25		0.24		0.25		−0.01

*Calculated from σ_I and σ_R.

Other data: [a] 0.20;[2,71] [b] 0.34;[2,71] 0.23 (C)[21], 0.23 (Dy)[19,128], and σ_p^- = 0.34 (A);[88] [c] 0.17;[2,71] [d] 0.20;[2,71] [e] 0.16;[2,71] [f] 0.07;[2,71] [g] σ_{p^-} = 0.83 (A)[88]; [h] 0.45 (C)[21]; σ_p^- = 0.65 (A)[88]; [i] σ_m = 0.34 and σ_p = 0.41 (DA).[129]

The group moments of the substituents increase in the series $CH=CHCF_3 < CF=CFCF_3 < C{\equiv}CCF_3 < CH=CHSO_3CF_3$, amounting to 2.79, 3.06, 3.38 and 4.93 D respectively[130,131]. As a result of the increase of the length of the dipole, these values exceed the group moments of CF_3 and SO_2CF_3 (2.51[132] and 4.32 D[104]). The dipole moments for the interaction with an amino-group in the *para*-position are 0.85, 0.94, and 2.71 D for the substituents $CH=CHCF_3$, $CH=CFCF_3$, and $CH=CHSO_2CF_3$ respectively and also exceed the μ_{int} for substituents without vinyl groups (μ_{int} = 0.49 and 1.46 D for CF_3 and SO_2CF_3).[130,131]

Despite the fact that the fluorine-containing unsaturated groups are electron-accepting in terms of their σ_m and σ_p constants, they are *ortho*, *para*-directing in electrophilic substitution reactions involving the aromatic ring[133], like other substituents of the type CH=CH–X, where X = NO_2, COOH, or $\overset{+}{N}(CH_3)_3$. Thus nitration of the compounds C_6H_5R results in a mixture of nitro-isomers having the following composition[133]:

R	*ortho*	*meta*	*para*
$CH=CH-CF_3$	46.5	3.5	50.0
$CF=CF-CF_3$	26.5	7.5	66.0
$CH=CH-SO_2CF_3$	27.0	15.0	58.0

Nitration of β-trifluoromethanesulphonylstyrene yields a considerable amount of the *meta*-isomer. This is because the SO_2CF_3 group, which has the highest σ_R constant, withdraws electrons from the *ortho*- and *para*-positions of the benzene ring and counteracts the formation

of the energetically favourable *ortho*- or *para*-quinonoid transition complex.

The pentafluorophenyl group, which we shall also consider in this section, should exhibit powerful electron-accepting properties. Indeed pentafluorophenol and pentafluorobenzoic acid exhibit much stronger acid properties (pK_a = 5.5 and 3.4)[129] than phenol and benzoic acid (pK_a = 9.98 and 4.2).[37] However, it has been found by ^{19}F NMR that the electron-accepting inductive effect of the C_6H_5 group is small and the conjugation effect is close to zero[129] The explanation is that the pentafluorobenzene ring in *m*- and *p*-$FC_6H_4C_6F_5$, which were used to determine the σ constants, is displaced from the plane by an appreciable angle. The electronic properties of the C_6Cl_5 group are very close to those of C_6F_5.

IX. SUBSTITUENTS WITH FLUORINE ATOMS LINKED TO HETEROATOMS (EF_n)

The σ constants for substituents of the type EF are listed in Table 10 in order of increasing Group number of the element. All groups of the type EF_n are powerful electron-accepting substituents in terms of both inductive and conjugation effects. The inductive effect of the EF_n group with the maximum number of fluorine atoms increases with the atomic number.

Table 10. σ constants for EF_n substituents (from ^{19}F NMR data).

Substituent		σ_m	σ_p	σ_I	σ_R
Group III	BF_2[2]	0.32	0.48	0.16	0.32
Group IV	CF_3[47,48]	0.44	0.49	0.39	0.10
	CCl_3[47,48]	0.30	0.31	0.29	0.02
	CBr_3[47,48]	0.26	0.27	0.25	0.02
	SiH_3[a]	0.05	0.10	0.01	0.09
	SiF_3[135,2]	0.54	0.66	0.42	0.24
	$SiCl_3$[135]	0.48	0.56	0.39	0.17
	$SiBr_3$[135]	0.48	0.57	0.39	0.18
	GeF_3[135]	0.85	0.97	0.74	0.23
	$GeCl_3$[135]	0.71	0.79	0.63	0.16
	$GeBr_3$[135]	0.66	0.73	0.59	0.14
Group V	PF_2[71,85]	0.48	0.59	0.38	0.21
	PCl_2[71,85]	0.53	0.61	0.45	0.16
	PF_4[71,85]	0.63	0.80	0.45	0.35
Group VI	SF_3[2,71]	0.70	0.80	0.60	0.20
	SF_5[2,136,6]	0.59	0.62	0.55	0.07
Group VII	IF_2[137]	0.85	0.83	0.86	−0.03
	ICl_2[137]	1.10	1.11	1.08	0.03
	IF_4[137]	1.07	1.15	1.00	0.15
	$I(OCOCH_3)_2$[137]	0.85	0.88	0.82	0.06
	$I(OCOCF_3)_2$[137]	1.28	1.34	1.22	0.12

Other data: [a]Calculated from δF;[134] [b]σ_m = 0.61(B), 0.63(A), and 0.61(P), σ_p = 0.68(B), 0.86(A), and 0.70(P), σ_I = 0.55(B), 0.56(A), and 0.53(P), and σ_R = 0.11(B), 0.27(A), and 0.12(P)[2,136].

Despite the fact that boron is less electronegative than carbon, under the influence of fluorine atoms the BF_2 group exhibits an electron-accepting inductive effect[2]. The higher σ_R constant of this substituent can be explained by the presence of a vacant *p* orbital in the boron atom to which the π electrons of the aromatic ring are displaced.

The σ_I constants gradually increase in the series of substituents with Group IV elements $CF_3 < SiF_3 < GeF_3$.[135] In the first two groups they are very close but on passing to GeF_3 the σ_I constant increases sharply. This is probably due to the increase of the polarity of the Ge–F bond with increase of the contribution of ionic structures of the type $ArGeF_2F^-$. The higher negative charges on the fluorine atoms in the SiF_3 and GeF_3 groups than in the CF_3 group are confirmed by the fact that the ^{19}F NMR signals for the first two groups are located in a higher field relative to trifluoromethylbenzene[135].

The σ constants of substituents with Group IV elements linked to chlorine and bromine atoms also increase on passing from carbon to silicon and germanium but their σ_I constants are lower than those of the fluorine analogues. This is because E–F bonds are the most polar[135]

The values of σ_R for the $SiHal_3$ and $GeHal_3$ groups greatly exceed the σ_R for the $CHal_3$ groups. This increase of the conjugation effect is accounted for by the involvement of the *d* orbitals of silicon and germanium in $(d-p)\pi$ conjugation. It is shown to the greatest extent in aryltrifluorosilanes and aryltrifluorogermanes where electron withdrawal by fluorine atoms promotes an increase of the $(d-p)\pi$ conjugation.

The dipole moment of phenyltrifluorosilane (2.77 D)[138] is higher than that of phenyltrichlorosilane (2.41 D)[138] and trifluoromethylbenzene (2.51 D)[132] which is consistent with the more marked electron-accepting properties of the SiF_3 group. It is also indicated by the increase of the dipole moment in the sequence $C_6H_5Si(CH_3)_2F <$ $C_6H_5Si(CH_3)F_2 < C_6H_5SiF_3$ (1.70, 2.55, and 2.72 D respectively)[139].

In electrophilic substitution reactions, for example in chlorination in the presence of $FeCl_3$, the $Si(CH_3)_3$ group is predominantly *ortho*, *para*-directing, activating the benzene ring. On gradual substitution of the methyl groups in $Si(CH_3)_3$ by fluorine atoms, the content of the *meta*-isomer in the reaction products increases, reaching 72% for the SiF_3 group, while the reactivity decreases by a factor of 1000 compared with the $Si(CH_3)_3$ group.[140,141]

The PF_2 group is a substituent with somewhat weaker electron-accepting properties than $P(CF_3)_2$.[85] The reason for this is the occurrence in the PF_2 group of an interaction between the *p* electrons of the fluorine atom and the *d* orbitals of the phosphorus, which acts in the opposite direction. In the PCl_2 substituent the $(p-d)\pi$ interaction between the chlorine and phosphorus atoms is weaker and therefore the electron-accepting inductive effect of the PCl_2 group is somewhat higher than that of the PF_2 group.

An increase of the number of fluorine atoms at the phosphorus atom leads to an increase of the constants σ_I and σ_R. The PF_4 group is one of the most powerful electron-accepting phosphorus-containing substituents. The pronounced electron-accepting effects of the PF_2 and PF_4 groups can be explained by the interaction of the π electrons of the aromatic ring with the vacant *d* orbitals of phosphorus, which become compact under the influence of the fluorine atoms and overlap fairly effectively with the *p* orbitals of the carbon atoms in the benzene ring[85]

Similar phenomena are observed in the SF_3 and SF_5 substituents. However, the conjugation effect of the SF_5 group proved to be smaller than that of SF_3 despite the higher number of fluorine atoms. Two *d* orbitals of the sulphur atom in the SF_5 group are involved in the formation of σ bonds and the remaining three vacant *d* orbitals, which have higher energies, are to a considerable degree saturated by the electrons of the five fluorine atoms and probably interact less effectively with the π electrons of the benzene ring. Only one *d* orbital of the SF_3 and PF_4 substituents is involved in the formation of σ bonds and

the remaining four vacant *d* orbitals interact fairly effectively both with fluorine atoms and with the π electrons of the aromatic ring[107].

Among all the substituents of the EF_n type investigated, only the SF_5 group is extremely resistant to hydrolysis. Nitration of phenylsulphur pentafluoride yields 80% of the *m*-nitro-isomer. The group moment of CF_5 is 3.44 D and μ_{int} for the interaction with an amino-group in the *para*-position is 0.6 D.[136]

Table 10 shows that groups with tervalent or quinquevalent iodine interact with an aromatic ring mainly via the inductive mechanism. The very high σ_I constants are probably due to the high polarity of the bonds between the iodine atom and halogen atoms or acyloxy groups. The ICl_2 and $I(OCOCF_3)_2$ groups, in which the contributions by the structures I^+Cl^- and $I^+(OCOCF_3)^-$ should be maximal, have the highest σ_I constants.

The accumulation of fluorine atoms at the iodine atom leads to an increase of the inductive effect and a considerable increase of the conjugation effect. The involvement of vacant *d* orbitals in substituents with a pentacovalent iodine atom in conjugation with the π electrons of the benzene ring is probably more effective than in the IF_2 and ICl_2 groups[137].

X. FLUORINE-CONTAINING SUBSTITUENTS WITH METAL ATOMS

Fluorine-containing substituents with a mercury atom have now been investigated (Table 11)[142]. The electronic properties of mercury-containing substituents are largely determined by their inductive effects. The constants σ_I of these substituents depend very markedly on the nature of the solvent. The lower the polarity of the solvent the higher the σ_I constant. The increase of the σ_I constants on passing from dichloroethane (DCE) to chloroform can probably be accounted for by the tendency of chloroform to form hydrogen bonds with electron-accepting groups linked to the mercury atom[143]. Mercury has vacant 6*p* orbitals and therefore solvents such as tetrahydrofuran (THF) may be coordinated to mercury atoms, which leads to a sharp decrease of the constants σ_I. For the same reason, the σ_R constants, determined by the interaction of the 6*p* orbitals of mercury with the ring π electrons, fall almost to zero in THF. The presence of electron-accepting substituents at the mercury atom (CN, CF_3, SCF_3) promotes the overlapping of the mercury 6*p* orbitals with the 2*p* electrons of the carbon atom in the benzene ring—$(6p - 2p)\pi$ interaction and an electron-accepting conjugation effect. The *p* electrons of the fluorine atom in the HgF substituent are displaced to the 6*p* orbitals of the mercury atom and probably further to the benzene ring, which leads to a weak electron-donating conjugation effect of this substituent.

Table 11. σ constants for substituents with a mercury atom (from ^{19}F NMR data).

Substituent	σ_I			σ_R		
	$CHCl_3$	DCE	THF	$CHCl_3$	DCE	THF
HgF[142]		0.34	0.18		−0.01	−0.01
HgCl[143]	0.31		0.17	0.04		0.01
$HgCF_3$[142]	0.27	0.16	0.06	0.05	0.03	0.01
HgCN[143]	0.23		0.07	0.11		0.02
$HgSCF_3$	0.37	0.32	0.18	0.05	0.04	0.02
$HgOCOCH_3$[143]	0.38		0.16	0.02		0.00
$HgOCOCF_3$[143]	0.48	0.37	0.22	0.04	0.03	0.00

XI. INDUCTIVE CONSTANTS σ^+ OF FLUORINE-CONTAINING SUBSTITUENTS IN ALIPHATIC COMPOUNDS

Taft's σ^+ constants[9], obtained mainly from the dissociation constants of aliphatic acids by means of the equation

$$\lg \frac{K}{K_0} = \rho^* \sigma^*$$

are used to characterise the inductive effect of substituents. Very exact correlations are achieved between the pK_a of R–COOH acids and the $\sigma^+(R)$ when two equations are employed[144]—for saturated acids [Eqn. (I)] and for unsaturated acids with an sp^2 hybridised carbon atom linked to the COOH group [Eqn. (II)]:

$$pK_a = -1.700\,\sigma^*(R) + 4.644\,, \qquad (I)$$

$$pK_a = -1.795\,\sigma^*(R) + 5.275\,. \qquad (II)$$

A similar equation [Eqn. (III)] has been found also for aliphatic alcohols of the type RCH_2OH:[144]

$$pK_a = -1.316\,\sigma^*(R) + 15.74\,. \qquad (III)$$

Table 12. Inductive constants σ^* for fluorine-containing substituents.

Substituent	σ^*	Substituent	σ^*
CH_3	0[9]	OCF_3	3.42[d]
F	3.10[10, 28]	SCF_3	2.74[d,e]
CH_2F	1.10[9, a]	$SOCF_3$	4.17[d,e]
CHF_2	2.05[9, b]	SO_2CF_3	4.55[d,e]
CF_3	2.60[10, 28, c]	NO_2	3.90[10]
CH_2CF_3	0.92[9]	$CH=CH_2$	0.57[144, f]
$CH_2CH_2CF_3$	0.32[9]	$CF=CH_2$	1.53[g]
$CH_2CH_2CH_2CF_3$	0.12[9]	$CH=CF_2$	1.17[g]
$CH(CF_3)_2$	1.34[51]	$CF=CF_2$	1.94[g,h]
$C(CF_3)_3$	1.48[51]	$CCl=CCl_2$	2.26[g]
CH_2SCF_3	0.99[108]	$CH=CHCF_3$	1.07[g]
CH_2SOCF_3	1.50[108]	$CH=CHCCl_3$	1.19[146]
$CH_2SO_2CF_3$	1.61[108]	C_6H_5	0.60[9]
$COCF_3$	3.70[145]	C_6F_5	1.10[147]
$N(CF_3)_2$	3.05[d]		

[a] 1.17;[144] [b] 2.00;[144] [c] 2.61;[147] [d] calculated from Eqn. (4); [e] calculated from Eqn. (V) for SCF_3, $SOCF_3$, and SO_2CF_3 groups (experimental values 2.77, 4.20, and 4.50); [f] 0.56[147] and 0.65;[148] [g] calculated from the pK_a for unsaturated acids[57] with the aid of Eqn. (II); [h] 1.73.[149]

The effects of substituents are additive in alcohols with the structure R′R″R‴COH, hydroxylamines R′R″R‴CNHOH, and oximes R′R″C=NOH.[145,146] However, on gradual substitution of the hydrogen atoms in the methyl group of acetic acid by fluorine or chlorine atoms or CF_3 groups, a "saturation effect" is observed instead of additivity[10,51].

The σ^* constants can also be calculated from Eqns. (IV) and (V):[10]

$$\sigma^* = 6.23\,\sigma_I \qquad \text{(IV)}$$

and

$$\sigma^*(R) = 2.8\,\sigma^*(CH_2R)\,. \qquad \text{(V)}$$

Table 12 lists the constants σ^* for fluorine-containing substituents found by the methods indicated. The σ^* for certain groups without fluorine are listed for comparison.

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The data obtained for the σ constants made it possible to derive correlation equations whereby one can estimate the electronic properties of new substituents the σ constants of which are still unknown. For example, the σ constants of fluorine-containing substituents of the type XCF_3 and $XCHF_2$ may be determined from the σ constants of XCH_3 substituents[10,53,54,89]:

$$\sigma_I(XCF_3) = \sigma_I(XCH_3) + \begin{cases} 0.20 & (n=2) \\ 0.10 & (n=3) \\ 0.06 & (n=4) \end{cases};$$

$$\sigma_c(XCF_3) = \begin{cases} 0.88\,\sigma_R(XCH_3) + 0.19 & (n=2) \\ 1.05\,\sigma_R(XCH_3) + 0.08 & (n=3) \end{cases};$$

$$\sigma_R(XCHF_2) = 0.71\,\sigma_I(XCH_3) + 0.28$$

where X are various elements or groups of atoms and n is the number of bonds between the benzene ring and the CF_3 or CH_3 group.

The electronic properties of fluorine-containing substituents incorporating only 12 of the elements in the Periodic System have now been investigated. Nevertheless many relations useful to chemists have been discovered; these are already being used and will undoubtedly find wider applications in various branches of organic chemistry.

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Oligomerisation of Acetylenes in the Presence of Transition Metal Compounds

L.P.Yur'eva

The literature data on acetylene cyclo-oligomerisation and polymerisation reactions in the presence of transition metal compounds are reviewed. Both catalytic reactions leading to the synthesis of benzene and cyclo-octatetraene derivatives and linear polymers and cyclo-oligomerisation reactions leading to the formation of organometallic compounds are considered. Modern ideas on the mechanism of acetylene cyclo-oligomerisation and polymerisation reactions are discussed in detail.
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I. INTRODUCTION

A wide variety of inorganic and organometallic compounds (OMC) of transition metals give rise to the cyclo-oligomerisation and polymerisation of acetylenes. Catalytic reactions result in the formation of benzene and cyclo-octatetraene derivatives and also linear polymers. In many cases the cyclo-oligomerisation products are formed as π-complexes with the transition metal. Arene and cyclobutadiene complexes are produced in this way. The reaction of acetylenes with metal carbonyls is frequently accompanied by the insertion of the carbonyl group, which leads to the formation of cyclopentadienones, tropones, quinones, and their π-complexes. When acetylenes react with σ-derivatives of transition metals, the formation of simple cyclotrimerisation products may be accompanied by the formation of products involving the σ-group. The metal atom can also participate in the formation of a heterocycle with M–C bonds.

II. CATALYTIC OLIGOMERISATION REACTIONS OF ACETYLENES

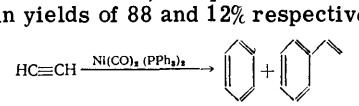
Since the discovery of the cyclo-oligomerisation of acetylenes in the presence of nickel compounds by Reppe in 1940, this reaction has become a convenient method for the synthesis of organic compounds which are otherwise difficult to obtain, such as cyclo-octatetraene, trivinylbenzene, and other benzene derivatives. An enormous number of original studies have been made on the cyclo-oligomerisation and polymerisation of acetylenes under the influence of transition metal compounds and many reviews have been written of which several may be recommended[1-6]. In the present review most attention has been devoted to studies in recent years.

The cyclotrimerisation of acetylenes is catalysed by transition metal compounds of various types, among which homogeneous and mixed metal carbonyls and catalysts of the Ziegler–Natta type are most frequently used. Certain organometallic compounds, salts, etc. also exhibit catalytic activity. The cyclotrimerisation of acetylenes is accompanied by linear polymerisation which becomes the main reaction under certain conditions.

The cyclotetramerisation of acetylenes takes place almost exclusively in the presence of nickel catalysts. Copper(I) salts catalyse the linear oligomerisation of acetylenes.

1. Catalysis by Metal Carbonyls

The first catalysts used in the cyclotrimerisation of acetylenes were carbonylphosphinenickel complexes[7-9]. When acetylene reacts with dicarbonyldi(triphenylphosphine)nickel in acetonitrile, the products are benzene and styrene (in yields of 88 and 12% respectively):



Detailed studies showed that monosubstituted acetylenes form a mixture of 1,2,4- and 1,3,5-trisubstituted benzenes[10-15]. The majority of disubstituted acetylenes (with the exception of but-2-yne-1,4-diol and its ethers[16] as well as monosubstituted acetylenes containing substituents such as t-butyl, COOH, CN, and halogens do not react.

Linear polymerisation of acetylenes occurs together with cyclotrimerisation. The preferential formation of benzene derivatives or linear polymers depends mainly on the nature of the substituent at the triple bond. More reactive monomers give rise mainly to aromatic products, while the yield of linear polymer increases for less reactive acetylenes.

The catalytic activity of the nickel atom and the nature of the product also depend on the nature of the ligand linked to the metal. For example, $Ni(CO)_3PPh_3$ is an effective catalyst of the polymerisation and cyclotrimerisation of acetylenes, while $Ni(CO)(PPh_3)_3$ and $Ni(PPh_3)_4$ are inactive in these reactions[7,17,18]. Reports have been published on catalysis by nickel tetracarbonyl[19-21]. $Ni(CO)_2[P(OPh)_3]_2$ promotes the aromatisation of acetylenes, while linear polymerisation takes place preferentially[17] in the presence of $Ni(CO)_2[P(CH_2CH_2CN)_3]_2$.

The cyclotrimerisation of tolane under the influence of iron, cobalt, manganese, nickel, molybdenum, and tungsten carbonyls has been investigated[20]. As shown below (see Section III), these metal carbonyls react with acetylenes, forming organometallic compounds of various types. Organic products are formed under more severe conditions. For example, tolane reacts with $Fe_3(CO)_{12}$ at 260–280°C with formation of hexaphenylbenzene (yield up to 75%); [20] at lower temperatures a number of organoiron compounds have been isolated[22,23]. Cyclo-octyne cyclotrimerises in the presence of $Fe(CO)_5$ even at room temperature[24].

Carbonyl derivatives of cobalt—$Co_2(CO)_8$, $MgCo_2(CO)_8$, $Hg[Co(CO)_4]_2$, and $RC_2R'Co_2(CO)_6$—exhibit a very high catalytic activity in the aromatisation of acetylenes. Both mono- and di-substituted acetylenes react. Acetylenes with various substituents give rise preferentially or exclusively to asymmetrically substituted benzenes[20,25]. When acted upon by $Hg[Co(CO)_4]_2$, substituted butadiynes are converted into a mixture of 1,2,4- and 1,3,5-trialkylnylbenzenes[26]. Non-conjugated terminal diacetylenes form, together with polymers, also dimers containing one aromatic ring and one triple bond[27]. The cyclotrimerisation of ferrocenylacetylenes in the presence of $Co_2(CO)_8$ has been described[28–30]. $[Co(CO)_3NO]$ has also been suggested as a catalyst[18,31].

Cobalt carbonyl and $RhM_4(CO)_{12}$ have been compared in the cyclotrimerisation of phenyl acetylene[32]. In catalysis by cobalt carbonyl 1,2,4-triphenylbenzene is formed 7–9 times faster than the symmetrical isomer; in catalysis by the rhodium compound the isomer ratio is 2:1.

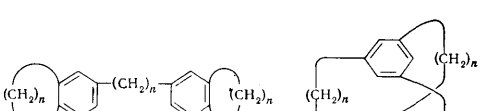
$[RhCl(CO)_2]_2$ has been used for the cyclotrimerisation of tolane[33].

Cyclotrimerisation also takes place in the presence of molybdenum and tungsten hexacarbonyls[20] and triacetonitriletricarbonyl[34] and arenetricarbonyl complexes of chromium and molybdenum[35].

2. Ziegler–Natta Catalysts

Acetylenes undergo linear polymerisation[36–38] and cyclotrimerisation[39–47] in the presence of a catalytic system comprising titanium halides or alkoxides and alkylaluminium derivatives. The R_3Al–$TiCl_4$ systems (R = ethyl or t-butyl) are usually employed to synthesise benzenes. The yields of the corresponding benzene derivatives and linear polymers depends markedly on the Ti:Al ratio[48,49]. Monosubstituted acetylenes do not decompose the catalyst but cyclotrimerise with formation of a mixture of 1,2,4- and 1,3,5-trisubstituted benzenes[28,50].

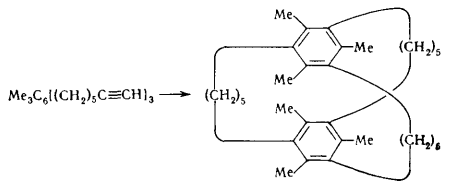
The reactions of conjugated and non-conjugated diacetylenes and triacetylenes have been investigated[27,51–55]. Hexa-2,4-diyne forms trimethyltripropynylbenzene (5%) together with polymers. Non-conjugated alkadiynes $HC{\equiv}C(CH_2)_nC{\equiv}CH$ produce, together with polymers, two types of trimers: (I) (in yields up to 13% for $n = 2$) and traces (less than 1%) of compound (II) containing two benzene rings linked by three polymethylene chains:



(I)

(II)

Cage compounds have been obtained in yields up to 50% from aromatic triynes[51]:



Acetylenes trimerise and polymerise in the presence of trialkylaluminium and vanadium[39,56–60] or cobalt[61,62] derivatives. The $i\text{-}Bu_3Al$–NiX_2 [63–65] and $i\text{-}Bu_3Al$–iron(III) naphthenate[66] systems polymerise acetylene. Et_2Zn–$Cr(OBu\text{-}t)_3$ induces the dimerisation of monosubstituted acetylenes to vinylacetylene derivatives[67]. The replacement of diethylzinc by triethylaluminium leads to the formation of alkylbenzenes.

It has been shown for the R_3Al–$VOCl_3$ and $i\text{-}Bu_3Al$–$TiCl_4$ catalytic systems that the activity of the catalyst is related to the formation of a reduced form of the metal[56,68].

3. Catalysis by Organometallic Compounds

Dicyclopentadienyl derivatives of titanium[69] and vanadium[70] polymerise acetylene. Many monosubstituted acetylenes give rise to the corresponding benzene derivatives in the presence of vanadocene and phenylacetylene produces a linear oligomer. A catalytic effect of tricyclopentadienyllanthanides in the cyclotrimerisation of certain acetylenes has been mentioned[71].

Acetylenes cyclotrimerise and copolymerise with olefins in the presence of di(cyclo-octatetraene)iron[72,73]. The linear polymerisation and cyclotrimerisation of acetylenes is catalysed by cyclo-octa-1,5-dienenickel halides[75] and π-allyl complexes of palladium and nickel[76–79].

Both catalytic and stoichiometric cyclisation and polymerisation reactions of acetylenes take place in the presence of diacrylonitrilenickel. Thus acetylene produces cyanoheptatriene, benzene, and cyclo-octatetraene (COT)[80,81]. Triphenylphosphine suppresses the formation of COT and the synthesis of benzene becomes a catalytic process. In the presence of an excess of acrylonitrile, the main reaction product is cyanoheptatriene (see also Cairns et al.[82]). Disubstituted acetylenes give rise to tetrasubstituted benzonitriles together with hexasubstituted benzenes[80,83]. Similarly hexaphenylbenzene and tetraphenylbenzaldehyde have been obtained from tolane and diacroleinnickel.

When acted upon by diacrylonitrilenickel, but-2-yne[20] and hexafluorobut-2-yne (HFB)[84] undergo linear polymerisation together with cyclotrimerisation. Propargyl alcohol, phenylpropiolaldehyde, propiolic and acetylenedicarboxylic acid esters, and phenylacetylene form polymers[80].

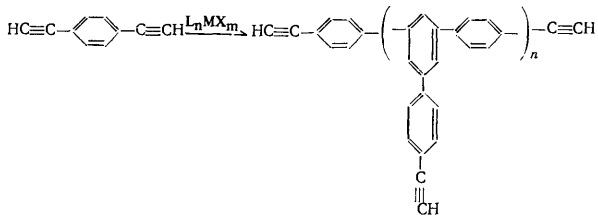
Dimesitylcobalt catalyses the trimerisation of but-2-yne[85]. The cyclisation of acetylenes in the presence of σ-aryl and σ-alkyl derivatives of other metals is a stoichiometric reaction and will be considered below (see Section III). Platinum and nickel σ-acetylides $(Ph_3P)_2M(C{\equiv}CPh)_2$ polymerise phenylacetylene[86,87].

2. Catalysis by Phosphine and Phosphite Complexes of Cobalt Subgroup Metals

Certain rhodium and iridium complexes catalyse the cyclotrimerisation and polymerisation of acetylenes[88].

Thus $RhCl(PPh_3)_3$ causes the polymerisation of HFB [89]. Dimers have been obtained from dialkylethynylmethanols [90]. Phenylacetylene produces a polymer together with the dimer [90-92]. Certain disubstituted acetylenes give rise to the corresponding benzene derivatives [93]. Rhodium and iridium complexes $RhH(CO)(PPh_3)_3$, $IrH(CO)_2(PPh_3)_2$, [94] and certain others [89,90] catalyse the cyclotrimerisation of alk-1-ynes.

Cobalt complexes, for example $CoBr[P(OEt)_3]_4$, have been used for the polycyclotrimerisation of aromatic diacetylenes [95-98]:



Complexes of zerovalent nickel with phosphines and certain other ligands of a similar type are active in the copolymerisation of acetylenes with butadiene [99].

5. Catalysis by Salts of Transition Metals and Their Complexes

Palladium(II) chloride and its benzonitrile complex $(PhCN)_2PdCl_2$ (BNP) [100-103], nickel compounds $(R_3P)_2NiX_2$ [60, 87,104], and $K_4Ni_2(CN)_6$ [105], and rhenium, niobium, and tantalum pentahalides and their adducts with NaX, KX, $POCl_3$, and amines [106-108] catalyse the cyclotrimerisation of disubstituted acetylenes.

Copper(I) salts catalyse the linear polymerisation of acetylenes. When acetylene is passed into an acid solution of CuCl in the presence of NH_4Cl, vinylacetylene, divinylacetylene, and polymers are formed [109,110]. These reactions have been reviewed in detail in monographs [111-113].

6. Other Catalysts

A number of catalytic systems comprising Group VIII transition metal salts and a hydride reducing agent, for example $(Ph_3P)_2NiCl_2$–$NaBH_4$), have been suggested for acetylene cyclotrimerisation and linear polymerisation reactions [18,92,114-118]. Acetylenes cyclotrimerise in the presence of metal oxide catalysts (chromoaluminosilicate, alumina–nickel oxide–molybdenum oxide, and others [119]). Various acetylenes are converted into dimers, benzene derivatives, and higher polymers in the presence of palladium on charcoal [120].

7. Cyclotetramerisation of Acetylenes

The cyclotetramerisation of acetylenes is catalysed almost exclusively by nickel compounds. Among compounds with other metals, $Zn[Co(CO)_4]_2$ is known; acetylene gives rise to about 3% of COT together with benzene [121].

The interaction of acetylene with bivalent nickel compounds (cyanide, acetylacetonate) takes place at temperatures in the range 80–120°C and pressures between 15 and 25 atm. [8,122] The yields of COT amount to 70 to 90%, in addition up to 15% of benzene is obtained as well as polymers and a nickel-containing product resembling cuprene. Insignificant amounts of styrene, 1-phenylbuta-1,3-diene, and vinylcyclo-octatetraene as well as traces of azulene and naphthalene are produced [123-128]. Under analogous conditions, substituted acetylenes form linear polymers and benzene derivatives [129]. In the mixed cyclotetramerisation of acetylene with mono- and di-substituted acetylenes, a number of mono- and di-substituted cyclo-octatetraenes were obtained [130-134].

Acetylenic alcohols, for examples 2-methylbut-2-yn-3-ol, form the corresponding isomeric tetrasubstituted cyclo-octatetraenes in the presence of the following catalytic systems: nickel tetracarbonyl and di(cyclo-octa-diene) nickel; nickel cyanide, acetylacetonate, and ethoxide; $NiCl_2$ – $NaBH_4$. [135] When acted upon by di-(π-allyl)- nickel propargyl alcohol and 2-methylbut-3-yn-2-ol are converted into linear dimers and cyclo-octatetraene derivatives [136]. The addition of phosphine suppresses the formation of the latter. The formation of small amounts of tetrasubstituted cyclo-octatetranes was observed also when $Ni(PX_3)_4$(X = = Cl or F) were allowed to act on propiolic acid esters [137]; in this case the main reaction products are benzene derivatives.

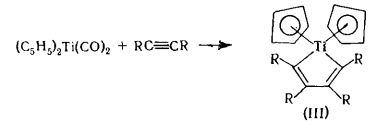
III. SYNTHESIS OF ORGANOMETALLIC COMPLEXES BY THE CYCLO-OLIGOMERISATION OF ACETYLENES

When acetylenes were allowed to react with various transition metal compounds, cyclo-oligomerisation resulted in the formation of all types of π-complexes known at present as well as compounds with an M–C σ-bond. The synthesis of organometallic compounds from acetylenes has been described in a number of reviews (see, for example, Refs. 2, 4, 5, and 138–142).

1. Reactions of Acetylenes with Metal Carbonyls

The reactions of acetylenes with the carbonyls of certain metals (iron, nickel) were investigated for the first time by Reppe [8,143], who isolated a number of organometallic compounds and organic cyclo-oligomerisation and carbonylation products.

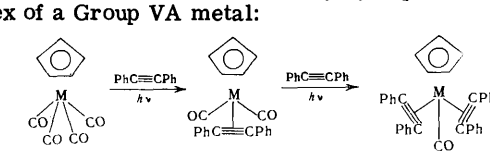
Acetylenes cyclo-oligomerise in the presence of carbonyl-cyclopentadienyl complexes of Group IVA and VA metals. The two carbonyl groups of dicarbonyldicyclopentadienyltitanium are displaced by phenylacetylene and tolane with dimerisation of acetylene and the inclusion of the metal atom in the ring [144]:



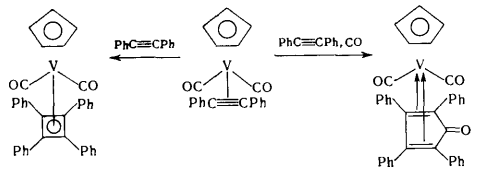
(III)

Acetylenic π-complexes and also π-complexes with other organic ligands and benzene and cyclopentadienone derivatives have been obtained from tolane and tetracarbonylcyclopentadienyl complexes of vanadium [145], niobium [146], and tantalum [147]. It was possible to trace the formation of cyclobutadiene, cyclopentadienone, and benzene structures in these reactions.

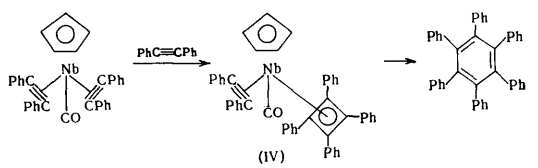
Two acetylene molecules can be introduced successfully into the molecule of the tetracarbonylcyclopentadienyl complex of a Group VA metal:



The ditolane complex of vanadium decomposes fairly readily with formation of tetracyclone. On heating, the monotolane complex combines with another tolane molecule with formation of a cyclobutadiene complex. In the presence of carbon monoxide, a tetracyclone complex is formed together with the cyclobutadiene complex[148]:



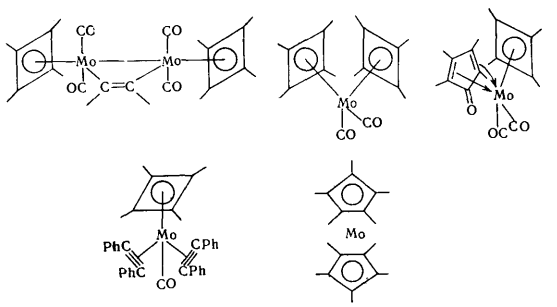
The ditolane complex of niobium combines with a third tolane molecule to form a mixed diphenylacetylene–tetraphenylcyclobutadiene complex (IV).[149] On heating, the complex decomposes with formation of hexaphenylbenzene:



The ditolane complex of tantalum undergoes similar reactions[147]. The structures of the niobium[149–153] and vanadium[154] complexes have been confirmed by X-ray diffraction.

Thus the formation of cyclic structures is preceded by the incorporation in the acetylene complex of a second and third acetylene molecule. The formation of the cyclopentadienone fragment is due to the insertion of a carbonyl group linked to the metal or of the carbon monoxide introduced into the system, which probably is also first coordinated to the metal. Hexaphenylbenzene is presumably formed as a result of an intramolecular interaction of the coordinated acetylene and cyclobutadiene. The parallel orientation of the triple bond of the acetylene ligand in relation to one of the sides of the cyclobutadiene ligand in complex (IV), which was established by X-ray diffraction analysis, suggested that the formation of hexaphenylbenzene proceeds via an intermediate complex with Dewar benzene.

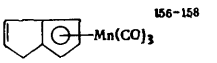
The following complexes have been obtained from tolane and molybdenum carbonyls [$Mo(CO)_6$ and (diglyme)$Mo(CO)_3$]:



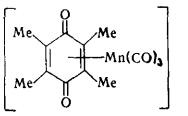
as well as tetracyclone and hexaphenylbenzene[155].

The reaction of triacetonitriletricarbonylchromium with tolane gives rise to a cyclopentadienone complex of chromium, which rapidly decomposes with formation of tetracyclone[34].

Carbonyl derivatives of manganese, $Mn_2(CO)_{10}$ or $CH_3Mn(CO)_5$, react with acetylene at an elevated pressure and temperature to form[156–158]



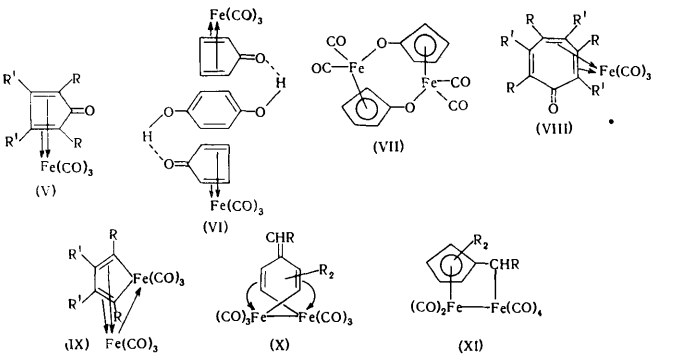
The reaction of but-2-yne with $[Mn(CO)_5]^-$ in sunlight leads to the formation of a mixture of products, one of which is duroquinone[159]. It is presumably formed from the intermediate duroquinone complex



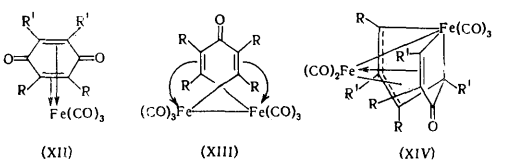
The most typical products of the reactions of acetylenes with iron carbonyls are organometallic complexes with new ligands formed as a result of the cyclo-oligomerisation of acetylenes with participation of the carbonyl group and/or the iron atom. Complexes of certain types are produced only from acetylene or its monosubstituted derivatives, while others are formed from disubstituted acetylenes.

The reaction of acetylene with $Fe(CO)_5$[8,143] or $Fe_3(CO)_{12}$ and $Fe_2(CO)_9$[138,160–164] yielded complexes (see Scheme 1) with cyclopentadienone [(V)–(VII)] and tropone (VIII) as ligands as well as metal-containing cyclic products [(IX)–XI) (R and R′ = H)].

Scheme 1



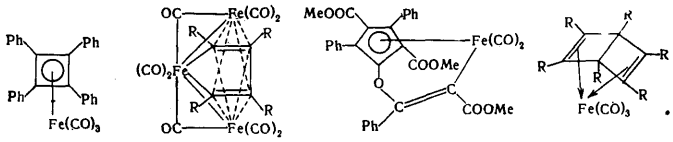
The formation of quinone complexes (XII)[24,165] and also complexes of types (XIII)[22,166] and (XIV)[138] is characteristic of dialkylacetylenes:



Cyclobutadiene (XV) and cyclopentadienone (V) complexes as well as di- and tri-nuclear metal-containing cyclic complexes (IX), (XIII), and (XVI) have been obtained from diarylacetylenes[22,23,167–173]. Complexes of types (V), (IX), (XIII), and (XVI) have been synthesised from diferrocenylacetylene[30].

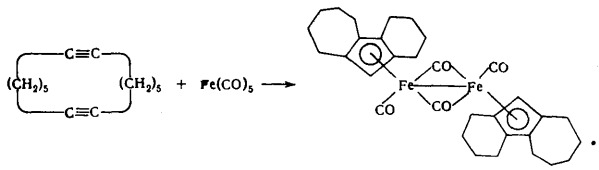
The complex (XVII) has been synthesised from ethyl phenylpropiolate and iron nonacarbonyl[174]. The structure of a complex (XVIII) with a hexasubstituted Dewar benzene as the ligand has been attributed to the product of the

reaction of the dimethyl ester of acetylenedicarboxylic acid with $Fe_2(CO)_9$ (Avram et al.[175]):

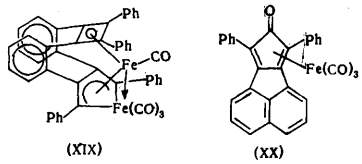


(XV) (XVI) (XVII) (XVIII)

Fluoroacetylenes form complexes analogous to (V) and (IX).[84,176-178] Only one of the two triple bonds is involved in the reaction of diphenylbutadiyne with iron carbonyls and the products are isomeric complexes of types (V), (IX), etc. with phenyl- and phenylethynyl-substituted ligands[26]. Both triple bonds of non-conjugated diacetylenes are involved in the reaction, for example[179]:



The reaction of *o*-di(phenylethynyl)benzene with $Fe(CO)_5$ and $Fe_3(CO)_{12}$ gives rise to a number of complexes[180], one of which has the structure (XIX)[181]. Acecycloneiron tricarbonyl (XX) has been obtained from 1,8-di(phenylethynyl)naphthalene and $Fe(CO)_5$ (Bossenbrock and Shechter[182]):



(XIX) (XX)

Many of the organoiron products described can be obtained by the reaction of acetylenic π-complexes of iron $RC_2RFe(CO)_4$ and $RC_2RFe_2(CO)_7$ with acetylenes[138].

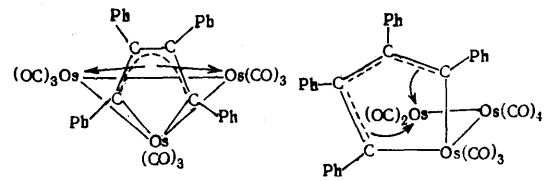
The structures of iron complexes were established on the basis of infrared and NMR spectroscopic data and chemical properties and in many cases also by specific synthesis. X-Ray diffraction structural studies have been made on the following complexes: (V),[183] (VIII),[184,185] (IX),[186] (X),[187,188] (XI),[188,189] (XIII),[190,191] (XIV),[192] (XV),[193] (XVI),[194] (XVII),[174], and (XIX).[181]

The formation of the ferracyclopentadiene structure was traced in the reaction of tolane with tri-iron dodecacarbonyl. Low yields of polynuclear complexes containing one[195] and two[22,194] acetylenic ligands were isolated from the reaction products under mild conditions. Determination of the structures of these intermediates by X-ray diffraction made it possible to deduce the mode of the gradual transformation of the acetylenic ligand into a metal-containing ring (see Scheme 2). In the first reaction stage carbonyl groups in $Fe_3(CO)_{12}$ are replaced by an acetylene molecule as in compound (XXI). Further substitution of CO results in the formation of a violet complex (XXII) which contains two independently coordinated acetylenic ligands. The violet complex then rearranges to the black isomer (XVI) containing the ferracyclopentadiene fragment. In the last stage one of the iron atoms is eliminated with formation of the stable dinuclear complex (XIX) with a metal-containing ring.

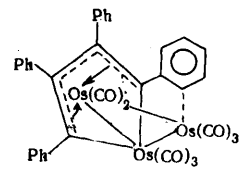
When phenylacetylene reacts with iron carbonyls, the complexes (V), (VIII), (IX), (XI), and (XIV) are formed, while the product of the reaction of *p*-bromophenylacetylene and $Fe_3(CO)_{12}$ is the complex (X).[23,138,196]

A characteristic feature of the behaviour of ruthenium and osmium dodecacarbonyls is a higher stability of the metal-containing cluster in the reaction with acetylenes compared with the corresponding iron carbonyl. After refluxing tolane with $Ru_3(CO)_{12}$ in petroleum ether, complexes analogous to the corresponding iron complexes (V), (IX), and (XVI) were isolated[197-202]. Under the reaction conditions, the dimethyl ester of acetylenedicarboxylic acid trimerises quantitatively to $C_6(COOCH_3)_6$.

The reaction of $Os_3(CO)_{12}$ with but-2-yne involves the formation of the osmium analogues (V) and (IX)[203]. Tolane gives rise to $(Ph_2C_2)_2Os_3(CO)_9$ (XXIII) which may be represented by the alternative structures (XIIIa) and (XIIIb)[204] and the complex $(Ph_2C_2)_2Os_3(CO)_8$,[204,205] which has the structure (XXIV) according to X-ray diffraction analysis[206]:



(XXIIIa) (XXIIIb)

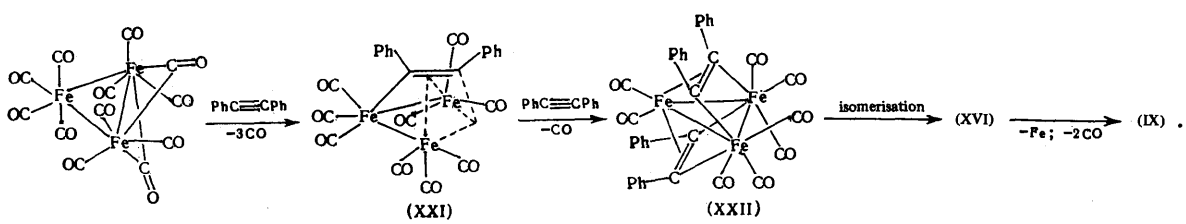


(XXXIV)

When carbon monoxide is allowed to act on (XXIII), the product is an analogue of the complex (IX).

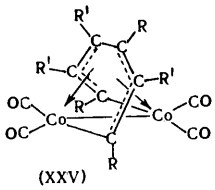
The cobalt carbonyls $Co_2(CO)_8$ and $Co_4(CO)_{12}$ react with acetylenes to form acetylenic π-complexes $RC_2R'CO_2(CO)_6$ and $RC_2R'CO_4(CO)_{10}$ and their cyclo-oligomerisation products—the complexes (XXV) and (XXVI), as well as

Scheme 2

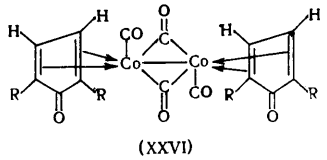


(XXI) (XXII)

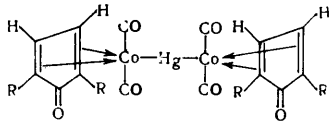
the corresponding cyclopentadienones and benzenes [25,176,207-211]. The structure (XXV) was established by X-ray diffraction [212]:



(XXV)



(XXVI)

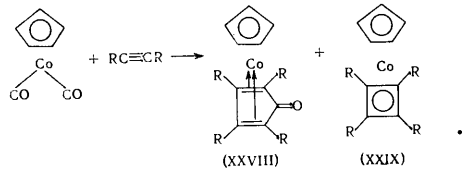


(XXVII)

Mercury tetracarbonylcobaltate reacts with disubstituted acetylenes to form acetylenic complexes, while the reaction involving monosubstituted acetylenes proceeds without the elimination of mercury and with formation of the cyclopentadienone complexes (XXVII) [25,138,213]. The complexes $R_2C_4H_2Co_4Hg_2(CO)_{12}$, which probably contain a cyclobutadiene ligand, have been obtained from certain monosubstituted acetylenes.

When acetylenehexacarbonyldicobalt reacts with acetylenes different from that coordinated to the metal atom, isomers of substituted benzenes and cyclopentadienones, with partial incorporation of the initial acetylene bound in the complex, are produced [25,214-217].

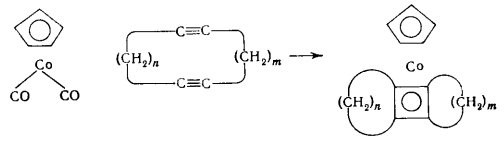
Disubstituted acetylenes dimerise in the presence of π-cyclopentadienylcobalt dicarbonyl with formation of cyclopentadienone (XXVIII) and cyclobutadiene (XXIX) complexes as well as hexa-substituted benzenes and tetrasubstituted cyclopentadienones [218,219]:



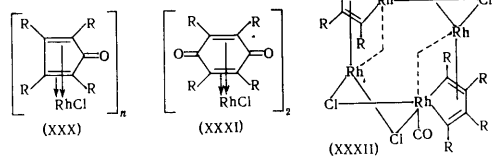
(XXVIII) (XXIX)

X-Ray diffraction structural analysis of compound (XXVIII) has been carried out [220,221].

Depending on R, the reaction involves the formation of complexes (XXVIII) [84,159,222,223] or (XXIX) [224] only. Macrocyclic alkadiynes undergo transannular cyclisation [225,226]:

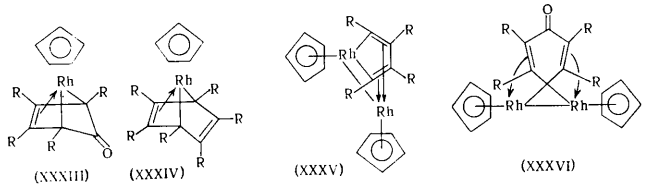


The reaction of disubstituted acetylenes with chlorodicarbonylrhodium leads to the formation, depending on the acetylene, of cyclopentadienones and quinones and their π-complexes (XXX) and (XXXI), as well as complexes with a metal-containing cyclic fragment (XXXII) [33,222,227-229] [the structure (XXXII) was established by X-ray diffraction [230]] and hexasubstituted benzenes:



(XXX) (XXXI) (XXXII)

The reaction of π-cyclopentadienylrhodium carbonyl with HFB leads to the complexes (XXXIII) and (XXXIV) [222] as well as metal-containing cyclic complexes (XXXV) and (XXXVI) [231]. The structure (XXXIV) was established by X-ray diffraction [232]:



(XXXIII) (XXXIV) (XXXV) (XXXVI)

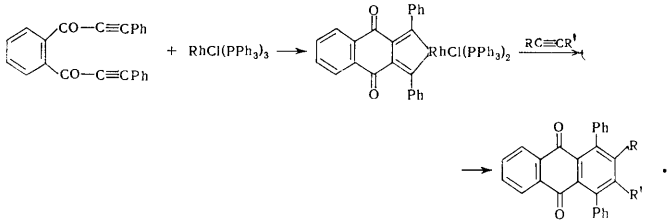
The complexes (XXXIII), (XXXIV), and (XXXVI) were obtained by treating the acetylene complex $[C_5H_5Rh(CO)]_2.(CF_3C_2CF_3)$ with HFB.

Di(pentafluorophenyl)acetylene yielded the pentafluorophenyl analogues of compounds (XXXIII) and (XXXV) and also hexa(pentafluorophenyl)benzene [223,233,234]. The complexes (XXXIV) have also been obtained from $(CH_3)_5C_5M(OAc)_2H_2O$ (M = Rh or Ir) and the dimethyl ester of acetylenedicarboxylic acid in the presence of hydrogen [235].

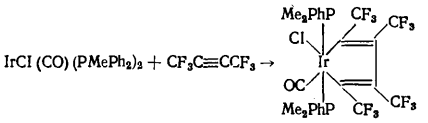
The reaction of $Ni(CO)_4$ with tolane [19] or cyclo-octyne [129] yields the corresponding cyclopentadienones and their nickel complexes.

2. Reactions of Acetylenes with Phosphine, Arsine, and Stibine Metal Complexes

As for the carbonyls, the substitution of phosphine and other similar ligands in the reaction with acetylene is frequently accompanied by the formation of cyclo-oligomerisation products. Rhodium and iridium form metal-containing cyclic products under these conditions. For example, the reactions of $RhCl(MPh_3)_3$ (M = Sb or As) with HFB [236-238] and of $RhCl(PPh_3)_3$ with *o*-di(arylpropionyl)benzene and 2,3-di(phenylpropionyl)naphthalene [239-243] yielded rhodiacyclopentadiene complexes, which can subsequently react with acetylenes whereby they are converted into benzene derivatives:



Similar reactions have been achieved for iridium complexes[244]:



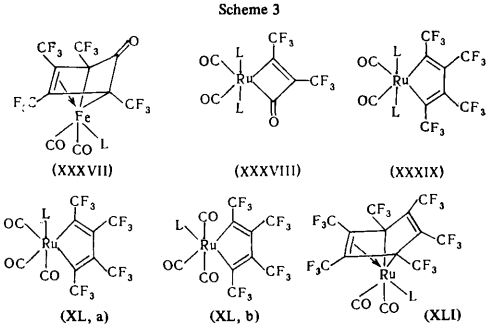
The reactions proceed via intermediate acetylene π-complexes, which were isolated when the reaction was carried out under milder conditions.

The cyclotrimerisation of HFB in the presence of tetra-(dimethylphenylarsine)nickel with formation of $(PhMe_2As)_2NiC_6(CF_3)_6$ has been described[245].

3. Reactions of Acetylenes with Carbonylphosphine and Phosphitocarbonyl Complexes of Group (VIII) Metals

The photochemical reaction of HFB with complexes of metals in the iron triad of the type *trans*-$M(CO)_3L_2$, where L = tertiary phosphine or phosphite, has been investigated[246]. The nature of the reaction product depends primarily on the metal and to a lesser extent on the reaction conditions. The reaction of iron with an excess of HFB yielded the complexes (XXXVII). The ruthenium complexes react differently depending on the reaction conditions. The complex (XXXVIII) was obtained from equimolar amounts of $Ru(CO)_3[P(OMe)_3]_2$ and HFB. The complexes (XXXIX) and (XL, a and b) are formed in the presence of HFB. When the reaction is carried out with more prolonged irradiation, the product is the complex (XLI) (see Scheme 3).

Scheme 3



The osmium complexes do not catalyse the cyclo-oligomerisation of HFB.

4. The Reactions of Acetylenes with Certain Transition Metal π-Complexes

At the instant of its formation dicyclopentadienyltitanium reacts with tolane[247] or propyne[248], forming compound (III). Together with a small amount of hexaphenylbenzene, the same complex is formed on thermal decomposition of di-(π-cyclopentadienyl)-σ-diphenyltitanium in the presence of tolane[249].

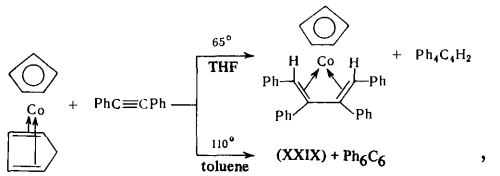
The rhodium complex of norbornadiene (NBD) reacts with an excess of but-2-yne to form an arene complex[250]:

$$[Rh(NBD)]^+ + MeC{\equiv}CMe \rightarrow [Rh(C_6Me_6)(NBD)]^+ .$$

In many instances acetylene substitutes an organic π-ligand, two or three acetylene molecules forming a new ligand.

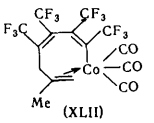
Thus the complexes (XXIX) have been obtained from cobaltocene and disubstituted acetylenes[84,251] including macrocyclic alkadiynes[225]. The complexes (XXIX) are formed also from cyclopentadienylcyclo-octatetraenecobalt[252,253] or cyclopentadienylcyclo-octa-1,5-dienecobalt[251,252].

Tolane reacts with π-cyclopentadienyl-π-cyclopentadienecobalt via the mechanism[253]

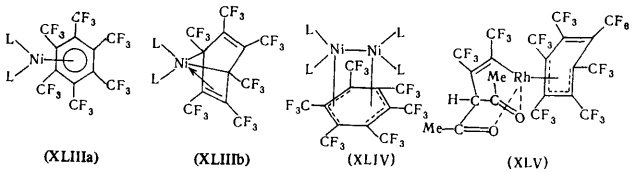


while its reaction with cyclo-octatraeneiron tricarbonyl results in the formation of the complexes (IX) and (XV)[253-255].

Together with polymerisation the reaction of π-2-methylallylcobalt tricarbonyl with HFB leads to the formation of the compound (XLII) produced by the insertion of two acetylene molecules in the cobalt-allyl bond[256]:

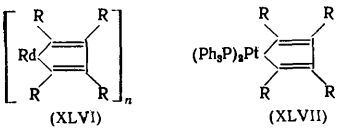


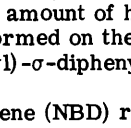
Di(cyclo-octa-1,5-diene)nickel reacts with HFB to form a mononuclear complex (XLIIIa) or (XLIIIb) and a dinuclear complex (XLIV) (L_2 = 1,5-C_8H_{12})[245]:



The displacement of cyclo-octa-1,5-diene by hexafluorobut-2-yne from acetylacetonatocyclo-octadienerhodium has been described[257]. According to X-ray diffraction data, the product has the structure (XLV)[258].

The action of certain acetylenes on dibenzylideneacetone complexes M(DBA)$_2$ (M = Pd or Pt) and Pt(DBA)$_3$ has been investigated[259,260]†. The product of the reaction of the palladium complex with the dimethyl ester of acetylenedicarboxylic acid is palladiacyclopentadiene (XLVI), which gives rise to hexasubstituted benzenes on heating with acetylenes R'S≡CR'. The reaction is catalytic for R' = COOMe:



The structure (XLVI) was established on the basis of the chemical behaviour and also spectroscopic data. The association of individual molecules is due to the involvement of the ester group in coordination to the metal of the type  Pd. Platinum complexes react more slowly with the dimethyl ester of acetylenedicarboxylic acid than the palladium analogue. The metal-containing

†In complexes of this type the metal–ligand bond is formed by the π-electron system of the carbonyl group.

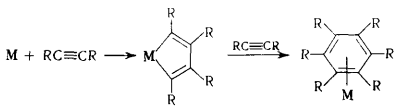
cyclic product was isolated in the form of a triphenylphosphine derivative (XLVII). Hexamethyl mellitate was also isolated from the reaction products, which is evidence of the greater ease of conversion of the metallocyclopentadiene into benzene in the case of platinum.

5. Cyclo-oligomerisation Reactions of Acetylenes Involving σ-Derivatives of Transition Metals

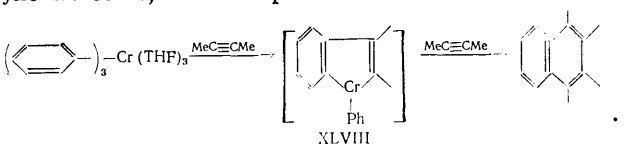
When triphenylchromium tristetrahydrofuranate reacts with but-2-yne, a number of organic and organochromium products are formed[261-264]. The reaction mode depends on the proportions of the reactants. Thus when less than 4 moles of the butyne per mole of Ph_3Cr are employed, the products are 1,2,3,4-tetramethylnaphthalene and its π-complex. An excess of the acetylene promotes the formation of hexamethylbenzene. When the reactant ratio is $Ph_3Cr : C_4H_6 = 1 : 6$, 40% of tetramethylnaphthalene 55% of hexamethylbenzene, and small amounts of the corresponding π-complexes are produced.

The authors believe that the reaction mechanism consists in the stepwise substitution of THF molecules in $Ph_3Cr(THF)_3$ by acetylene. The coordinated acetylene molecules cyclise with formation of aromatic systems and the corresponding π-complexes. The effect of the reactant ratio on the composition of the reaction products is evidence that the displacement of THF by acetylene takes place in steps. The phenyl group linked by a σ bond to chromium can also participate in the intramolecular reaction, which results in the formation of tetramethylnaphthalene.

The possible formation of a five-membered metal-containing ring, which then combines with a third acetylene molecule and is converted into a π-bonded benzene ring, has been suggested[265]:



In order to account for the formation of tetraphenylnaphthalene, a mechanism involving stages in which the butyne is inserted in the phenyl–chromium bond with formation of styrylchromium, its cyclisation to "benzochromole" (XLVIII), and the reaction of benzochromol with a second butyne molecule, has been put forward[266]:



XLVIII

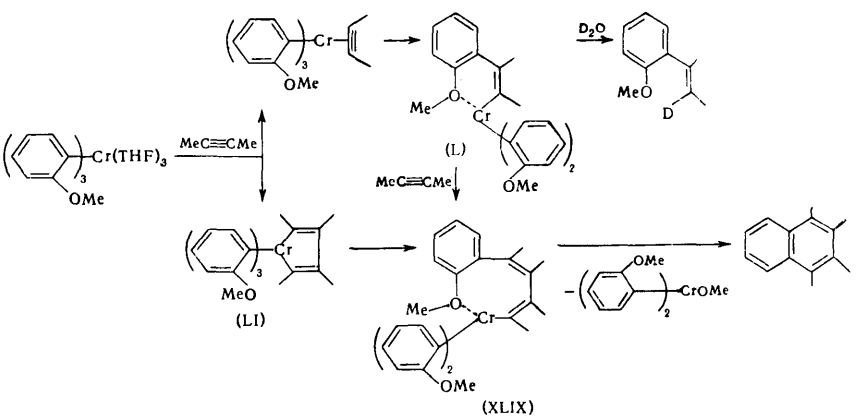
However, objections have been raised to the formation of (XLVIII) as a precursor of tetramethylnaphthalene[267]. When but-2-yne reacts with tri-(2-methoxyphenyl)chromium, 1,2,3,4-tetramethylnaphthalene is formed together with *cis*-2-(2-methoxyphenyl)but-2-yne and 2,3-di-(2-methoxyphenyl)but-2-ene. Since the elimination of the methoxy-group from the *o*-anisyl substituent is observed only in the formation of tetramethylnaphthalene, the authors believe that the *o*-anisylbutadienechromium compound (XLIX) is more likely to be its precursor. The chromium complex can be formed in its turn as a result of the reaction of the σ-vinyl derivative of chromium (L) with a second but-2-yne molecule or as a result of the transfer of the aryl group within the metal-containing ring (LI) formed from two acetylene molecules (see Scheme 4).

Tolane does not form arene complexes with triphenylchromium, the only products being hexaphenylbenzene, tetraphenylnaphthalene, 9,10-diphenylphenanthrene, terphenyl, and tetraphenylethylene[262,268]. Acetylene and monosubstituted acetylenes polymerise. *trans*-Isomers of 1,6-diphenylbuta-1,3-diene and also biphenyl and the conjugated *trans*-polyene $Ph-(-CH=CH-)_n-Ph$ were obtained from acetylene at −70°C.[269] HFB forms a linear polymer[84].

Various aryl derivatives of chromium can be used as cyclising agents[262,270,271]. If the *ortho*-positions are blocked, for example in trimesitylchromium, the only reaction product is a hexa-substituted benzene.

Like the phenyl group, an alkyl group linked by a σ bond to chromium can also participate in the formation of a new ring[263,265,272]. Thus the reaction of tolane with triethylchromium tetrahydrofuranate leads to the formation of 1,2,3,4-tetraphenylbenzene in addition to hexaphenylbenzene, the role of the chromium atom consisting not only in the elimination of the hydrogen atom from the

Scheme 4

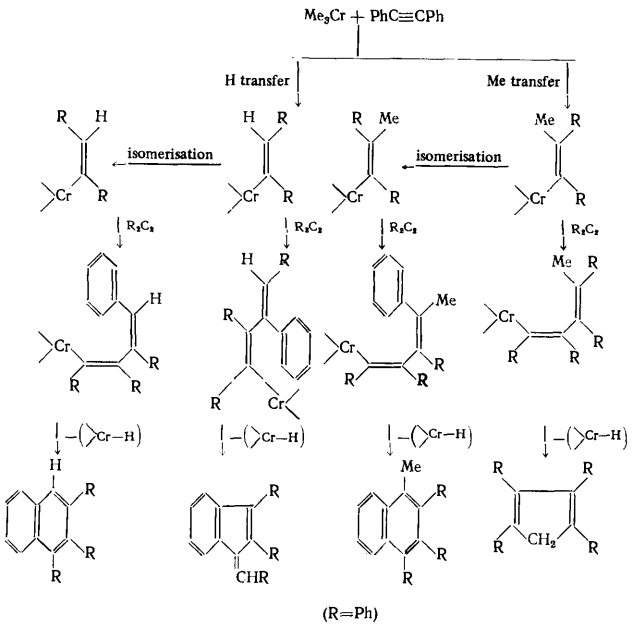


(XLIX)

CH_3 group of the ethyl substituent but also in the dehydrogenation of the resulting dihydrotetraphenylbenzene to an aromatic product. Trimethylchromium gives rise to phenyl derivatives of cyclopentadiene, benzene, and naphthalene [265 269 272-275].

The formation of certain reaction products may be interpreted in terms of metal hydride elimination from isomeric σ-butadienyl derivatives of chromium in accordance with Scheme 5 (Sneeden and Zeiss [276]):

Scheme 5



Tri-n-butylchromium forms with oct-4-yne and but-2-yne a complex mixture of products, from which the corresponding hexa-alkylbenzenes were isolated [270]. Trivinyl chromium [277] and triallylchromium [278] react with but-2-yne to give, together with hexamethylbenzene, condensation products involving σ-groups. Tri-β-styrylchromium forms only hexasubstituted benzenes [279].

The cyclisation of butyne to di(hexamethylbenzene)-chromium on reaction with a mixture of chromyl chloride and triethylaluminium has been described [280, 281]. The methyl derivative of chromium Li_3CrMe_6 does not react with phenylacetylene [273]. The cyclotrimerisation of disubstituted acetylenes in the presence of σ-derivatives of bivalent chromium has been described [273,278,282].

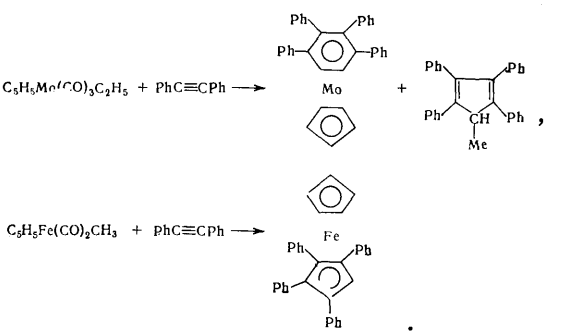
σ-Derivatives of bivalent manganese and cobalt (diphenylmanganese and dimesitylcobalt) cyclotrimerise but-2-yne with formation of hexamethylbenzene and arene π-complexes [283,284]. Naphthalene derivatives are not formed in this case. The π-complex obtained from Ph_2Mn and but-2-yne has the structure of benzene(hexamethylbenzene)manganese(I) [285]. Hexamethylbenzene is formed on cyclotrimerisation of butyne, while the second σ-linked ligand (benzene) is formed from the σ-phenyl group as a result of a σ–π rearrangement.

As a rule acetylene cyclisation reactions in the presence of the organometallic compounds considered are stoichiometric. Dimesitylcobalt, which acts as a catalyst in the reaction with butyne, is an exception. A constant amount (up to 20%) of the corresponding π-complex is always formed in this process. Dimesitylcobalt reacts also with acetylene: the stoichiometric trimerisation to benzene is accompanied by a catalytic reaction involving the formation of a solid polymer. The reaction also yields a certain amount of dibenzenecobalt [286].

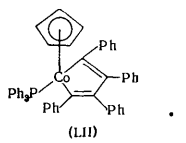
The reaction of tolane with dimesitylnickel(II) results in the formation of hexaphenylbenzene and the complex $[(Ph_2C_2)_4Ni]_n$. [263,282,287] Diethylnickel also induces the cyclisation of tolane to hexaphenylbenzene and provides the ethyl group for mixed cyclisation. However, nickel, being a weaker hydrogen acceptor than chromium, is incapable of abstracting hydrogen from the dihydrobenzene compound (1,2,3,4-tetraphenylcyclohexa-1,3-diene), which is in fact the final product of this reaction [272]. HFB polymerises under the influence of diethylnickel [84] and tolane cyclises also in the presence of dimesityliron [263,282].

The methyl derivatives of many metals $M(Me)_n$ (M = Ti, Zr, V, Nb, Mo, Mn, Fe, Ru, Co, Rh, or Pd) react with tolane to form hexaphenylbenzene, tetraphenylcyclopentadiene, and 1,2,3-triphenylnaphthalene [265,273]. The reaction of tolane with $(Ph_3P)_3RhMe$ yielded the following products: triphenylnaphthalene, tetraphenylbutadiene and a cyclisation product incorporating the σ-methyl group–tetraphenylcyclopentadiene [288].

On reaction with σ-alkyl-π-cyclopentadienyl complexes of molybdenum and iron carbonyls, tolane cyclo-oligomerises with insertion of the alkyl group σ-linked to the metal [254,289]:



The reaction of tolane with π-cyclopentadienyltriphenylphosphinecobalt(III) iodide in the presence of isopropylmagnesium bromide leads to the formation of the metal-containing cyclic complex (LII) [290,291]:



(LII)

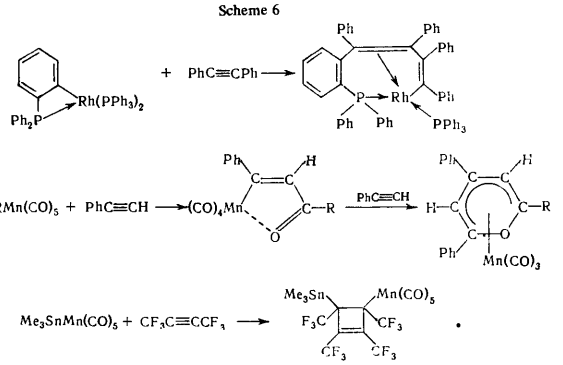
Acetylene and phenylacetylene undergo linear oligomerisation in the presence of σ-methyltris(triphenylphosphine)cobalt(I) [292]. For example:

$$(Ph_3P)_3CoMe + HC{\equiv}CH \rightarrow (Ph_3P)_2Co(CH{=}CH)_nMe .$$

The insertion of two molecules of acetylene derivatives in the σ-bonds Rh–C (Keim [293]) (the structure of the product was confirmed by X-ray diffraction [294]), Mn–C (Booth and

Hargreaves[295]), and Mn–Sn (Bichler et al.[296]) has been described (see Scheme 6).

Scheme 6



The reaction of but-2-yne with a σ-trifluoromethyl derivative of platinum yielded a cyclobutadiene complex[297].

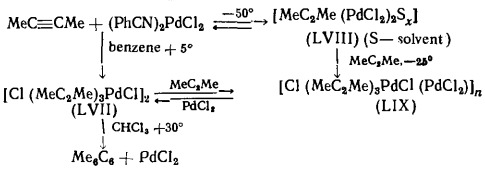
6. Reactions of Acetylenes with Transition Metal Salts

The reaction of acetylenes with bivalent platinum compounds has been investigated in greatest detail. The reaction proceeds in different ways depending on the nature of the substituents, conditions, etc. On treatment with palladium(II) chloride or its benzonitrile complex $(PhCN)_2PdCl_2$ (BNP) in benzene, diarylacetylenes yield π-cyclobutadiene complexes (LIII) together with hexasubstituted benzenes[100–103]. When the reaction is carried out in alcohol[100,103,298–303], the products are the *endo*-ethoxycyclobutenyl complexes (LIV)[103] [the structure of (LIV) has been established by X-ray diffraction[304]], which are converted under the influence of hydrogen halides into cyclobutadiene complexes (LV).

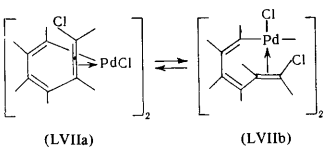
The cyclobutadiene complexes are not intermediates in the synthesis of benzenes[100,260,305]. For example, the reaction of (LIII) with tributylphosphine in the presence of tolane leads to the formation of the corresponding cyclooctatetraene in 92% yield; not even traces of hexaphenylbenzene are formed in this reaction.

The complexes (LV) were obtained from t-butylphenylacetylene and BNP; the formation of cyclotrimerisation products was not observed[173,306]. The structure of the cyclobutadiene complex (LVI) has also been attributed to the complex obtained from *o*-di(phenylethynyl)benzene and $PdCl_2$:[307,308]

Acetylenes containing less bulky substituents behave differently from those discussed above. But-2-yne reacts with $PdCl_2$ in benzene to form the complex (LVII)[260,309,310]. When the reaction was carried out in chloroform, two intermediates—the acetylenic π-complex (LVIII) and the complex (LIX)—differing from (LVII) by including $PdCl_2$ in their composition, were detected:

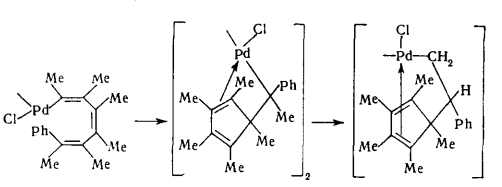


On heating, (LVII) decomposes with formation of hexamethylbenzene; treatment with triphenylphosphine, triphenylarsine, or triphenylstibine in the cold results in the formation of 5-vinylpentamethylcyclopentadiene with a small amounts of hexamethylbenzene. The structure of the product produced by the insertion of three acetylene molecules in the Pd–Cl bond was attributed to the complex on the basis of physicochemical data and the nature of its chemical reactions[260,310,311]. In this complex the ligand can exist as two conformers (LVIIa) and (LVIIb):



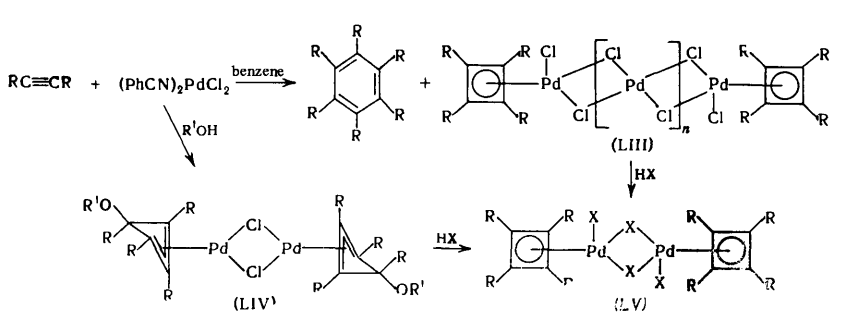
(LVIIa) (LVIIb)

The reaction of but-2-yne with "phenylpalladium chloride" yields a complex having the structure (LX), probably as a result of the cyclisation of (LXI) with a subsequent 1,2-hydride shift[312]:

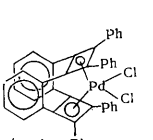


(LXI) (LX)

Together with the expected 1,2,4- and 1,3,5-isomers of trimethyltriphenylbenzene (yields 58 and 39%), the reaction of methylphenylacetylene with BNP in benzene gives rise to a small amount (3%) of the 1,2,3-isomer[102,260,310].



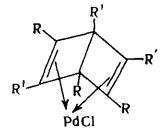
(LIII) (LIV) (LV)



(LVI)

The formation from methyl- and ethyl-phenylacetylenes in the presence of $PdCl_2$, together with hexasubstituted benzenes, of complexes containing acetylene tetramers and having the compositions $(PhC_2R)_4PdCl$ and $(PhC_2R)_4Pd_2Cl_2$ [299,313] has been reported.

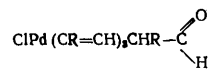
The structure of a complex of Dewar benzene (LXII, R = R' = COOMe) has been attributed to the product of the reaction of the dimethyl ester of acetylenedicarboxylic BNP:[175]



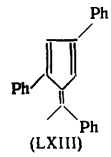
(LXII)

Acetylene and its monosubstituted derivatives undergo linear oligomerisation under the influence of palladium salts. Thus treatment of acetylene with $PdCl_2$ results in the formation of *trans*-alka-1,3,5,7,...polyene as the main product[314]. Stable σ-organometallic polyene products with the general formula $PdCl(CR{=}CR')_nX$ were isolated in the reactions of acetylene, vinylacetylene, and phenylacetylene[315-321]. Acetylene compounds undergo similar reactions in rhodium(III) chloride solutions[321].

The reaction of dialkylethynylmethanols with $PdCl_2$ in aqueous solutions has been investigated[322-325]. The following structure has been proposed for the complexes on the basis of infrared spectra[326-329]:

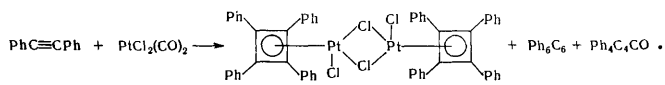


The reaction of phenylacetylene with BNP yielded fulvene (LXIII) and tetramers of unknown structure, tentatively dihydropentalenes[260]. The interaction of BNP with other monosubstituted acetylenes has also been described[310,330-332].

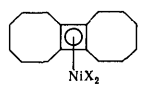


(LXIII)

In contrast to palladium salts, derivatives of bivalent platinum form mainly acetylenic π-complexes with acetylene. The cyclo-oligomerisation reaction has been described in only one instance[333]:



Nickel salts react with cyclo-octyne with formation of a complex to which the cyclobutadiene structure (LXIV) was attributed[129]. Another reaction product is the corresponding benzene derivative:

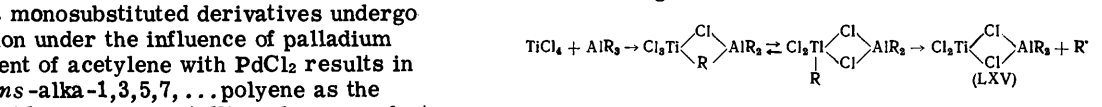


(LXIV)

The possible formation of the cyclobutadienegold complex[334] $[(C_4H_4)AuCl_2]^+$ when acetylene is passed into $AuCl_3$ solutions has been suggested[335].

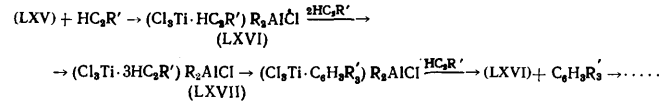
IV. THE MECHANISMS OF ACETYLENE CYCLO-OLIGOMERISATION AND POLYMERISATION REACTIONS IN THE PRESENCE OF TRANSITION METAL COMPOUNDS

The problem of the mechanisms of acetylene cyclo-oligomerisation and polymerisation reactions is now the subject of persistent attention of many chemists. Kinetic investigations involve considerable difficulties in view of the high rate and high heats of these reactions[17]. Such studies have been made on the cyclotrimerisation of hex-1-yne in the presence of the $i\text{-}Bu_3Al\text{-}VOCl_3$ catalytic system, which proceeds at a comparatively low rate. The reaction is described by a second-order equation with respect to the alkyne[57]. It has been shown that a tervalent form of titanium is catalytically active in the presence of $i\text{-}Bu_3Al\text{-}TiCl_4$.[68] The catalytic complex (LXV) is formed via the following mechanism:



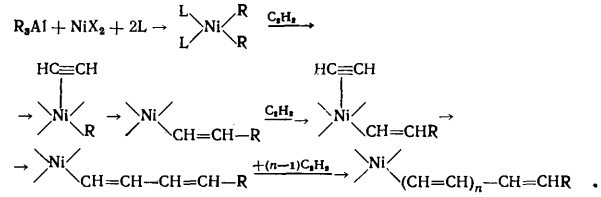
(LXV)

An acetylene molecule reacts with the titanium atom entering into the composition of the catalytic complex with formation of the monoacetylene complex (LXVI), which subsequently combines with two acetylene molecules in the rate-determining stage. In the octahedral complex (LXVII) three acetylene molecules cyclise with formation of a benzene derivative, which is displaced from the complex by a new acetylene molecule, etc.:



It has been shown that the polymerisation of phenylacetylene in the presence of the $Et_3Al\text{-}TiCl_3$ catalytic system is a first-order reaction with respect to the monomer[336]. The authors suggest that the mechanism of the formation of cyclic products is not determined by the simultaneous reaction of three monomeric units in a single step, the rate-determining step involving the abstraction of the linear trimer from the catalytic centre with ring closure.

The kinetics of the polymerisation of acetylene in the presence of $i\text{-}Bu_3Al\text{-}Ni(acac)_2$ have been investigated[337]. The initiation reaction is of first order with respect to the monomer and the order of the propagation reaction is close to zero. The following reaction mechanism including the stage involving the formation of an acetylene π-complex with subsequent insertion of the coordinated acetylene in the Ni–C σ-bond has been proposed:



It proved possible to isolate intermediate complexes incorporating the monomer and having the compositions $i\text{-}Bu_2Ni.C_2H_2.Bipy$ and $i\text{-}Bu_2Ni.C_2H_2.(PPh_3)_2$ in the reaction of acetylene with $i\text{-}Bu_3Al\text{-}Ni(acac)_2$ in heptane in the presence of stabilising ligands (triphenylphosphine or bipyridyl). The complexes polymerise acetylene at −10°C.

The study of the kinetics of the dimerisation of acetylene to vinylacetylene in the presence of copper(I) complexes led to the following mechanism for this reaction involving stages with formation of an acetylene π-complex and its conversion into a σ-acetylide with subsequent insertion of a second acetylene molecule in the Cu–C σ-bond [338–340]:

$$C_2H_2 + [Cu_nCl_{n+1}]^- \rightleftarrows \underset{\pi\text{-complex}}{[C_2H_2Cu_nCl_{n+1}]^-} \xrightleftharpoons[-H_3O^+,\,-Cl^-]{+H_2O} \rightleftarrows \underset{\sigma\text{-acetylide}}{[Cu_nCl_nC{\equiv}CH]^-} \xrightleftharpoons{C_2H_2} \underset{\pi\text{-complex}}{[Cu_nCl_nC{\equiv}CH\,(C_2H_2)]^-} \xrightarrow{\text{slow}}$$

$$\rightarrow [Cu_nCl_nC_4H_3]^- \xrightarrow[\text{fast}]{+H_3O^+ + Cl^-} [Cu_nCl_{n+1}]^- + C_4H_4 \ .$$

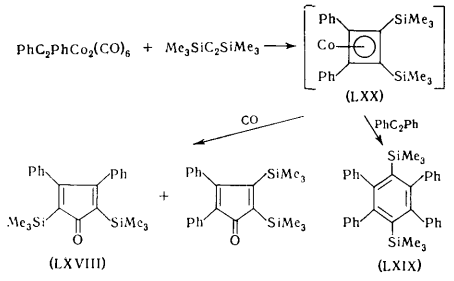
A number of studies have been made on the effect of the polarity of the solvent and various additives on the cyclo-oligomerisation reaction. It was found that the cyclotrimerisation of acetylenes catalysed by metal carbonyls and catalysts of the Ziegler–Natta type is insensitive to a change in solvent polarity. This enabled a number of workers [20,44,83] to put forward the hypothesis that a ionic mechanism of these reactions is unlikely. However, the hypothesis of an ionic mechanism has received increasing recognition recently. These ideas will be considered below.

In most studies ideas concerning the mechanism of the interaction of acetylenes with transition metal compounds were based on the nature of the final reaction products and the structure of intermediates. It is now generally accepted that the first stage of the reaction is a π-complex type of coordination of the acetylene to the metal. The formation of acetylene π-complexes under certain conditions and the possibility of obtaining from them acetylene cyclo-oligomerisation products were frequently pointed out above.

There are two main points of view on the problem of the ways in which coordinated acetylene is subsequently transformed into the final reaction product. The first is that the coordinated acetylene molecules react with one another, the process being accompanied by the formation of new C–C bonds and carbon ring closure. A six- or eight-membered ring can be formed either by the simultaneous formation of three (or four) C–C bonds or via the intermediate formation of the cyclobutadiene ring. The second view presupposes the conversion of the acetylene π-complex into a σ-compound (a metal-containing ring, a σ-ethynyl or a σ-vinyl derivative) with subsequent insertion of acetylene in the metal–carbon bond.

The hypothesis of the intermediate formation of cyclobutadiene complexes has been frequently put forward by a number of workers [142,334,341]. Evidence in support of this hypothesis comes from the conversion of an acetylene complex of niobium into a diacetylene complex and further into a mixed cyclobutadiene–acetylene complex, which splits off hexaphenylbenzene on heating [146,149] (see above).

Heating of diphenylacetylenedicobalt hexacarbonyl with di(trimethylsilyl)acetylene unexpectedly results in the formation, together with other products, of 3,4-diphenyl-2,5-di(trimethylsilyl)cyclopentadienone (LXVIII) and 2,3,5,6-tetraphenyl-1,4-di(trimethylsilyl)benzene (LXIX) [25,138,168]. According to the authors, the most probable mechanism of the synthesis of these products consists in the intermediate formation of the cyclobutadiene complex (LXX), which can then undergo ring expansion in any conceivable manner:



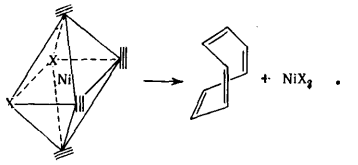
The problem of the possible intermediate formation of cyclobutadiene complexes on cyclotrimerisation of acetylenes was studied in relation to 1,1,1-trideuteriobut-2-yne [266,342,343]. If the reaction proceeds via a cyclobutadiene complex, all three possible isomeric benzenes should presumably be formed. The 1,2,3-$(CD_3)_3$-4,5,6-Me_3C_6 isomer is absent from the products of the reaction involving triphenylchromium, dimesitylcobalt, dicobalt octacarbonyl, di(acrylonitrile)nickel, and i-Bu_3Al–$TiCl_4$. In the presence of $AlCl_3$, the 1,2,3-isomer is formed quantitatively (on the assumption of the intermediate formation of a cyclobutadiene structure‡), while on treatment with BNP its yield is intermediate between the two extreme values. As already mentioned, similar results were obtained in the cyclisation of phenylmethylacetylene in the presence of BNP [102,310], which is consistent with the cyclobutadiene hypothesis. However, it has been shown [100,305] that cyclobutadiene complexes of palladium are not intermediates in the synthesis of benzenes. It has been suggested that dynamic processes involving the intermediate complex (LVII), accompanied by the migration of the substituents, are responsible for the "unexpected isomers" [260].

The hypothesis of the simultaneous coordination of several acetylene molecules around the metal atom was put forward for the first time by Reppe [122] and was developed further in subsequent investigations [80,83,345–348] (see also Refs. 349 and 350). The acetylene cyclo-oligomerisation reaction is a many-centre process with simultaneous formation of C–C bonds. These ideas have been developed in detail in relation to the cyclotetramerisation of acetylene under the influence of nickel compounds.

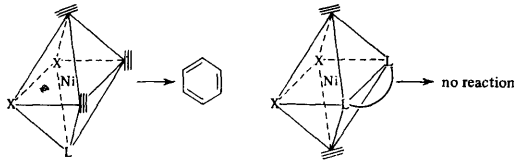
Paramagnetic (at least in solution) nickel(II) complexes with low-field ligands–di(salicylaldehydo), di(acetylacetonato)-, and di-(*N*-alkylsalicylaldimino)-nickel and nickel cyanide are catalytically active in the synthesis of COT. These complexes have an octahedral structure or can readily acquire it. Planar nickel(II) complexes with high-field ligands—phthalocyanine or dimethylglyoxime complexes—are inactive. The yield of COT is proportional to the rate of ligand exchange in the complex. Under the influence of acetylene, the coordinate bonds

‡But-2-yne reacts with $AlCl_3$ under milder conditions with formation of Dewar hexamethylbenzene [344]. This result is also consistent with the hypothesis of the intermediate formation of a cyclobutadiene structure with subsequent addition of an acetylene molecule as in the Diels–Alder reaction.

are ruptured and in the resulting intermediate complexes the four acetylene molecules are arranged favourably for closure of the eight-membered ring:



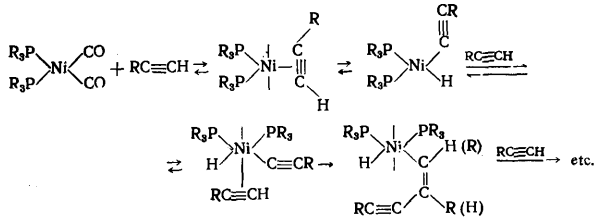
On addition of triphenylphosphine, which blocks one coordination site in the complex, COT is not formed and the reaction product is exclusively benzene. The addition of substances capable of blocking two coordination sites at once [$\alpha\alpha'$-bipyridyl, *o*-phenanthroline, and 1,2-bis-(diphenylphosphino)ethane] fully deactivates the catalyst in the cyclo-oligomerisation reaction:



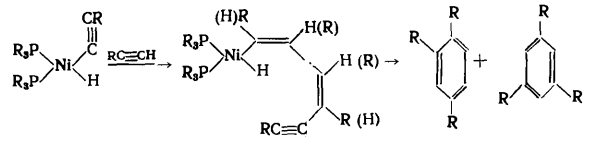
The formation of COT in the presence of $Zn[Co(CO)_4]_2$ can be accounted for by dinuclear catalysis. Two acetylene molecules are coordinated around each of the two cobalt atoms with simultaneous formation of new C–C bonds [121,351]. This hypothesis is open to many objections. In particular it cannot explain the preferential formation of 1,2,4-isomeric substituted benzenes in the cyclotrimerisation of asymmetric acetylenes.

The essential feature of the hypotheses concerning the mechanism of the cyclisation and polymerisation of acetylenes discussed reduces to the postulate of the intermediate formation from the acetylenic π-complex of an organometallic compound with metal–carbon σ-bonds; chain growth takes place as a result of the insertion of π-coordinated acetylene in the M–C bond.

The mechanism proposed [17] explains satisfactorily the formation of linear polymers in the reactions of terminal acetylenes with metal carbonyls. On the basis of the finding that deuteriated hept-1-yne reacts much more slowly with dicarbonyldi(triphenylphosphine)nickel than its non-deuteriated analogue, the authors proposed a mechanism based on the oxidative addition of acetylene to the metal with formation of an acetylide–hydride complex. The insertion of acetylene in the M–C bond leads to the formation of a σ-vinyl derivative:

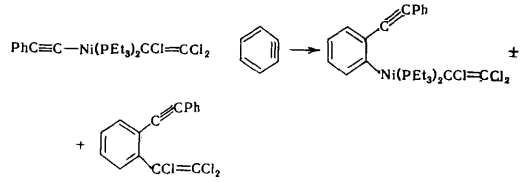


In the presence of a favourable conformation, ring closure may take place with formation of benzene derivatives:

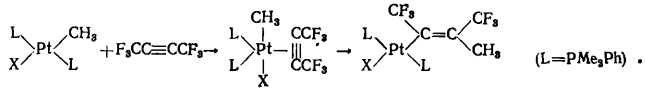


A similar mechanism has been proposed for the polymerisation of alk-1-ynes in the presence of rhodium(I) and iridium(I). [90,91,94]

The occurrence of certain reaction stages has been confirmed experimentally. Thus the formation of hydride-acetylide compounds is observed when certain terminal acetylenes add to the coordination-unsaturated iridium complex $IrCl(CO)(PPh_3)_2$. [352] The insertion of acetylene in the metal-alkynyl group has been described for the interaction of nickel acetylide with dehydrobenzene [353]:



In platinum complexes coordinated acetylene has been inserted in the Pt–CH_3 bond [354–356]:

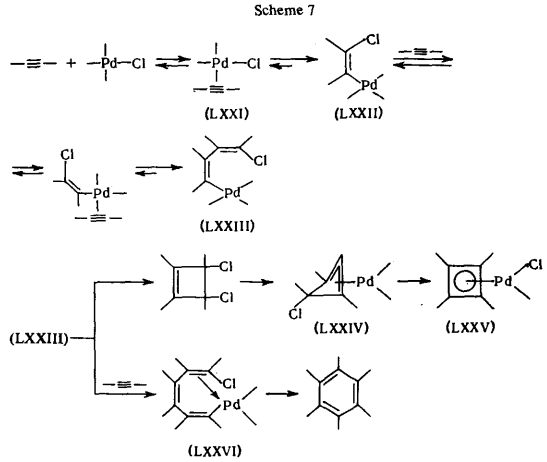


The formation of iridium complexes containing both a σ-vinyl group and a π-acetylenic ligand, $(Ph_3P)_2Ir(CR=CHR)(RC_2R)(CO)$ (R = CF_3 or $COOCH_3$), can also serve as evidence in support of the mechanism proposed [357].

Finally linear polymerisation of phenylacetylene with participation of nickel and platinum acetylide complexes has been achieved [86,87,358].

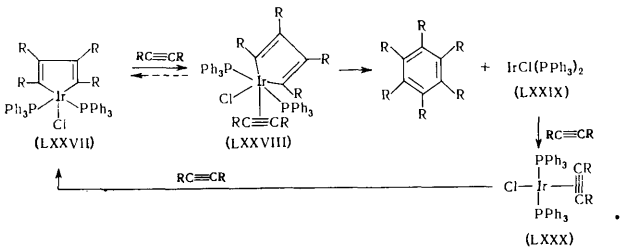
In the polymerisation of alkynes in the presence of transition metal halides of the type $(R_3P)_2NiX_2$, [104] BNP, [100,309] $PdCl_2$, and $RhCl_3$ [321] a σ-vinyl derivative may be formed as a result of the insertion of acetylene in the M–Hal bond. Thus Scheme 7 has been proposed for the cyclo-oligomerisation of acetylene in the presence of BNP. [260,309,310,312] The acetylene π-complex $(RC_2R)\cdot(PdCl_2)_2S_X$ (LXXI) formed initially is converted in the rate-determining stage into the σ-vinyl intermediate (LXXII), which subsequently coordinates a second acetylene molecule and is converted into (LXXIII). The reaction pathways of the latter depend on the size of the substituents in acetylene. For bulky substituents (Ph, t-Bu), cyclisation into inactive cyclobutene or cyclobutadiene complexes (LXXIV) or (LXXV) is observed. For small substituents (Me), a third acetylene molecule is inserted with formation of (LXXVI), which cyclises to hexamethylbenzene.

Scheme 7

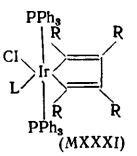


The polymerisation of acetylene in the presence of Ziegler–Natta catalysts can be explained similarly by the insertion of acetylene in an M–R bond[359].

In order to account for the formation of benzene derivatives from disubstituted acetylenes in the presence of nickel catalysts, the hypothesis of the intermediate formation of a metal-containing cyclic complex was put forward[17]. It was developed further in subsequent investigations[5,32,100,290,352,360]. The reaction mechanism for iridium as an example is as follows[361]:



The reversible addition of acetylene to the coordination-unsaturated cyclic iridium compound (LXXVII) leads to the formation of the intermediate complex (LXXVIII), which then decomposes with liberation of hexasubstituted benzene and the moiety (LXXIX). The latter combines with an acetylene molecule to form the acetylene complex (LXXX), which is in turn converted into the cylic iridium complex (LXXVII), etc. The changes involving the conversion of (LXXX) into (LXXVII) and of (LXXVII) into a benzene derivative have been achieved experimentally. The capacity of the coordination-unsaturated complex (LXXVII) to react with CO and tertiary phosphines with formation of the hexacoordinate complex (LXXXI),



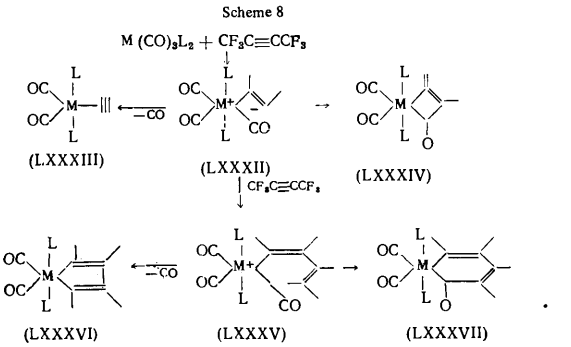
suggests that the stage involving the formation of (LXXVIII) is also likely. A similar series of transformations has been achieved for rhodium complexes[236,239–243].

The employment of the metal-containing cyclic compound hypothesis in relation to non-stoichiometric cyclisation reactions of acetylenes in the presence of σ-alkyl and σ-aryl metal derivatives was described above (Section III).

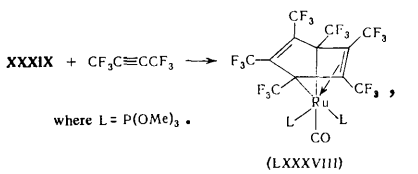
The attempts to apply the metal-containing cyclic compound hypothesis in the version described in order to account for the reaction of HFB with carbonylphosphine (phosphitocarbonyl) complexes of iron, ruthenium and osmium of the type $M(CO)_3L_2$ [L = PMe_2Ph or $P(OMe)_3$] have encountered many objections. In particular the formation of, for example, the complex (LXXXIV) cannot be accounted for in terms of the "insertion reaction" of carbon monoxide (more correctly the migration of the alkyl group), since electronegative substituents in σ-linked alkyl groups are known to hinder strongly the insertion of CO in the M–C bond.

Scheme 8, postulating the formation of an intermediate ionic product (LXXXII), has been proposed as an alternative to the "insertion reaction". This product is either converted into an acetylene π-complex (LXXXIII) with elimination of CO or the metallocyclobutenone (LXXXIV) is formed as a result of the intramolecular attack of the carbanion on the coordinated carbonyl group. Compound (LXXXII) can also react with a second acetylene molecule, forming the ionic intermediate (LXXXV), which yields as a result of similar reactions either the metallocyclopentadiene (LXXXVI) or the complex (LXXXVII) as a precursor of cyclopentadienone.

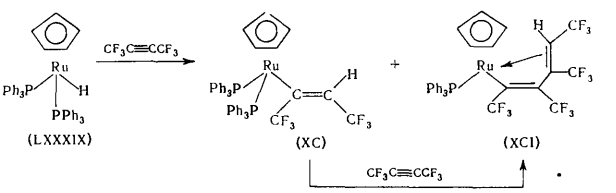
Scheme 8



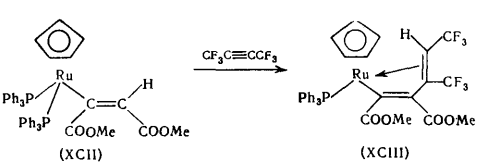
The formation of the complex (LXXXVIII) from (XXXIX) on irradiation is consistent with the hypothesis that the benzene ring is formed from the metallocyclopentadiene:



The mechanism in which the formation of ionic intermediates is postulated has been confirmed in studies by other investigators. When π-cyclopentadienyldi(triphenylphosphine)ruthenium hydride (LXXXIX) reacts with HFB, the complexes (XC) and (XCI) are formed[362]:



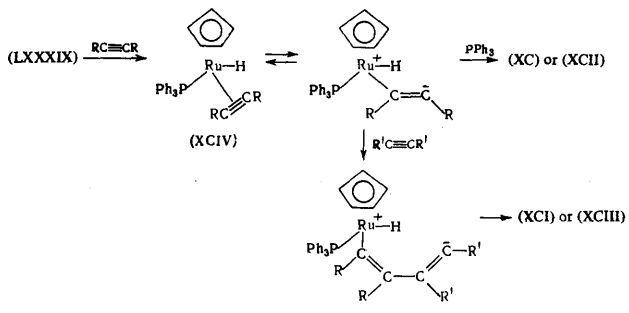
Compound (XCII) was similarly obtained from (LXXXIX) and the dimethyl ester of acetylenedicarboxylic acid. The reaction of (XCII) with HFB yields a complex which has the structure (XCIII) according to X-ray diffraction data:



The formation of (XCIII) cannot be accounted for from the standpoint of the insertion of acetylene in the M–C bond, since one would expect in this case the formation of the isomeric product $C_5H_5Ru(PPh_3)[C(CF_3)=C(CF_3)-C(COOMe)=CH(COOMe)]$. Evidently (XCIII) is formed as a result of the insertion of HFB in the C–H bond in (XCII). Scheme 9, in which the formation of ionic

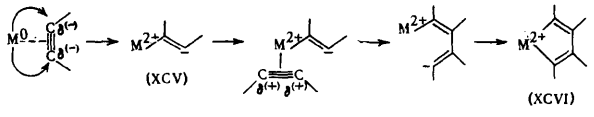
intermediates is postulated as in Scheme 8 discussed above, has been put forward on the basis of the data obtained for the reaction:

Scheme 9

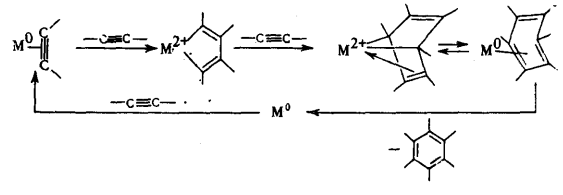


A similar mechanism has been proposed for the cyclo-oligomerisation of acetylenes with participation of zero-valent palladium and platinum complexes (Scheme 10).[260] The hypothesis of the formation of dipolar intermediates (XCV) is based on the observed acceleration of the reactions in polar solvents. A second acetylene molecule is coordinated to the metal which is already in a +2 state of oxidation as a result of which the acetylene is activated in relation to the nucleophilic agent and undergoes intramolecular attack by the vinyl anion:

Scheme 10



It has been suggested that the subsequent conversion of the metal-containing cyclic product (XCVI) into a benzene derivative involves the formation of a π-tetrahaptobenzene complex:



Thus an obligatory stage in all the cyclo-oligomerisation and polymerisation reactions of acetylenes in the presence of transition metal compounds is the formation of acetylene π-complexes. The pathways followed in the subsequent conversion of the π-complexes into the final products can apparently be different depending on the nature of the metal and the acetylene.

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Polymeric Chemotherapeutic Agents with Carcinolytic Activity

I.Iliev, M.Georgieva and V.Kabaivanov

The review deals with advances in research on the applications of polymeric compounds in active cancer chemotherapy and prospects for its development. The principal aims to which efforts are at present directed are indicated and arguments are adduced in support of the necessity for a further and comprehensive development of this problem. Attention is concentrated on the employment of synthetic polyelectrolytes as transporting agents for active chemotherapeutic preparations. The bibliography includes 52 references.

The treatment of different types of cancer is one of the most important problems being solved at present in medicine. The widespread occurrence of these affections in all parts of the world, their wide pathological variety, and the absence in certain cases of means for a complete cure — all these necessitate an active search for chemotherapeutic antitumour agents.

There exist several hypotheses at present concerning the nature of cancer and the mechanism of its occurrence and development. One can now state with complete certainty that cancer constitutes the formation of new tissue (tumour), which arises in different parts of the human organism as a result of continuous uncontrolled division of cancer cells. Usually this is a result of the response of the organism to the action of various external and internal irritants, toxic substances, physical (ionising radiation and others) and biological agents (certain types of viruses and hormones), etc.[1].

The concept of "cancer" is collective[2] (carcinomas, sarcomas, lymphomas, etc.). The wide variety of forms of cancer and their morphological, aetiological, and clinical differences make it necessary to select specific agents to treat the disease. The principal modern methods for the treatment of a cancer are surgery, radiotherapy, hormonotherapy, chemotherapy, and combined procedures[3]. When chemotherapy is used in the fight against cancer, it is necessary to overcome a specific difficulty — the identical response of normal and cancer cells to chemotherapeutic agents.

Many authors believe[3-5] that chemotherapeutic preparations used in modern practice can be divided into four principal groups: alkylating agents, antimetabolites, antibiotics, and preparations of plant origin. Larionov[4] includes hormonal preparations among them. Boesen and Davies[5] distinguish yet another group, combining all preparations with anticancer activity which cannot be included in any of the four groups stated above in terms of the principle of their action.

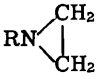
Antimetabolites are largely structural analogues of compounds important to the organism, such as vitamins, hormones, and aminoacids.

Antibiotics are not as effective against cancer cells as against bacterial infections. However, their capacity to influence the metabolism of tumours and also the virus theory of certain forms of cancer[6] resulted in the use of many antibiotics in the fight against cancer. Actinomycins have been most widely used.

Among preparations of plant origin, the alkaloids colchamine and vinblastine show the highest antitumour activity.

The main group of preparations includes alkylating compounds with anticancer activity. It has been most thoroughly investigated and a large number of carcinolytic preparations employed in clinical practice belong to it. The different types of biological alkylating agents, the mechanism of their action, the kinds of tumours which they effectively inhibit, the methods for the enhancement of their selectivity, and the prospects of finding new preparations have been considered in detail in reviews[4, 7-9].

A common property of biological alkylating agents is their capacity to alkylate the nucleophilic centres of biological systems under very mild conditions (aqueous solution at pH 7 – 7.5, temperature 37°C). The following nucleophilic centres are encountered in biological systems: anions of organic and inorganic acids and ionised sulphydryl groups and thioethers. The main alkylating compounds employed are β-chloroethylamines $R_2NCH_2CH_2Cl$, epoxy-compounds $R_2CH-CH-CH_2$ (O), aziridine derivatives



and alkanesulphonic acid esters.

It has been established that many alkylating agents react *in vitro* directly with the functional groups of proteins and nucleic acids. They attack the carboxy- or hydroxy-groups of aminoacids and phosphoric acids.

In order to account for the biological activity of alkylating substances, two hypotheses have been put forward[7]: (1) the formation of cross-links between two points in the same biomacromolecule or between two different biomicromolecules; (2) local polymerisation. In the latter case compounds capable of being alkylated and containing reactive groups are polymerised in the organism with formation of macromolecules. The majority of investigators tend to give preference to the first hypothesis. On the other hand, the second hypothesis makes it possible to detect the carcinolytic activity of certain alkylating polymers[10].

The principal requirement which must be met by alkylating agents (as well as all other anticancer chemotherapeutic agents) is selectivity of their action. The selectivity is measured by the so called chemotherapeutic index, which is defined as the ratio of the therapeutic and toxic doses of the given preparation[9].

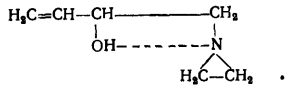
The high reactivity and low specificity of alkylating compounds introduced into the organism frequently preclude their employment as chemotherapeutic agents. Thus the idea arose that an inert carrier, which as a rule exhibits a specific affinity for the particular system toward which the therapeutic activity is directed, be employed.

An important principle of the preparation of chemotherapeutic compounds with high selectivity and low toxicity involves the employment of latent activity[8]. The principle is based on the possibility of introducing into the organism inactive preparations which are gradually converted into their active form under the influence of enzymes. Such preparations may be high-molecular-weight compounds.

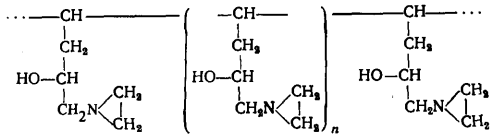
The successful application of polymers in all branches of medicine stimulated the synthesis of polymeric medicinal preparations with carcinolytic activity. Krentsel'et al.[11]

state that interest in polymeric materials increased particularly after the development of methods for stereospecific polymerisation whereby it is possible to synthesise rigorously ordered macromolecules, which were previously known only among natural compounds. The same workers believe that there are three promising trends in the synthesis of polymeric antitumour preparations.

The first important trend involves the synthesis of physiologically active polymers from physiologically active monomers. Alkylating aromatic preparations derived from di-(2-chloroethyl)amines, derivatives of aziridine, and ethylene derivatives in which the double bond is activated by groups such as NO_2, SO_2R, COR, etc. are believed to be the most promising in this respect. In the synthesis of such preparations the main factor is the endeavour to increase the selectivity by controlling the length of the macromolecule and the content of functional groups. In most cases polymerisation of monomeric anticancer alkylating substances of such types is difficult and advances in this field are so far insignificant. The first positive result was achieved by Lidaks and Hillers[12], who polymerised the familiar antitumour preparation ethoxen (1-azirindino-2-hydroxybutene):

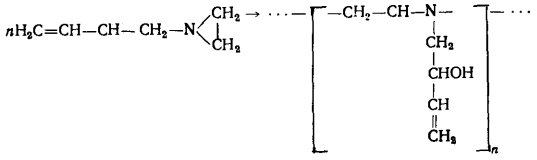


The main task in the synthesis was to achieve polymerisation via the double bonds and to prevent the opening of the aziridine ring. This was done by employing hydrogen peroxide at 100°C as the initiator. According to the authors, the resulting physiologically active polymer has the following structure:



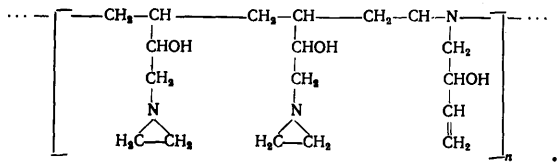
This structure presupposes the complete retention of the aziridine ring, which is unlikely. The polymeric preparation obtained was used in the treatment of the carcinoma of the alimentary canal and the stomach and was administered *per os*, which ensured good contact with the surface of the tumour and prevented a premature reaction of the reactive alkylating aziridino-group. The polymer exhibits almost the same anticancer activity against sarcoma S-45 in mice as the initial monomer, but is less toxic.

Subsequently it was established[11] that the polymerisation of ethoxen proceeds not only via the double bonds but also via the opening of the aziridine ring:



When synthesised by thermal polymerisation, the polymer includes up to 37% of units containing the aziridine ring, 58.8% of such units are retained on radical polymerisation under the influence of benzoyl peroxide and 67 to 68% on radiation-induced polymerisation (using γ-rays from a cobalt source). Thus the maximal antitumour effect is to be expected for the polymer obtained by γ-irradiation.

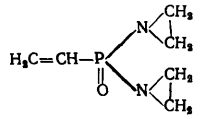
This polymer probably has a structure of the type[11]



i.e. of each three monomeric molecules two enter the growing chain as a result of the dissociation of the C = C double bond and one as a result of the opening of the ring.

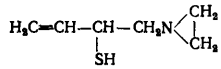
Shimanskaya[13] has listed the following other promising monomeric aziridine derivatives which are of interest for the synthesis of anticancer polymeric preparations:

bis(1-aziridinyl)vinylphosphine oxide:

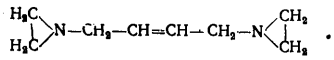


(the presence of the phosphoryl group might have increased the latent activity of the polymer);

1-aziridino-2-mercaptobut-3-ene (mercapto-analogue of ethoxen):

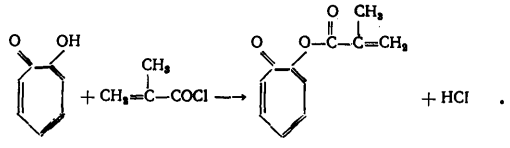


1,4-diaziridinobut-2-ene (product of the addition of aziridine to butadiene):

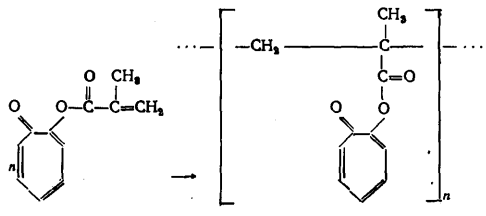


Cornell and Donaruma[14, 15] used 2-methacryloxytropone as the monomer. They assumed that the corresponding polymer would exhibit a moderate physiological activity, since at the biological pH it should be insoluble and resistant to biological decomposition. Indeed, the polymer obtained from 2-methacryloxynitrile[11, 12] does show a weak physiological effect. On the other hand, the homopolymer of methacryloxytropone exhibits a higher carcinolytic activity in relation to experimental strains.

Methacryloyloxytropone is a product of the reaction between tropolone and methacryloyl chloride:



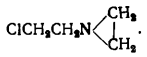
The polymerisation can be represented by the following scheme:



The authors do not explain the mechanism of the anticancer activity of the polymer which they synthesised. The carcinolytic activity of the monomer is probably due to the structural similarity between tropolone, colchicine, and other troponoids of this kind, the physiological activity of

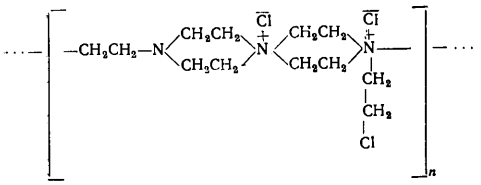
which is known. Colchamine is an analogue of this group substances among preparations of plant origin.

Galstyan[16] reported studies on the anticancer activities of the polymeric preparation Kh-1. This chloroalkylating preparation, obtained by Avetyan and Matsoyan[17], has been investigated clinically and introduced into chemotherapeutic practice under the name "polychlorimine". 2-Chloroethylaziridine, which constitutes a combination of two groups with a high cytostatic activity,

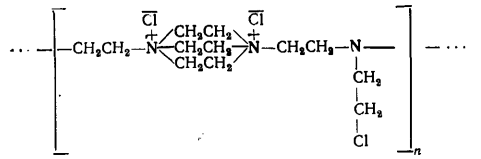


was used as the monomer for its synthesis.

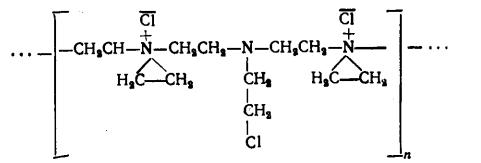
The monomer is unstable and polymerises readily in the presence of water. Controlled polymerisation was achieved in aqueous dimethylformamide solution at 30 – 40°C for monomer : water : dimethylformamide ratios of 1 : 5 : 1. The analytical data lead to the conclusion that the fundamental unit of the resulting linear polymers contains two ammonium ions formed by cyclisation. Three probable versions (A – C) of the structure of the polymer chain have been put forward:



(A)

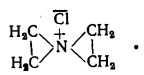


(B)



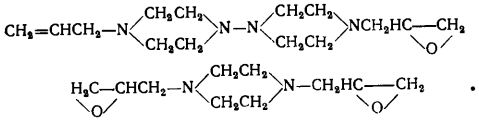
(C)

The authors believe that polymerisation proceeds via a cationic mechanism involving self-initiation with participation of a quaternary ammonium salt produced from the monomer:



The mechanism of the anticancer activity of the preparation has not been established. Its effectiveness can hardly be accounted for solely by the presence in the chain of a large number of active alkylating groups. This could lead to an extremely high toxicity and would reduce the selectivity of the polymeric chloroalkylating agent. The preparation is probably a polyelectrolyte. Thus, bearing in mind certain characteristics of cancer cells, which will be discussed below, one can assume that the effectiveness of the preparation is based on its combined action as a polyelectrolyte and as an active alkylating agent.

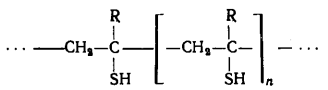
It would probably be interesting to obtain and test polymeric analogous of a number of compounds containing the epoxy-group, for example:



The copolymerisation of methacrylic acid with alkylating derivatives based on it is also interesting.

According to Krentsel' et al.[11], a second important trend in the synthesis of polymers with carcinolytic activity involves the formation of simple macromolecules containing physiologically active groups. Such studies are also important because they make it possible to explain the influence which a given polymer structure can exert on the reactivity of physiologically active functional groups. Polymers containing sulphydryl and imidazole groups are particularly interesting in this respect[18]. These polymers can inhibit the influence of ionising radiation, which is responsible for the carcinogenic degeneracy of cells.

Polyvinylmercaptans with various substituents in a side chain may be quoted as a possible example:



The presence of phenolic rings increases the resistance of polyvinylmercaptans to oxidation.

Certain reports concerning the use of polymeric molecules as carriers of active anticancer low-molecular-weight substances can also be referred to studies of this kind. The inclusion of an active sarcolysine preparation in the molecules of a number of polymers and copolymers (the copolymers are conventionally designated by K_2, K_7, K_{10}, K_{12}, etc.) led to the synthesis of effective agents with a comparatively low toxicity and high selectivity[19].

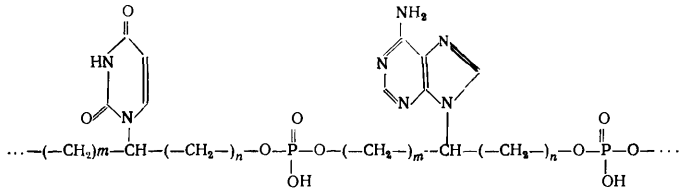
Vernick and Hoppe[20] discovered that the polyvinylpyrrolidine – iodine complex has an inhibiting effect on Walker carcinosarcoma 256. The possibility of using polyvinylpyrrolidine as a polymer forming complexes with various cytostatic substances and increasing their selectivity has also been reported by other workers[21].

A third, exceptionally promising but unfortunately as yet uninvestigated type of synthesis of polymeric carcinolytic substances is asymmetric synthesis[22]. The synthesis may be based on the relation demonstrated by many investigators between the stereoisomerism of chemical substances, in particular sarcolysin derivatives[23, 24], and their carcinolytic activity. The method of polymerisation on polymeric matrices might find an application here[25].

The study of the use of polymeric analogous of natural macromolecules to suppress the selective action of the enzyme RNA-polymerase[26] showed that polymers with a specific configuration may inhibit the synthesis of protein and arrest the growth of malignant tumours. It has been suggested[26] that it might be possible to synthesise polymers whose structure would resemble various enzymes with a rigorous alternation of a large number of aminoacids in the monomeric unit with an appropriate chain length and appropriate distances between individual units. Such "depressant polymers" can "recognise", via one of their units much more readily than low-molecular-weight chemotherapeutic substances, the appropriate enzyme centre susceptible to

attack and block its activity. Merrifield's method — solid-phase polymerisation — is most suitable for the synthesis of such polymers[27].

The synthesis of a polymer of this kind was achieved by Hillers[28], who obtained oligomeric polynucleotides complementary to natural aminoacids and having the following structure:

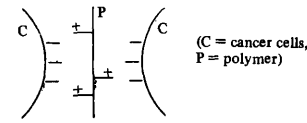


In all the instances mentioned, the activity was explained on the basis of the already established mechanisms of the action of alkylating substances on biological centres or the mechanisms of the suppression of the activity of enzymes responsible for cell division. Polymeric preparations exhibit almost identical activities in relation to both cancer and normal cells. Therefore, even a slight qualitative difference between such cells has been the subject of numerous wide-scale investigations in order to find new ways for the inhibition of the growth of tumours.

Another interesting type of study, which gives rise to the possibility of creating various combinations and modifications of polymeric substances, involves the use of polyelectrolytes. Both polycations and polyanions, i.e. polybases and polyacids, can probably be used with equal success.

The majority of natural and biological polymers are polyelectrolytes. They include, for example, peptides and enzymes[29, 30]. The surface of normal and cancer cells has a definite electrical charge. The possibility of the formation of electrostatic bonds between natural or synthetic polyelectrolytes and a biopolymer of a living organism constitutes yet another basis for the inhibition of tumour growth. For example, by binding a suitable polyelectrolyte to enzymes e.g. deoxyribonuclease responsible for cell division, one might retard or arrest such division. It is then necessary to protect the organism from the toxic action of the polyelectrolytes, since they act with equal force on both cancer and normal cells[29]. Cationic polyelectroyltes proved to be the most selective. This may be attributed to the negative surface charge of the cells, arising mainly from ionised phosphate or carboxy-groups.

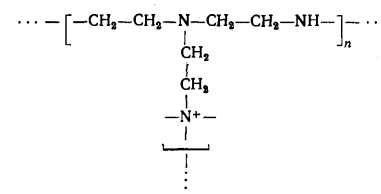
On the basis of studies by a number of investigators, Ambrose et al.[31] showed by electrophoresis that the negative charges arising on the surfaces of normal and cancer cells are of different magnitudes. Subsequently these workers[32] confirmed this by experiments with cancer cells from mouse kidneys and lungs. They tested synthetic polycations as antitumour preparations *in vitro*. Polyethyleneimine ... $-[-CH_2CH_2NH-]_n$ ..., polyvinyl-4-butylpyridine, and polyhexamethylenediguanidine ... $-[-(-CH_2-)_6-\underset{\underset{NH}{\|}}{C}-NH-\underset{\underset{NH}{\|}}{C}-NH-]_n-$... were tested. It was found that only polyethyleneimine exhibits a fairly marked antitumour activity. The highest efficiency is obtained at a low concentration of the test polymers. The agglutination of tumour cells in such experiments confirms the hypothesis that the cancer cell has a higher negative charge than the normal cell. According to these investigators, this can be explained by a decrease on the surface of cancer cells of the number of Ca^{2+} ions, which play the role of an intercellular adhesive. A decrease of the number of these ions on the surface of cancer cells impairs the intercellular linkages. Polycations which combine with the negatively charged surface neutralise the surface charge. This increases the adhesion between the cells and causes the agglutination of the tumour cells[33].



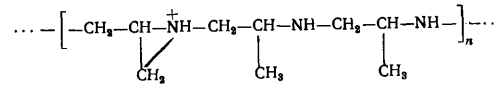
It has been shown that the units of sialic acids are responsible to a greater extent than phosphate residues for the formation of the negative surface charge of cancer cells[33, 34].

In accordance with the latest research, Moroson[34] believes that, apart from the Coulombic cytostatic binding of cancer cells described above, polycations in general enhance the immune response of the organisms to cells transplanted from the outside. Polycations of the following types were investigated *in vivo* and *in vitro*:

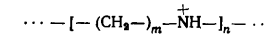
Polyethyleneimines with molecular weights of 600, 1800, 60 000, and 100 000:



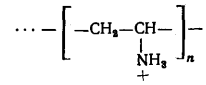
Polypropyleneimine with a molecular weight of 10 000 to 15 000:



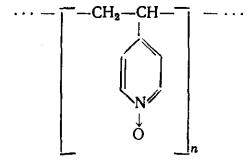
A polyamine with a molecular weight of 30 000 – 50 000:



Polyvinylamine with a molecular weight of 10 000 to 300 000:



Poly(vinylpyridien *N*-oxide) with a molecular weight of 100 000:



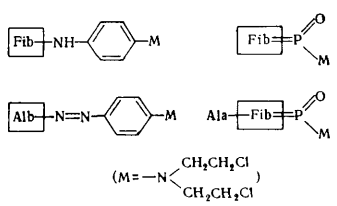
These polymers have basic properties and in the neutral form each of the four nitrogen atoms carries a positive charge. The mechanism of the polymerisation of the ethyleneimine [aziridine] monomer includes a stage involving the formation of a quaternary immonium ion and then interaction with yet another ethyleneimine molecule. Polyethyleneimine molecules with a higher molecular weight (in excess of 100 000) has been obtained by treatment with ethylene chloride.

Apart from inhibiting the growth of tumours by direct electrostatic addition, some investigators believe that polycations are capable of transporting powerful cytostatic substance to the cancer cells. In his experiments, Woodman[35]

employed for this purpose chitosan (a copolymer of hexosamine and *N*-acetylhexosamine), polyethyleneimine, polypropyleneimine, diethylaminodextran, "polybrene" [poly-1, 5-dimethyl-1, 5(diaza-undecamethylene dimethobromide)], and other polymers. These high-molecular-weight compounds are capable of forming complexes with iododeoxycytidylic acid and thus transporting iododeoxyuridine — an active metabolite. The presence of polycations probably facilitates the passage of the active metabolite through the membrane of the cell after its enzymatic decomposition (cell dephosphorylation[8]) or even the entire polycation–metabolite complex may pass into the cell. As a result, the activity of nuclear deoxyribonuclease is inhibited.

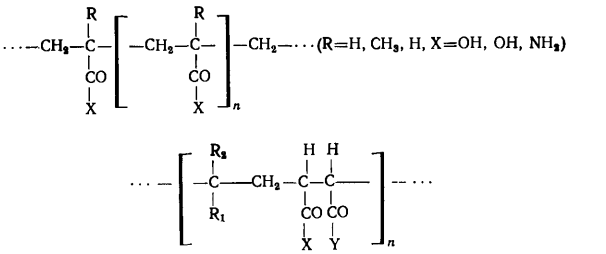
Ryser[36] and Larsen[37] observed an increase of the transmitting capacity of a cell membrane model (thiolated gelatin) in the presence of polycations. Larsen and Thörling[38] therefore explained their observation of the anticancer inhibiting effect of diethylaminodextran and the sodium salt of sulphonated dextran by the facilitation of the passage of the macromolecule through the cell membrane.

The possibility of the transport of cytostatic agents of another type with the aid of polycations is also of great interest. Experiments with complexes of methotrexate, chlorambucil, etc. and polyethyleneimine proved unsuccessful, since these complexes dissociate in 0.015 M NaCl. Nitrogen mustard gas, linked covalently to albumin (a natural polyelectrolyte) as well as a phenylalanine–mustard gas polymer did not exhibit the expected antitumour activity[39]. However, the diphenylamine analogue of mustard gas and some of its derivatives exhibited a high chemotherapeutic selectivity. These preparations proved to be effective in relation to certain mouse tumours[40]. Some derivatives of nitrogen mustard gas linked to biopolycations of the type of albumin, globulin, and fibrinogen showed a high latent activity[40]



Regelson and coworkers[41] discovered that many synthetic heparinoid polyanions exhibit a comprehensive antitumour activity. Regelson attributes this activity to the anticancer activity of heparin itself, which is an inhibitor of cell division. Heparin is a sulphomucopolysaccharide—a natural anionic hydrophilic polymer, which acts as a coagulator. While the causes of the anticancer activity of polycations are known comparatively accurately, for polyanions there are numerous likely mechanisms and hypotheses. It has been suggested that polyanions bind Ca^{2+} and Mg^{2+} ions, keeping them on the surface of the cell, which promotes cohesion among the cells. As mentioned above, cancer cells are distinguished by impaired intermolecular adhesion owing to a lower coverage of the surface by Ca^{2+} or Mg^{2+} ions. Polyanions can also combine with various biopolycations (enzymes), which results in a decrease or complete disappearance of the activity of enzymes, promoting uncontrolled cell division. Polyanions also inhibit the activity of nuclear deoxyribonuclease of cancer cells.

Regelson investigated the sodium salt of polyethylenesulphonic acid (molecular weight 15 000 – 35 000)[42] as the first analogue of heparin and demonstrated its anticancer activity on various types of tissue culture. Later, in order to confirm this hypothesis, he investigated the anticancer activity of other polyanions — polyacrylic acid and ethylenemaleic acid anhydride[43], both pure and hydrolysed. Polyanions in the amidoacid form have also been examined. They differ by the density of electrical charges:



(R_1=H; H; H: H; H; H; CH_3; CH_3
R_2=H; H; H; H; CH_3; CH_3; CH_3; CH_3
X=OH; NH_2; NH_2; NH_2; ONH_4; NH_2; ONa; NH_2
Y=OH; ONH_4; OH; NH_2; ONH_4; ONH_4; ONa; NH_2)

It was found that the amidoacid form of the copolymer of ethylene and maleic anhydride exhibits a broad spectrum of antitumour activity, while the hydrolysed form inhibits most effectively the growth of sarcoma 180 (equally toxic doses were compared). The highest effectiveness is, however, achieved when the carboxamide groups are distributed along the main copolymer chain. The enhanced anticancer activity of the cobalt, copper, and nickel salts of the copolymer of ethylene and maleic anhydride against Walker sarcoma in mice was also discovered by Hodnett et al.[44]

Another polyanion, a pyran copolymer, investigated by Merigan, Regelson and coworkers[45–48], exhibits an interesting antitumour activity. To facilitate its elimination from the organism (with urine), it is convenient to employ a polymer with a molecular weight of 17 000. It was established that the pyran copolymer induces the formation in the organism of an active interferon, giving rise thereby to a broad spectrum of carcinolytic activity[49]. Interferon, which is a low-molecular-weight protein, exhibits a universal antiviral activity. It appears in the cells of many animals and man as a result of the action of virusus and viral nucleic acids. Its activity against carcinogenic viruses has been demonstrated[49].

The monomeric pyran ring is formed in the polymer chain after the copolymerisation of divinyl ether with maleic anhydride (in a pure form and with a 50% admixture of the amidoacid form) or by the interaction of methyl vinyl ether with maleic anhydride (also in a pure form and with a 50% admixture of the amide). Other methods of synthesising this ring are also known, for example, by the reaction of maleic anhydride and styrene. It has been established that methylation of 50% of the carboxy-groups does not block the formation of interferon, while amidation sometimes does have a blocking effect. The capacity of these copolymers to induce the formation of interferon depends on the steric accessibility of the carboxy-groups at the instant of their addition to cancer cells. Copolymers without free carboxy-groups are inactive[45].

Finally, special mention should also be made of the search for carcinolytic substances directly related to Szent-Gyorgyi's interesting hypothesis concerning the essential nature of the cancer cell[50]. According to his view, the cells of a living organism are in a state of equilibrium in the presence of free methylglyoxal. By virtue of its high activity, only traces of methylglyoxal are required for normal cell reproduction. The division of normal cells begins as a result of the liberation of the enzyme glyoxalase,

which inactivates methylglyoxal. When the cell is capable of binding glyoxalase, division ceases at the required instant. If the cell loses this capacity, it changes, according to Szent-Gyorgyi's idea, from a normal to a cancer cell. Possibly special administration of glyoxalase-inactivated methylglyoxal from the outside might have a definite therapeutic effect. Polymeric carriers have the ability to maintain a constant therapeutic concentration of methylglyoxal liberated on gradual decomposition of the polymer chain. Experimental evidence for the anticancer activity of methylglyoxal and its derivatives has been published in a number of studies[51, 52].

Despite the vigorous development of the applications of polymers in all branches of medicine and particularly their recent use in chemotherapy, carcinolytic activity has been demonstrated or even investigated for only a small number of polymeric preparations. The reason for this is probably lack of an exhaustive explanation of the mechanism of carcinogenesis and of the control of cell division as well as the mechanism of the antitumour activity of various polymeric substances. This hinders the search for new preparations and forces investigators to study mainly the available commercial polymers with suggested carcinolytic activity.

There is no doubt that polymers constitute an exceptionally promising field for the search for antitumour agents. They are particularly suitable for the application of the principle of latent activity (by employing carrier polymers with marked carcinolytic properties). Complexes with an ionic linkage or polymers modified by a covalently linked agent might transport the active form in a combined state to the cancer cell, where, as a result of a chemical change (decomposition, reduction, oxidation), the cytostatic activity against malignant formations may be liberated. Vast possibilities are also inherent in the use of synthetic polycations as covalent or ionic carriers of alkylating agents. Thus, there are many possibilities in polymer cancer chemotherapy which have not yet been utilised.

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Translated from *Uspekhi Khimii*, **43**, 196-198

Editorial Note

The translated reviews by V. Herout and H. Z. Levinson published in this issue describe the trends in studies designed to elucidate the role of low-molecular-weight products as regulators in biological systems. Until recently the problem of chemical control was developed mainly in relation to the control of functions at the level of the organism. This problem was investigated in greatest detail for the hormonal system of mammals. During the last 15–20 years, the range of these studies has expanded significantly—new data have been obtained on hormonal control in lower animals too, particularly in arthropods, as well as in higher and lower plants.

The problem of the possible role of metabolites excreted by the organism to the surrounding medium has remained much less thoroughly investigated. Numerous facts long known to biologists have shown that these substances can function as regulators in specific interrelations between organisms. Thus it has been shown at the level of a phenomenological description that many biological phenomena, such as, for example, the mutual influence of plants (allelopathy), the interrelation between plants and insects, and the wide variety and complexity of control in communities of social insects and certain behavioural responses of fish can be accounted for only if it is assumed that chemical substances excreted by individuals into the medium play the role of regulators acting on the behaviour and vital activity of other individuals. However, owing to the inadequacy of analytical methods, the apparent analogy between hormonal control within the organism and control in social groups involving metabolites entering the medium (in "hormonal" amounts) for a long time remained largely a speculative hypothesis, which has been reflected in the appearance of terms such as "ectocrines","exohormones", and "environmental hormones".

Quite recently (at the end of the 1950s and at the beginning of the 1960s) the idea of the regulatory importance of the metabolites excreted into the medium received rigorous experimental support as a result of the employment of new physical chemical methods (chromatography, NMR, and mass spectrometry). The studies by Butenandt and Karlson, who isolated the sexual attractant (pheromone) of the silkworm and established its structure, can probably be regarded as the beginning of this new period in research on exohormones. Further studies showed that the system of chemical communication employing signalling substances (pheromones) is present not only in insects but also in higher animals, up to primates.

Even more complicated and varied chemical control mechanisms have been observed in studies on non-trophic relations in biocenoses—stable communities of various species of living organisms populating a given region. Owing to the external and dense network of trophic relations (food chains—"who eats whom") subtler relations of a purely regulatory signalling type have been discovered in communities. In other words, it has been found that ecology cannot be restricted to the study of the energy flux and metabolism in communities but must also take into account the no less important flux of signalling substances carrying information about the presence, behaviour, and physiological state of various species constituting the given biological system. This aspect of ecological studies is in fact reflected in the term "chemical ecology" which appeared recently. Some idea about the subject and scope of this concept is provided by the titles of the articles in the collected volume "Chemical Ecology" published in the USA in 1970: "Plants and Chemical Environment", "Chemical Interactions between Plants and Insects", "Hormonal Interactions between Plants and Insects", "Intraspecies Chemical Communication in Animals", "Chemical Protection Against Arthropods", etc.

For chemists the most significant aspect of this problem is the question of the nature of the substances whereby chemical control processes are achieved. It appears evident (apparently G. Frenkel' was the first to draw attention to this) that metabolites involved in basal metabolism, providing the organism with energy and constructional material, cannot behave as chemical regulators of this kind (because such metabolism is of the same type for all living beings) and that these must consist of substances the metabolism of which is fairly specific to various species. The set of such natural products, sometimes referred to as "secondary metabolites", is extremely large, particularly in plants. Isoprenoids, alkaloids, certain aliphatic and aromatic compounds, and antibiotics are usually included among them. Some of these substances (for example steroids) are known to be involved in the control of the most important biological functions at the level of the organism. However, it remained obscure for a long time whether the majority of the others fulfil any kind of function in nature or whether they are simply the metabolic "waste" of the organisms producing them. Chemical ecological data have now demonstrated convincingly that at least some of the "secondary metabolites" do in fact play the role of regulators in the interrelations between organisms at the level of populations and communities.

Thus both at the level of the organism and at the level of communities of organisms, there is a characteristic chemical communication channel between individual components of the biological system, certain types of low-molecular-weight natural products being widely used as signals.

The problem of the way in which this chemoregulating system functions is still obscure, but in one of its main aspects the problem is essentially one of chemoreception. One must emphasise that the latter hardly reduces to the problem of the mechanism of signal reception by specialised organs of taste and smell in animals but embraces the entire range of interactions of the signal molecule with the receptor in a particular biological system.

Another important aspect of the problem of chemical control is related to the study of the question of the organisation of the system governing the chemical communication channel. Interesting data on this question were obtained by Sutherland, who found that in many cases the hormonal control system in the animal organism is constructed as a system of primary messengers (hormones), which induce in the target cells the formation of a secondary messenger (cyclic adenosine 3,5'-monophosphate, cyclic AMP). Possibly the principle of this type of hierarchy of signal systems is as common as the principle of the hierarchy of the control systems in biological organisation.

The entire range of problems associated with chemical control is of undoubted interest to chemists. The literature on this general problem is extremely large and could not be covered by the two reviews published here. Therefore we felt it necessary to include an additional list of references, which provides more complete information about the principal trends in studies on chemical control phenomena.

This list of references, divided into several fairly arbitrary sections, is quoted at the end of the list of references in Levinson's review.

ADDITIONAL REFERENCES

I. General Problems of Chemical Ecology

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Effect of Impurities on Radiation-chemical Processes in Crystals of Inorganic Salts

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Research results obtained on radiation-chemical processes in crystals of inorganic salts having composite anions (nitrates, sulphates, oxyhalides, etc.) containing various chemical impurities are analysed. The effect of water of crystallisation on the mechanism of the radiolysis and on the radiation-chemical resistance of inorganic compounds is examined. The role of heterophase additives (of a mixture of inorganic substances), the conditions of exposure, and the mechanism of transfer of energy in irradiated systems are discussed. The contributions of various factors (ionisation potentials of lattice ions, electron affinity of radiolysis products, lattice parameters, electrophysical properties of impurities, etc.) to the radiolysis of inorganic salts are estimated. Possible ways of controlling the radiation resistance of exposed materials are discussed.
The bibliography includes 121 references.

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I. INTRODUCTION

Research on the effect of ionising radiations on crystalline compounds has been especially widely developed during the past 15–20 years, largely because of the need to ascertain how corpuscular radiation and γ-rays affect the diverse structural materials employed in reactor engineering and also to establish the general features of radiation and radiation-chemical processes in various substances. Close attention has been paid in particular to the physical and chemical phenomena produced by ionising radiations in ionic compounds. This is associated e.g. with problems of trace techniques and the monitoring of radiations, study of the radiation stability of materials, and also attempts at a scientific approach to the change in properties of irradiated compounds. All these aspects require in some way a knowledge of the general mechanism (or mechanisms) of radiation-chemical processes in various classes of compounds.

Radiation and radiation-chemical processes have hitherto been most fully studied in crystals of alkali-metal halides, in nitrates, and in oxyhalides. Efforts have been directed mainly at identifying the products of radiolysis, studying the kinetics of their accumulation and annealing, establishing qualitative and quantitative relations between the yield of radiolysis products and the lattice energy,

linear energy transfer, pressure, and temperature, and recently at establishing the effect of various impurities on radiation-chemical processes. Impurities can sometimes have a decisive effect on the radiation-chemical resistance† of irradiated compounds, which can be utilised for controlling radiation-chemical processes in crystalline substances.

Although contributions increase annually, no systematic review and analysis has yet been made of the results scattered in many papers and journals, which may even in some degree hinder research in this field. The present Review attempts to fill the existing gap.

No claim is made to complete coverage of all the material. For example, the large section concerned with the radiation-thermal decomposition of solids is omitted, nor are many aspects of the action of radiation on alkali-metal halides considered. Attention is paid mainly to salts having composite anions. Deliberate restriction in the selection of material is due to the desire to adhere more closely to the essence of the question, without encumbering the paper with a mass of additional factual data. Nevertheless, references to the appropriate papers can always be found in the text.

II. GENERAL ASPECTS OF THE RADIOLYSIS OF INORGANIC SALTS

The experimental information that has accumulated on the radiolysis of salts of various acids shows that many features of radiation-chemical processes depend on the chemical composition of the test materials. Despite this, however, it is always possible to distinguish a large group (or groups) of typical primary and secondary reactions taking place whatever the compound irradiated. It is also noteworthy that the general processes do not exclude the presence of individual specific elementary reactions in the radiolysis of certain salts.

The primary processes of radiolysis comprise mainly the ionisation and excitation of anions A and cations C or the excitation of groups of ions according to fundamental schemes[1,2] of the type

$$h\nu \rightsquigarrow (K^{z_K}, A^{z_A}) \rightarrow (K^{z_K}, A^{z_A})^* \text{ or } (K^{z_K})^*, (A^{z_A})^* \quad (1)$$

$$h\nu \rightsquigarrow (K^{z_K}, A^{z_A}) \rightarrow K^{z_K-n}, A^{z_A-m}, (m+n)e^-, R_A^* , \quad (2)$$

where z is the ionic charge and R_A* are the excited radicals formed from the anions. Repeated ionisation is improbable, so that m and n are usually unity.

Because there are two main types of primary interaction of radiation with matter, the radiolysis of salts occurs in two ways—through secondary reactions of excited molecules and secondary interconversions of ionisation products—but it is often very difficult to determine the contributions of ionisation and excitation in the primary and subsequent stages of radiolysis. The reason is that present-day techniques (conductivity measurements, electron spin resonance) enable only ionised products to be reliably and fairly simply identified in a solid. The role of excited species in radiation-chemical processes must usually be assessed from indirect results. However, many analyses have recently been made of the formation of excited states and their role in various radiation processes.

† The radiation-chemical resistance of a salt is usually characterised by the extent of decomposition of the compound (Section II).

According to Lushchik, for example, a cascade of secondary electrons produces a series of electronic excitations of the ions of the main substance (of energy ~ 100 eV). These electronic states are unstable, and pass rapidly into stable electronic states of low energy—excitons and electron–hole pairs of energy ~ 10 eV—which determine the final radiation effects—luminescence, formation of colour centres, dislodged atoms, and subsequent radiation-chemical reactions—in ionic crystals[3,4]. Analogous phenomena can be observed as a result of the self-trapping of holes formed at low and even room temperature[5,6].

Elango et al.[7-10] showed in a series of experiments that colour centres are formed in alkali-metal halide crystals on exposure to light and soft X-rays. They consider that the main role is played by excitons, whose decay is able to initiate the formation of ionised species. In several papers the formation of excited species has been regarded as the primary stage of radiolysis[10-12].

Excited and superexcited electronic states evidently play an important part in radiation-chemical reactions[13,14]. However, analysis of numerous papers shows (without going into the mechanism of the primary act of absorption of the radiated energy and the intermediate stages of its transfer) that the conventional separation of all radiation-chemical reactions into two groups (reactions 1 and 2) is probably legitimate. It must be borne in mind that under certain conditions reaction (1) may precede the ionisation of cations and anions.

Certain workers usually distinguish two temperature regions when considering typical secondary reactions in the most thoroughly studied ionisation branch of radiolysis, in each of which a characteristic group of reactions takes place[1,14,15]. At low temperature (up to ~ 200°K) processes involving the recombination of radicals R with an electron are most often observed:

$$R + e \rightarrow (R^-)^* \rightarrow R^- + h\nu , \quad (3)$$

or

$$R + e \rightarrow (R^-)^* \rightarrow \text{product} . \quad (4)$$

In sulphates of alkali and alkaline-earth metals, for example, the reaction

$$SO_4^- + e \rightarrow (SO_4^{2-})^* \begin{cases} \nearrow SO_4^{2-} + h\nu \\ \searrow SO_3^- + O^-,\ (SO_3^- + O + e) \end{cases} \quad (5)$$

takes place[16], with formation of the initial sulphate ion and its radical dissociation products. At low temperatures dimerisation of the primary radicals

$$R + R \rightarrow R_2 \quad (6)$$

or

$$R_1 + R_2 \rightarrow R_2' \quad (7)$$

is also possible. The above reactions are typical of organic compounds and certain composite inorganic salts[17]:

$$ClO_3 + ClO_3 \rightarrow Cl_2O_6 . \quad (8)$$

In the region of ~ 200°K the most probable processes involve the decay of composite radicals into simple radicals and stable products:

$$R \rightarrow R_1, R_2, R_3 \ldots \text{(stable products)} . \quad (9)$$

For example[1,17]

$$ClO_3 + e \begin{cases} \nearrow ClO_2^- + {}^1/_2 O_2 \\ \searrow Cl^- + {}^3/_2 O_2 \end{cases} . \quad (10)$$

The above classification of primary reactions is, of course, extremely arbitrary, and individual deviations from the suggested scheme are possible in particular cases. Thus the dimerisation of radicals or processes resembling (8) are often observed at temperatures above 200°K.[1,15-19]

It is not only difficult but also dubious to introduce exact limits to these temperature regions without specifying the compounds. Even with a definite substance the temperature ranges within which particular radiation-chemical reactions occur may shift with the nature and the quantity of various impurities, the "biography" of the crystal, etc. It is therefore advisable to refine this concept (classification) in subsequent investigations.

Besides the above reactions there are still quite a large number of intermediate reactions of primary and secondary radicals, molecules, and fragments of composite anions or cations. Such processes fall into the main types[1]—(i) reactions between R and its breakdown products with the formation of composite radicals, e.g. $ClO-ClO_3^-$ and $N_2O_3^-$ in chlorates and nitrates respectively; (ii) interaction of thermalysed electrons with radicals and anions (processes 3–6); (iii) reactions of atomic oxygen with anions and radicals, e.g. the interaction of O and NO_2^- in the nitrates, and of ClO_3^- and O in chlorates and perchlorates; and (iv) reactions among excited molecules, ions (breakdown), and atoms with the formation of O_2 and O_3^- in oxy-salts, etc.

The formation of various products in irradiated salts may depend in larger or smaller degree on many factors. Substances that are less subject to the action of radiation possess several specific features responsible for their radiation.resistance[20]. *Radiation resistance* (or stability) is taken to be the ability of substances to withstand the action of radiation without change in their structure-sensitive properties, and could be measured by the stored energy[21-23]. This concept is close to the *radiation-chemical resistance*, which determines the extent of radiation chemical changes in an irradiated specimen, and is characterised by the yield G of the corresponding product (or decomposition of the whole compound).

The radiation-chemical yield of a particular product depends on a large number of properties of the solid, the radiation, and the conditions of irradiation. No unequivocal general quantitative relations have yet been established between G and the various parameters of the test systems. Only in isolated cases have the first steps in this direction been taken.

These two criteria, representing in different ways the interaction of radiation with a given compound, are almost identical. With alkali-metal halides, for example, a sharp distinction cannot be made between them, the differences being purely terminological. It is therefore more expedient (and even essentially more correct) to replace them by a concept such as *radiation resistance* defined by the totality of changes in the irradiated specimen due to the action of radiation. The *radiation yield* (G)—the quantity of various products (F-centres, localised holes, dislodged atoms, radicals, ions, new molecules, etc.) formed in the specimen by the absorption of 100 eV of radiant energy—must obviously be adopted as an [inverse] measure of radiation resistance. This preserves all the previously established relations for the variation in properties of exposed substances, determined by the stored energy or the radiation-chemical yield: it unites the purely "physical" and purely "chemical" approaches to the phenomenon.

The type of bond is usually very important. When various oxides are exposed in a reactor, for example, their radiation stability diminishes in the sequence

$$Al_2O_3 > BeO > ZrO_2 > SrO\ .$$

The covalent character of the bonds increases in a similar sequence[20]. Furthermore, radiation stability decreases from metallic to ionic, covalent, and molecular bonds[20,24]. These rules hold in series of compounds of the same type. However, the correlations are purely qualitative and extremely tentative.

The stability towards radiation usually increases with increase in the *lattice energy*[21-25], which is evidently one of the main characteristics determining the radiation resistance of solids. Thus the properties of ionic crystals of low lattice energy change considerably more strongly in the exposed zone than those of substances of high lattice energy. However, the resulting reversible radiation disturbances disappear far more slowly in compounds of the latter type[21,26].

The sensitivity of inorganic ionic compounds to radiation is largely dependent on the composition and on the nature of the bond. Thus in ionic crystals containing composite anions, in contrast to binary ionic salts such as alkali-metal halides, the bonds between elements in the lattice may be strong, with a small volume of free interstices‡, and hence little probability that atoms (ions) will be displaced from their normal positions. In many cases, therefore, a correlation is observed between the yields of radiolysis products from ionic salts and the free volume V_{fr} of the unit cell, defined as the difference between the volume of the cell and that of the ions occupying it[27-29]. The relation between radiolysis yields and free volume, noted by almost all authors, probably represents a cage effect. For a first-order or pseudounimolecular radiolytic process G and V_{fr} are related by the formula[29]

$$G = f[\exp(-k/V_{fr})]\ . \qquad (11)$$

The free volume—a phenomenological characteristic of the properties of crystals—is a parameter representing the cooperative character of the bonds in a solid that are responsible for solid-phase reactions. The disintegrating ion is usually more weakly bound in crystals with large free volumes (loose lattices): i.e. the probability of dissociation and of escape of radiolysis products from the cell is increased, while reverse processes of recombination diminish. Hence the initial yields of radiolysis products should increase, in series of compounds of the same type in which the cation or the anion is replaced (presumably also with bonds of the same character and the same lattice structure), as the free volume increases[27,28]. But macroscopic diffusion is also increased in loose crystals, which may tend to diminish the yields G.[30]

The nature of the cation has an appreciable effect on the yield G, which e.g. with nitrates increases in the sequence[28,30-33]

$$Li < Na < Rb < Cs < K$$

$$Cd,\ Ag < Pb < La < Ba\ .$$

In this case the properties of the cation must evidently also be taken into account, especially in series of salts having the same anion, besides the above role of the free volume.

‡ It makes sense to compare the volume of free interstices with the size of the lattice ions in series of salts of the same type.

Thus with silver and cadmium halides rise in the ionisation potential of the cation intensifies the irreversibility of radiolysis and increases the yield of decomposition products[34,35].

The effect of the free volume is usually decisive where the variation of ionisation potential in a series of salts of the same type is small. In salts with like anions and the same or almost the same free volumes the radiation resistance is higher in the compound whose cation has the lower ionisation potential. This is probably due to the polarising effect of the cation on the anion. Such interaction was reflected in the empirical dependence of the efficiency of decomposition of salts of the same type on the ratio of the ionisation potentials of the cations[1,36]:

$$G = G_A E_A + G_c E_c \frac{I_{M_1^+}}{I_{M_2^+}} \quad , \qquad (12)$$

where G_A and G_C are the efficiencies of decomposition of the salts calculated per 100 eV of energy absorbed solely by anions and by cations respectively, E_A and E_C their ionicities, and the I the ionisation potentials. This formula describes well the radiolysis of several halogenates at not very high temperatures (Fig. 1).

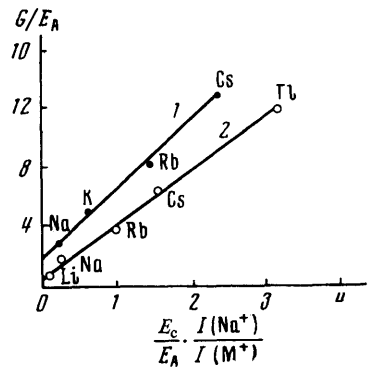

Figure 1. Dependence of radiolysis of salts on ionicity of anion and cation allowing for ionisation potential of cation[1]: 1) chlorates; 2) bromates.

Where ionisation processes predominate in the formation of the primary products, increase in their *electron affinity* involves a decrease in the radiolytic decomposition of the salts. This rule is illustrated by the selenates, sulphates, and carbonates of alkaline-earth metals (barium, calcium). In these compounds the primary products of radiolysis are the radical-ions SO_4^-, SeO_4^-, and CO_3^-, whose relative electron affinities are approximately 1 : 1.3 : 2§. The total yield of paramagnetic species from the salts follows the same sequence.

Where the formation of the primary radiolysis products involves rupture of bonds in the anion, the subsequent radiation processes depend on the electron affinity of these products. Alkali-metal nitrates, chlorates, bromates, and iodates can be included in this group of salts (with a readily broken bond in the anion). In this case increase in the electron affinity of the primary products is accompanied by an increase in the overall efficiency of decomposition of the salt. Thus because ClO_2 in chlorates possesses a greater electron affinity than does NO_2 in nitrates, the reaction

$$ClO_2 + e^- \rightarrow (ClO_2^-)^* \rightarrow ClO^- + O \qquad (13)$$

goes more strongly than does

$$NO_2 + e^- \rightarrow (NO_2^-)^* \rightarrow NO^- + O \; . \qquad (14)$$

Therefore the total yield of radiolysis products should be higher (under the same conditions) e.g. in potassium chlorate than in potassium nitrate, as is observed experimentally. The electron affinity of ClO_2 actually governs reaction (13) to some extent. However, the final yield of radiolysis products from reaction (14) largely depends on competition between deactivation of the excited state and dissociation of $(NO_2^-)^*$ into NO^- and O. Salts of this type conform to the relation

$$A_1/A_2 = K \frac{G_1(O_2)}{G_2(O_2)} \; , \qquad (15)$$

where A_1 and A_2 are the electron affinities of the primary products of radiolysis in the salts, and K is a constant representing all the factors other than electron affinity that influence the radiolysis (type of cation, free volume of lattice, energy of bond, etc.). In the above salts, for example, $A_{NO_2} = 1.62$ and $A_{ClO_2} = 3.43$, while $G(O_2)_{KClO_3} = 2.0$ and $G(O_2)_{KNO_3} = 0.8$.[31] Formula (15) is probably general in character, and can be used for the approximate comparison of radiation resistance in series of analogous salts of the second group.

The above examples show that radiation-chemical processes in salts, and hence the yield of individual products, depend on many factors governing the individual and collective interactions in the undisturbed and irradiated crystal lattice.

The linear energy transfer and the dosage rate are also very important in radiolysis[37-45]. Several investigations have recently been made on these aspects, including experiments on the exposure of various salts to heavy accelerated particles. For example, the bombardment of nitrates with protons changes substantially the rate of formation of nitrite, the initial yields of which are 0.50, 0.92, 1.65, and 2.00 for sodium, rubidium, caesium, and potassium nitrates respectively[38-41]. The γ-irradiation of these salts results in lower initial yields—approximately 0.3, 0.6, and the range 1.0–1.2 for the potassium and caesium salts[27,31].

Exposure of compressed pellets of sodium nitrate to protons produces a maximum yield of nitrite if the specimens are at +180°C.[40,42] At the same time a monotonic decrease in $G(NO_2^-)$ from 1.6 to 0.6 is observed with increase in the linear energy transfer from 2 to 6 eV $Å^{-1}$. At lower temperatures the yield of nitrite first increases and then falls with increase in the linear energy transfer (Fig. 2). These effects are well explained by the enhanced probability of reverse processes with large linear energy transfers (too high density of primary defects in the track), which ultimately lowers $G(NO_2^-)$. It is assumed further that local heating in the track tends to accelerate the radiation-chemical processes. Two regions of radiolysis are therefore distinguished: in the low-temperature range (the track is at a higher temperature than the matrix) local heating in the tracks is of decisive importance; in the high-temperature region the

§ The electron affinities were taken for the species in the gas phase (from standard tables).

yield of radiolysis products is affected mainly by processes of recombination in regions having a high content of primary products (the yield $G(NO_2^-)$ decreases).

It has been concluded[43] from a study of the radiolysis of alkali-metal azides, perchlorates, and nitrates by cobalt-60 γ-quanta and by protons that the variation in yield of products cannot be explained by thermal effects in the track even with large linear energy transfers. It was also shown that the bombardment of azides, nitrates, and especially perchlorates by protons diminishes the dependence of the yield on the free volume of the unit cell.

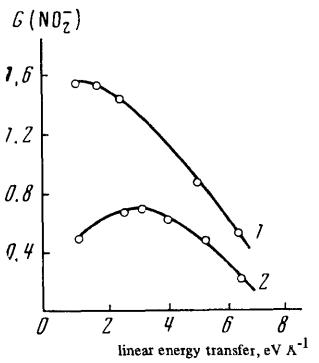

Figure 2. Variation in yield of nitrite in proton-irradiated compressed sodium nitrate pellets for radiolysis at: 1) 180°C; 2) 25°C[40].

Several investigators prefer to explain the variation of yield with linear energy transfer solely by thermal effects in the tracks[37,38]. It was also suggested that charges may be displaced in the region of the tracks, with intensified dissociation of lattice ions[39].

The effects of dosage rate on radiation-chemical processes in various salts involve problems closely similar to the influence of linear energy transfer on yield, but have not yet been studied in adequate depth. Most of the relevant publications reveal no variation in yield at different dosage rates[39,44-50]. For example, variation in the rate of electron irradiation from 10^{17} to 10^{20} eV g^{-1} s^{-1} produces hardly any change in $G(NO_2^-)$ in potassium, sodium, caesium, and lead nitrates[48], a conclusion supported by other work[46,47] for a wider range of dosage rates (10^{15}–10^{20} eV g^{-1} s^{-1}) and other forms of radiation. Similar conclusions can be reached also for chlorates and bromates[49,50].

The above examples still do not give complete clarification of this field. Thus there are indications that yields of primary radicals vary with different intensities of self-irradiation in radioactive alkaline-earth metal sulphates[51-53]. Experiments with strontium sulphate crystals exposed to cobalt-60 γ-quanta have also shown that at room temperature the radical concentration ratio $C_{SO_4^-}/C_{SO_3^-}$ decreases from 2.9 to 2.1 with increase in the dosage rate from 6.2×10^{13} to 6.2×10^{16} eV g^{-1} s^{-1} (in both cases the absorbed dose was $\sim 10^{20}$ eV g^{-1}). At low dosage rates the total concentration of paramagnetic centres increases at the same time by almost 30%. The observed effects are probably caused by accelerated recombination of radicals in "hot zones" (or points), whose concentration is higher at high dosage rates[54].

The nature of the cation can exert a great influence on primary radiation-chemical processes (in series of salts of the same type, e.g. alkali-metal nitrates). Several workers consider that the yield of radiolytic decomposition products from the anion depends not only on its ionicity but also on interaction of the cation with the radiation[30,31,33,55]. Ionisation of the cation and the transfer of excitation energy (charge) from cation to anion play an important part here[1,33,56].

In concluding this Section we note that such factors as degree of dispersion, pressure, and temperature also affect the occurrence of radiation-chemical processes in crystals of inorganic salts. Increase in the dispersity of crystalline nitrates is accompanied by increase in $G(NO_2^-)$, an effect attributed to oxygen trapped in the crystal surface[55], which usually promotes the reverse reactions. Furthermore, gaseous products may migrate to the surface of fine particles, where they may react chemically among themselves and with the surrounding medium, as has been observed in the radiolysis of powdered succinic acid[57].

The effect of temperature is largely dependent on the mechanism of radiolysis and the reverse reactions, which are accelerated by heating. In sodium, potassium, and rubidium nitrates, for example, the yield of NO_2^- increases with rise in temperature above $\sim$ 130°C[41,57-61]. With sodium nitrate this is attributed[59,60] to an increased probability that excited $*NO_3^-$ ions will break down into NO_2^- and O. In the case of rubidium[41] and potassium[59] nitrates the observed increase in $G(NO_2^-)$ is ascribed to polymorphic transitions in crystals. The irradiation of potassium[16], barium, calcium, and strontium sulphates at high temperatures stimulates the breakdown of excited sulphate ions resulting from the recombination of primary SO_4^- radical-ions with electrons:

$$SO_4^- + e \rightarrow \overset{*}{SO_4^{2-}} \rightarrow SO_3^- + O^-(O + e)\,. \qquad (16)$$

A reaction of type (4) without destruction of $*SO_4^{2-}$ occurs between −196° and −50°C. There are examples in which temperature has hardly any effect on radiolysis. Thus the yields of Cl, ClO^-, Cl_2^-, O_2^-, and ClO_2 in potassium chlorate remain almost unchanged between 77° and 300°K[58].

Changes in the crystal lattice caused by pressure have an appreciable influence on the yields of radiolysis products, owing to the slowing down or acceleration of radiation-chemical reactions. Increase in pressure (preliminary compression) usually lowers $G(NO_2^-)$ in nitrates[41]. Analogous effects occur if the irradiated crystals and the surrounding medium (air, an inert gas) are under pressure[61]. The dependence of the yield of radiolysis products on pressure and temperature (both these parameters usually vary in experiments) is quite complex, and largely determined by the mechanism of primary and secondary reactions[61].

All the above features of the radiolysis of inorganic compounds depend in considerable measure on the presence of impurities, which are directly or indirectly involved in radiation-chemical processes.

III. EFFECT OF WATER OF CRYSTALLISATION ON RADIATION-CHEMICAL PROCESSES IN CRYSTALS

The effect of water of crystallisation (which can also be regarded as an impurity in the matrix of the main material) on radiolysis was first noted in 1952 during an

investigation of the photochemical decomposition of lanthanum nitrate[62]: the crystal hydrate was found to decompose more rapidly than the anhydrous salt. Somewhat later a similar effect was observed in the same salt on exposure to γ-quanta[46]. Baberkin and Proskurin then undertook a detailed study of the radiolysis of a series of hydrated nitrates of bivalent cations[63,64]. On exposure to cobalt-60 γ-rays at room temperature the tetrahydrate of calcium nitrate decomposed several times more rapidly than the anhydrous salt (Table 1).

Table 1. Effect of water of crystallisation on the radiolysis of calcium nitrate[63].

Compound	$G(NO_2^-)_{part}$	$G(O_2)_{part}$*
Cryst. $Ca(NO_3)_2$	0.25	—
Cryst. $Ca(NO_3)_2.4H_2O$	1.50	0.37±0.02
Molten $Ca(NO_3)_2.4H_2O$	0.13	0.02±0.01

* G_{part} represents the yield of radiolysis products taking into account the ionicity and the weight of the component of the hydrate from which they have been formed.

The yield of nitrite in aqueous calcium, cadmium, zinc, and magnesium nitrates varies with the dosage rate of γ-rays[64], passing through a minimum at 0.8×10^{16} eV g^{-1} s^{-1} (dose 7×10^{19} eV g^{-1}) in the case of the calcium and cadmium salts. The other two nitrates show a similar variation in $G(NO_2^-)$, but at an exposed dosage rate of 1.2×10^{16} eV g^{-1} s^{-1}. This is evidently connected with a change in the rate of certain radiation-chemical processes depending on the density of ionisation of the crystals with increase in the linear energy transfer. Furthermore, the increased yield of nitrite was attributed to reactions such as

$$H_2O + e^- \rightarrow H_2O^- \rightarrow H + OH^- \text{ aq.} \quad (17)$$

$$2H + NO_3^- \rightarrow NO_2^- + H_2O\,. \quad (18)$$

On present-day views it is legitimate to introduce these reactions, since the nitrate ion is considerably more efficient than water in capturing electrons.

Study of the radiolysis of sodium nitrate containing various quantities of adsorbed water (this salt is hygroscopic) shows[65] that the yield of the nitrite ion increases smoothly with increase in the content of water molecules in the crystal lattice of the nitrate (Fig. 3). A possible explanation of this increase in yield was the involvement of H and OH radicals of water in the decomposition of the nitrate ion, e.g.

$$NO_3^- + H^\cdot \rightarrow NO_2^\cdot + OH^-\,. \quad (19)$$

More probably increase in the water content of sodium nitrate is accompanied by a diminution of the cage effect, and the reverse reactions involving recombination of NO_2 are inhibited. It must be noted that the investigation was in effect made on the heterogeneous system $NaNO_3$–H_2O; nevertheless the yield of NO_2^- was determined by the energy absorbed not by the salt but by the whole "mixture". When the ionicity of the components is taken into account, therefore, the dependence of $G(NO_2^-)$ on the water content of sodium nitrate may be different.

Formation of H·, OH·, $HO_2^\cdot$, and O_2^-—radicals whose concentration increases with increase in the number of molecules of water of crystallisation—is usually observed in irradiated crystalline hydrates of various salts[66–75].

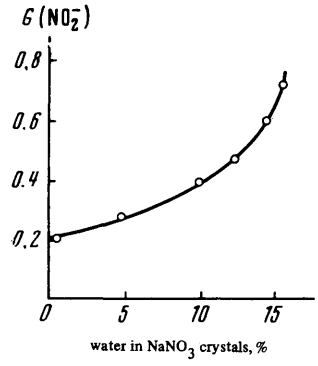

Figure 3. Variation of yield of nitrite in γ-irradiated sodium nitrate with water content of crystals[65].

Furthermore, electron spin resonance has revealed in certain salts (e.g. $BeSO_4.4H_2O$, $BeSO_4.2H_2O$, $CaSO_4.2H_2O$, $ZnSO_4.6H_2O$, $ZnSO_4.H_2O$) a paramagnetic centre (g = 2.000 ± 0.001, H = 4 ± 1 oersteds), probably due to a stabilised electron[69]. Water of crystallisation impedes[68,75] the radiation decomposition of certain salts. Thus Table 2 shows that the total yield diminishes by a factor of ten on passing from the anhydrous salt to the tetrahydrate.

Table 2. Yields of radiolysis products from beryllium sulphate and its crystalline hydrates*[69].

Compound	Temperature	G_{total}	$G_{part}(SO_3^-)$	$G_{part}(H, OH, HO_2)$
$BeSO_4$	room	0.12	0.12	—
	−196°	0.43	—	—
$BeSO_4.2H_2O$	room	0.02	0.045	—
	−196°	0.22	—	3.3
$BeSO_4.4H_2O$	room	0.005	0.016	—
	−196°	0.13	—	0.8

* Irradiation with γ-quanta (^{60}Co); dosage rate 1000 r s^{-1}.

However, radiolysis products accumulate in the same way in beryllium sulphate and in its hydrates: the concentration of paramagnetic centres increases initially, and then decreases slightly from absorbed doses of ~ 3×10^{20} eV g^{-1} (Fig. 4). Similar relations are obtained even at low temperatures, and also if the distribution of absorbed energy in the crystal according to the ionicities of the main substance and of water is taken into account[68,69].

The above results suggest that water of crystallisation exerts some "protective" action on the crystalline matrix. In the radiolysis of sulphates the water molecules may donate electrons to the primary SO_4^- radicals formed on exposure, tending to transform them to the initial state SO_4^{2-}. It is also possible that the water of crystallisation

"takes to itself" part of the radiant energy and disseminates it through the lattice, which ultimately leads to heating of the whole specimen. The hypothesis that products of the radiolysis of water take part in radiation-chemical processes with radicals of the main substance is not considered[68,69], since the yield of radiolysis products in specimens having a high content of water of crystallisation remains depressed as the temperature of the experiments is lowered to −196°C (Table 2), when reactions between radicals can be neglected.

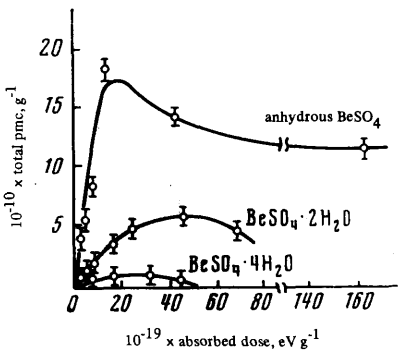

Figure 4. Accumulation of sum of paramagnetic centres (pmc) in γ-irradiated beryllium sulphate and its hydrates at room temperature[69].

Interaction between products of the radiolysis of water molecules probably occurs in the crystalline hydrates of transition metals ($MnSO_4.H_2O$, $NiSO_4.6H_2O$, $CoSO_4.7H_2O$).[73] Thus the suggested mechanism of the radiolysis of manganese sulphate hydrate by γ-irradiation may involve a reaction such as

$$MnO(SO_4) + H_2 \rightarrow MnO_2 + 2H^+ + SO_3^{2-} . \qquad (20)$$

The hydrogen and the intermediate compound of quadrivalent manganese are formed by radiolysis of the initial compound. The crystalline hexahydrate of ammonium iron(II) sulphate undergoes extensive decomposition after treatment with hard X-rays, to give products such as Fe^{3+}, SO_3^{2-}, and H_2 in maximum yields of 1.8, 0.43, and 0.35 respectively[74]. Chemical interaction between products of the radiolysis of water and the main compound is assumed also here.

Aqueous sulphates of copper, magnesium, zinc, and chromium remain almost undecomposed by cobalt-60 γ-rays. The radiant energy is mainly adsorbed by the water of crystallisation, which decomposes into oxygen and hydrogen. In $Li_2SO_4.H_2O$ exposed at the temperature of liquid nitrogen to accelerated electrons (1 MeV), for example, appreciable decomposition of the sulphate ion could not be detected even by such a sensitive method as electron spin resonance[72,75,76].

Although the effect of water of crystallisation on the radiolysis of salts has not yet been finally settled, existing experimental results indicate that the water is able to protect the matrix of the main substance from destruction when the radiolysis products do not undergo chemical reactions with ions or radicals of the compound[68,69]. If, however, water or its radiolysis products are involved in radiation-chemical processes, decomposition of the salts is promoted.

Further investigations on these lines will help to provide a deeper understanding of radiation-chemical processes in crystalline hydrates.

IV. RADIATION-CHEMICAL PROCESSES IN CRYSTALS OF INORGANIC SALTS CONTAINING IMPURITIES

Experimental workers encountered the effect of impurities on the radiolysis of solid compounds literally in the first investigations of radiation-chemical processes in inorganic compounds. However, systematic research on this aspect has been undertaken only recently.

In 1958 Cunningham and Heal expressed the view that impurities and lattice defects have no significant influence on the radiolysis of potassium nitrate[47]. This largely unfounded statement was very soon refuted. For example, not only the yield of nitrite but also the kinetics of the accumulation (annealing) of the radiolysis products are changed in potassium nitrate contaminated with strontium, lead, thallium, and sulphate ions[77]. The strongest effect is exerted by strontium and lead(II) ions, which produce cationic vacancies in potassium nitrate (the impurities were introduced into the crystals by fusing the nitrates and potassium sulphate with potassium nitrate at 340°C). It was also noted that thallium(I) ions, which are electron donors, increase the yield of nitrite, whereas strontium and lead(II) ions lower the yield. This is due to competition between impurities and radiolysis products for the electrons involved in the radiation-chemical processes. It is significant also that sulphate ions, which give anionic vacancies, hardly affect the rate of annealing of defects, whereas lead and strontium impurity ions accelerate the annealing.

Tervalent rare-earth metal ions inhibit the radiolysis of crystalline nitrates; those which are able to pass into the quadrivalent state (primarily Ce^{3+} and Pr^{3+}) are less effective[78]. Donor–acceptor interaction between impurity and radiolysis products probably occurs here also. The authors assume, as in their early papers[77,79], that the inhibition of radiolysis by impurity rare-earth metal ions is due to the resulting cationic vacancies, which facilitate recombination processes in the irradiated system.

A similar view was developed[80] in an investigation of the radiolysis of sodium nitrate contaminated with calcium ions replacing sodium isomorphously in the crystal lattice. However, decomposition of the nitrate is intensified in this case, although the proportions of the radiolysis products remain unchanged.

Impurities in potassium nitrate crystals which should produce neither cationic nor anionic vacancies (potassium hydroxide was introduced by fusion) nevertheless do affect radiolysis[81,82]. The yield of nitrite in potassium nitrate contaminated with the hydroxide is higher than in pure specimens. Furthermore, the yield at a dosage of $\sim 2.5 \times 10^{18}$ eV g^{-1} first increases with the alkali concentration, and then decreases, approaching the value of $G(NO_2^-)$ for the pure salt. These results are explained by the effect of hydroxide ions on the localisation and the decay of excited states of nitrate ions. It is also possible that hydroxide ions may take part in radiation-chemical reactions with radiolysis products of potassium nitrate.

The radiolysis of potassium nitrate is inhibited by contamination with nitrite and perchlorate ions[83]. The yield of nitrite in the impure crystals is 1.15, which compares

with the 1.7 obtained[81] for the pure crystals. A mechanism of acceptor–donor interaction[71-80] probably operates here.

According to the views developed earlier, univalent anionic impurities, included isomorphously in the lattice of potassium nitrate, compete with radiolysis products in reactions involving electrons, which may either accelerate or retard (depending on the mechanism of radiolysis) breakdown of the crystalline matrix.

It has also been shown[83] that the yields of radiolysis products from potassium nitrate (NO_2^- and O_2) increase sharply at temperatures above 128°C, when potassium nitrate undergoes a transition from a rhombic to a trigonal structure.

Lykhin and Boldyrev made a detailed investigation of the radiolysis of sodium nitrate contaminated with silver, thallium(I), strontium, and lead(II) ions, introduced into the crystals by fusing the nitrates with sodium nitrate[84]. The products were exposed to X-rays in air. The experiments support the main concept of the authors that bivalent ions facilitate breakdown of an excited nitrate ion by generating cationic vacancies in the potassium nitrate lattice. This occurs because the cage effect diminishes in the vicinity of a cationic vacancy. Therefore the yield of the nitrite ion is increased in sodium nitrate contaminated with bivalent cations. On the other hand, vacancies promote annealing reactions (the yield falls), which occur at an appreciable rate at high temperatures. As a result of competition between these processes the yield of nitrite becomes even smaller in the impurity crystals, relative to that in the pure crystals, as the temperature of irradiation is raised (Fig. 5).

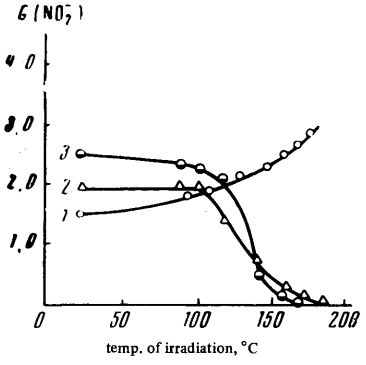

Figure 5. Dependence of yield of nitrite on temperature of irradiation[84] for: 1) pure KNO_3; 2) KNO_3 + 2.5 mole % Sr^{2+}; 3) KNO_3 + 2.5 mole % Pb^{2+}.

Several workers have observed that annealing processes are accelerated in crystals in which impurities have created cationic vacancies (and thereby facilitated the movement of products of radiolysis)[15,59,77,85-87]. Thus Mohanty has demonstrated that aluminium ions present in lead nitrate increase appreciably the rate and the degree of annealing of radiation disturbances in exposed crystals[87]. Contamination with bivalent cations (strontium, lead) accelerates considerably annealing processes in potassium nitrate[59,77]. The effect of impurities is especially noticeable during the initial periods of annealing (Fig. 6). It is significant that the sulphate ion, which should form anionic vacancies, has no effect on annealing (curves *1* and *2*).

An investigation of annealing in proton-irradiated crystals of sodium, potassium, and rubidium nitrates (contaminated with calcium, cadmium, and strontium) has led to the conclusion[15] that annealing is decisively affected by impurities producing cationic vacancies, on which intermediate products of radiolysis may even "accumulate". The donor–acceptor properties of the impurities are regarded as of no significance. This view cannot be fully accepted, since the acceleration of annealing observed in crystals of alkali-metal nitrates is not entirely unambiguous.

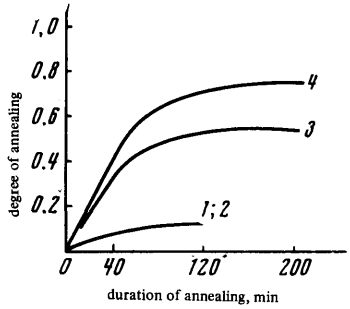

Figure 6. Effect of impurities on the post-radiation (absorbed dose 20.8 Mrad) annealing of potassium nitrate crystals at 130°C[85]: 1) pure specimen; 2) KNO_3 + 1.5 mole % K_2SO_4; 3) KNO_3 + 2.5 mole % $Sr(NO_3)_2$; 4) KNO_3 + 2.5 mole % $Pb(NO_3)_2$.

The slowing down of annealing processes in rubidium and caesium nitrates contaminated with carbonate ions (0.6–3 mole %) is attributed to an increase in the yield of nitrite when the crystals are irradiated with protons[88]. The carbonate ions are assumed to be balanced in the nitrate lattice by an increase in the number of interstitial ions and a decrease in the number of cationic vacancies. The increased yield is therefore due to a slowing down of radiation annealing on cationic vacancies. In addition to this mechanism, colour centres formed on anionic vacancies (some result from the incorporation of carbonate ions) may prevent the recombination of electrons with radicals by promoting the breakdown of radical products to nitrite.

The decrease in rate of radiolysis of sodium nitrate containing isomorphous silver nitrate as impurity is explained by Cunningham solely by the acceptor properties of silver ions[89,90].

Similar conclusions have been reached for the radiolysis (by X-rays) of lead azide containing a homophase impurity (silver or copper ions)[91,92]. The radiation decomposition of the azide is accelerated quite considerably by silver ions, the effect tending to saturation at an impurity content of ~ 10 mole %. The introduction of copper ions into the azide produces a sharp decrease in rate of radiolysis proportional to their content. Experiment shows that radiolysis is accelerated by impurities that increase the concentration of electrons in the material,

and slowed down by impurities that diminish the number of free electrons. This rule holds, of course, only if electrons are involved in reactions tending to increase the yield of radiolysis products[29,79,93].

We cannot in general confine our attention to the donor–acceptor action of impurities when considering the effect of foreign ions on radiolysis. Indeed, change in the nature and concentration of various defects in the preparation of crystalline compounds may affect also the fate of excited states. This indicates the complicated and multistage character of the influence of homophase additives on the radiolysis of solid compounds. When the impurity enters the lattice isomorphously, replacing ions of the main substance at lattice points and producing no vacancies, the impurity may act mainly by taking part in radiation-chemical reactions. For example, the increase in the yield of radicals observed in experiments with irradiated crystals of potassium perchlorate is due to the diminished probability of the recombination of electrons with radicals caused by the impurity silver ions, which act as acceptor centres for electrons[94]. But the effect of impurity copper ions in accepting electrons is probably balanced by a diminished concentration of anionic vacancies, and the copper ions act only as centres of recombination:

$$ClO_4^- + Cu^{2+} + e \rightarrow ClO_4 + Cu \rightarrow ClO_4^- + Cu^+ . \qquad (21)$$

As a consequence of these reactions the degree of decomposition of potassium perchlorate decreases[94].

The results of experiments with impure crystals can sometimes be explained by redistribution of the radiant energy and the localisation of electrons (holes) in specimens with defects. Thus powdered crystalline barium sulphate contaminated with nitrite and nitrate ions exhibited inhibited radiolysis of the main substance with intense decomposition of the impurity. This is explained by a hole–exciton mechanism of transfer to the impurities of the energy absorbed by the whole crystal lattice. Defects such as vacancies formed in the vicinity of an impurity may serve as sites for the localisation of holes and the destruction of excitons, which will lead to decomposition of the impurity[95–98].

Preferential radiolysis of impurities has been observed in crystals of sodium sulphate, lithium sulphate monohydrate[99], and strontium phosphate[100]. Various impurities of both donor and acceptor types—nitrite, sulphite, nitrate, and formate ions, hydrogen peroxide, methanol, benzene—were studied in the latter work. In all cases the impurity ions underwent considerable radiolysis. Their effect on the course of radiolysis of the carrier material largely depended on their donor–acceptor properties and on the transfer to the impurities of the energy absorbed by the crystal.

One consequence of the work on the radiolysis of contaminated barium sulphate is to establish that energy absorbed in an irradiated crystal can be transmitted to considerable distances[97]. Such a process is evidently quite possible, since energy transfer has already been observed between spatially separated rare-earth metal ions in crystals of the chlorides and bromides of various elements[101,102].

A purely electron–hole mechanism of the effect of impurities on the concentration of radiation defects has been postulated[103]. The number of localised holes in γ-irradiated α-alumina at 77°K increases proportionally to the content of the impurity ion Ti^{4+}. The latter, being located at an Al^{3+} lattice point, captures an electron, thus presenting its recombination with a hole.

There are indications that radicals formed from impurities may interact chemically. In fused potassium chloride crystals containing hydroxide and cyanide or nitrite impurity ions, for example, photolysis was followed by formation of a radical type of impurity HNO_2^-. Such reactions as

$$\rightsquigarrow HO^- \rightarrow H^\cdot + O^-$$

and

$$H^\cdot + NO_2^- \rightarrow HNO_2^- \qquad (22)$$

probably occur in this system[104].

At the conclusion of this Section it must be noted that the concept of the donor–acceptor effect of impurities on radiolysis, the vacancy mechanism, the transfer of the radiated energy from the matrix to impurity ions, and the mutual stabilisation of defects have long been successfully used in investigating the radiolysis (or coloration) of alkali-metal halide crystals. The literature on this problem is vast, so that it is sufficient to give merely a few examples. Thus transition-metal impurities (nickel, copper) in sodium chloride accelerate the decay of F-centres[105]. Traces (0.01 wt.%) of chromium, manganese, iron, cobalt, and nickel are electron traps and sources of vacancies (potassium chloride and bromide crystals)[106]. Contamination with sulphate, nitrate, and hydroxide ions diminishes the probability of the formation of F-centres, since radiolysis products of the impurities (O_2^-, O, etc.), being centres for the capture of electrons, compete with anionic vacancies for electrons[107]. A detailed analysis has been made[108,109] of the effect of bivalent cations (Pb^{2+}, Sr^{2+}, Ca^{2+}) and anions (S^{2-}) on the kinetics of accumulation and the stability of colour centres in potassium chloride and other alkali-metal halide crystals. Fairly complete reviews of the effect of impurities on the accumulation of various colour centres in alkali-metal halide crystals can be found[20–24,110–112].

In all cases the results have been explained (independently of the test material) in terms of the effect of vacancies created in the crystal lattice by the introduction of impurities. The donor–acceptor properties of impurities and ions of the main substance have also frequently been considered. Mechanisms involving the transfer of excitation energy from the lattice to impurities have been far more rarely analysed, although the role of such processes in a solid is quite large[3–9,20,113].

Little study has been made of the participation of impurities in intermediate reactions with radicals produced by irradiation of the crystalline matrix, the effect of the mode of inclusion of the impurity in the lattice (isomorphous or non-isomorphous), and other questions.

V. RADIOLYSIS OF MIXTURES OF INORGANIC SUBSTANCES

Although the effect of foreign impurities on radiation-chemical processes has now been studied fairly thoroughly, little work has yet been done on the radiolysis of salts with heterophase additions[90,114–118]. The first paper on the effect of impurities forming an independent phase on the radiolysis of inorganic compounds appeared only in 1967[114]. This showed that powdered thorium dioxide and nickel and zinc monoxides (particle size 90–140 μm) added in amounts of 1.5–7 mole % accelerate the radiolysis of ammonium nitrate by X-rays (the degree of radiolysis was assessed

from the total gas evolution). The efficiency of catalysis by the additives varied in the sequence

$$ThO_2 > ZnO > NiO > \text{pure } NH_4NO_3 .$$

The electronic work function φ in these oxides increases from nickel to thorium. Impurities of low work function were regarded as donors of electrons in the irradiated system. Therefore the above additives, by raising the concentration of electrons, accelerate the intermediate stages of radiolysis, which leads to the more intense gas evolution observed experimentally.

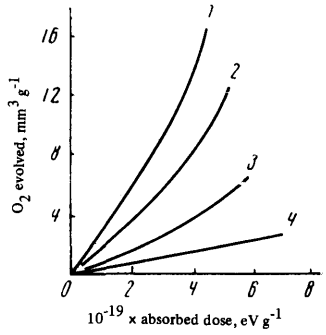

Figure 7. Radiolysis of sodium nitrate by X-rays at room temperature: 1) $NaNO_3$ (+3.5 mole % ZnO); 2) $NaNO_3$ (+3.5 mole % ThO_2); 3) pure $NaNO_3$; 4) $NaNO_3$ (+3.5 mole % CoO).[115]

This conclusion was confirmed by these workers on several new systems[92,115]. Thus Fig. 7 illustrates the radiation-chemical decomposition of potassium and sodium nitrates containing mechanically admixed powdered oxides of thorium, nickel, cobalt, and zinc. In these experiments, too, impurities of low work function accelerated radiolysis, and those with high values of φ slowed it down. By analogy with homophase additives, the impurities probably affected reactions such as[115]

$$\rightsquigarrow NO_3^- \rightarrow NO_3 + e , \quad (23)$$

$$NO_3 + e \rightarrow NO_3^- + O , \quad (24)$$

$$NO_3^- + e \rightarrow \overset{*}{N}O_3^{2-} \rightarrow NO_2^- + O^- . \quad (25)$$

A comprehensive investigation has been made of the effect of heterophase additions on the radiation-chemical stability of lead azide[116,117]. The additives used were the oxides of zinc, cadmium, cobalt, and nickel. The first two accelerate considerably the evolution of nitrogen from the azide when the mixtures are exposed to X-rays. Nickel and cobalt oxides retard the radiolysis of the azide under the same conditions. It was also found that these additives have no effect on the activation energy of radiolysis. From the results of numerous experiments the fully justified suggestion was made[116] that donor–acceptor interactions between the compounds in the mixture undergoing irradiation were of decisive importance. Introduction of a heterophase impurity of donor type increases the steady-state concentration of electrons in the irradiated system, whereas acceptor impurities have the opposite effect. As a result, radiation-chemical reactions involving electrons in silver azide are either slowed down or accelerated, e.g.

$$\rightsquigarrow N_3^- \rightarrow N_3^0 + e , \quad (26)$$

$$N_3^0 + e \rightarrow N_3^- . \quad (27)$$

Analogous effects have been observed in perchlorates[117]. It should also be noted that the donor or acceptor character of impurities is greatly dependent on the type of systems in contact during exposure, and may not coincide with assessments based on the measured work functions of the pure oxides in the absence of irradiation.

Processes entailing the redistribution (and primary distribution) of energy in heterogeneous systems under irradiation (transfer of charges, migration of excitons) should also be very important in these cases. These phenomena accompanying radiolysis can be represented by the proposed[117] empirical relation

$$v_d/v_0 = 1 + f\left(\alpha \frac{I_d}{I_0} - 1\right), \quad (28)$$

where v_0 and v_d are the rates of radiolysis of the pure salt and of the salt with the additive, I_0 and I_d are the corresponding absorbed dosage rates, α is a constant defining the transfer (redistribution) of energy between the components, and f is the fraction by weight of the heterophase additive. Experiments show that the radiant energy may actually undergo redistribution even when particles of the mixtures are in poor contact. The mechanism of such transfer is not yet clear. However, there is direct evidence that radiant energy absorbed in crystalline mixtures is able to migrate at least to distances up to 60 Å.[118]

Heterophase impurities would probably have a weaker effect than similar homophase impurities on the radiolysis of the main substance. For example, the yield of NO_2^- radicals falls with increasing contamination of barium sulphate with the nitrate ion, to reach a minimum when the latter forms a separate phase[97,98]. Hence transfer of the radiant energy, absorbed in the matrix of the main substance, to the heterophase nitrate impurity is difficult. Although heterophase additives are less effective, study of the effect of foreign mechanical inclusions on the radiolysis of various salts is a promising line of research on the radiation chemistry and the physics of solids. Heterophase additives are very easy to "introduce", a factor which may be decisive in work with impurities, limiting the experimental possibilities. Investigations in this field will probably enable new methods to be developed for systematically varying the radiation resistance of various compounds.

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Experiment shows that external actions on a crystal, varying the mobility and the steady-state concentrations of charged species and excited states, change the rate of radiation-chemical processes. The direction of these changes can be predetermined and even controlled if the mechanism of radiolysis is known. The introduction of impurities into a crystal may be an effective method for monitoring and controlling processes of radiolysis.

Analysis of the experimental results shows that several mechanisms have been suggested for the effect of impurities on radiolysis, corresponding to the actual processes occurring in the crystal lattice.

1. Donor–acceptor interaction of impurity and products of radiolysis. The specific effect of an impurity is

largely dependent in this case on radiation-chemical processes in the exposed crystals. For example, stages of radiolysis having a radical mechanism or involving excited states will be relatively insensitive to donor or acceptor impurities.

2. Generation of vacancies by impurity ions. Vacancies may provide a site for the localisation of electrons or holes capable of increasing the mobility of the products of radiolysis, which will accelerate recombination processes. The same defects can often have opposite effects on the rate of radiolysis. For example, the addition of cadmium ions, which create cationic vacancies in the lattice of silver salts, enhances the radiation resistance of silver oxalate[119] but promotes decomposition of silver carbonate[119-121]. In this case the mechanism of the radiolysis of the specific compound is also decisive.

3. Transfer of the energy of the radiation absorbed by the lattice to the impurity, as occurs in organic systems[113]. The impurity itself decomposes, protecting, as it were, the main compound.

4. Acceleration and extension of the radiolytic decomposition of salts by interaction of radiolysis products of "impurity" molecules and matrix components. This mechanism is typical of crystalline hydrates or compounds with considerable inclusions of water molecules.

Research workers have so far paid less attention to the role of impurities in the intermediate stages of radiation-chemical reactions. The mechanism of the introduction of foreign atoms into the lattice, and hence the specific mode of participation of the impurity in radiation and radiation-chemical processes, have not always been studied in detail.

The preparation of specimens—quenching, thermal and radiation conditioning—is very important in radiation-chemical investigations. Due attention will probably also be paid to this factor in future work.

In conclusion it must be noted that the action of an impurity is usually a complicated multistage process: only in very rare cases is its role determined by a single one of the above mechanisms. And the first advances in this direction support the hope that reliable methods (and a theoretical basis) will be developed for controlling the radiolysis of inorganic compounds.

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Structure and Behaviour of Aluminate Ions in Solution

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The most important published data on the composition and structure of aluminate ions in solutions of different concentrations and pH values are systematised and analysed. The views of various workers on the types of interaction present in aluminate solutions are discussed. The significance of different hypotheses and models of mononuclear and polynuclear aluminate ions is examined in the light of the results of recent physicochemical investigations.
The bibliography includes 154 references.

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I. INTRODUCTION

The structure of aluminate ions in solution is among the most important problems in the chemistry of aluminium and also in the production of alumina by alkali methods [1,2]. Even the fundamental nature of these solutions (colloidal [3-14], or true solutions [15-25]) remained controversial until quite recently. The lack of general agreement on the nature and structure of aluminate ions in solution is due to the complexity of their behaviour and to the inconsistency of many of the experimental results which have been reported. Nevertheless, the most reliable experimental results appear to be consistent with the ionic model of aluminate solutions [1,2,19-25].

However, the problem of the composition and structure of the aluminate ion in solutions of different concentrations and pH values is still not finally settled. Hence, the structural differences between unsaturated and supersaturated solutions, and the decomposition mechanism of aluminate solutions, are also still unclear [1,2,19-23,26-28].

It is generally agreed that the predominant species in aluminate solutions (at least, in unsaturated solutions at high pH) is the mononuclear aluminate ion [22-26,29-32], although divergent views are held on the structure of this ion. The following compositions have been proposed: AlO_2^-, [22,29-31,33-41] $AlO(OH)_2^-$, [22,29-30,33] $Al(OH)_4^-$, [22,24-26,29-31,33,42-65] and $Al(OH)_4.2H_2O^-$. [19,51,66] Several workers [22,29,30,33] believe that the first three types of mono-aluminate ion can coexist in aluminate solutions as singly-charged anions with different degrees of hydration:

$$Al(OH)_4^- \rightleftharpoons AlO(OH)_2^- + H_2O \rightleftharpoons AlO_2^- + 2H_2O, \qquad (1)$$

the equilibrium being shifted towards the right by increase of temperature and concentration.

The formation of measurable amounts of ions of the $Al(OH)_5^{2-}$ and $Al(OH)_6^{3-}$ type, reported in most of the textbooks and monographs on the chemistry of aluminium, is not confirmed by experimental results [23,24].

Published information on the presence and on the existence region of poly-nuclear hydroxo aluminium complex anions in alkaline solutions is scarce, and contradictory [22,25,28,31,32]. However, this type of information is highly relevant both to the behaviour of metastable aluminate solutions and to the more general problem of poly-nuclear complex formation in solutions [67,68]. Furthermore, the control of industrial processes for the production of alumina requires a full understanding of the structure of the aluminate ions and of the phenomena which occur in supersaturated solutions.

The aim of this review is to survey and discuss critically the most important recent work which can serve as a basis for the further development of our views on the structure and behaviour of aluminate solutions.

II. RESULTS OF SPECTROSCOPIC INVESTIGATIONS

A wide range of spectroscopic methods has been applied to the study of the composition and structure of aluminate ions: Raman spectroscopy (RS), [31,39-41,52,62,63] infrared spectroscopy (IRS), [39,63,69,70] ultraviolet spectroscopy (UVS), [28,32,53,57,58,66] nuclear magnetic resonance (NMR), [30,51,60,61,63,71,72] and also X-ray [73,74] and acoustic (ultrasonic) spectroscopy [71,75].

The earliest reported (1952) RS spectra of dilute aluminate solutions [52] contained two lines (310 cm^{-1} and 615 cm^{-1} respectively) with relative intensities in the ratio of 1 : 5. The authors did not comment on the polarisation of these lines. From these results, they concluded that the $Al(OH)_4^-$ ion corresponds to the T_d model, although they were unable to observe the $\nu_3(F_2)$ line at 720 cm^{-1} which that model predicts. They merely state that the line is too weak to be observed experimentally. Further evidence in favour of the tetrahedral configuration was obtained from the values of the force constants calculated [76] by Hertzberg's method from the T_d model, which agreed satisfactorily with the values calculated from Gordy's equation [77] relating force constants and electronegativities in tetrahedral molecules. It should be noted, however, that neither the T_d nor the O_h symmetry is fully consistent with the observed [52] spectra of the aluminate ion, since the former symmetry should give four Raman-active (normal) vibrations (including two at similar energies), and the latter symmetry should give three active vibrations [52,78]. In any case, conclusions made from Raman spectra should be confirmed by IR spectroscopy whenever possible.

Lanaspeze and Eyraud[62] agreed with these conclusions[52], although they observed only one ν_1 line (at 615 cm^{-1}) in the Raman spectra of their aluminate solutions. They, also, did not comment on the polarisation of this line.

More recent work[31,39-41,63] on the Raman spectra of aluminate solutions covers a range of pH values and concentrations, as well as exploiting the helium–neon laser as a source of radiation. Only one of these investigations[63] is in partial agreement with the previous work[52,62]. Carreira and coworkers[39] found that at pH $\geqslant$ 13 the Raman spectra contain only one line, at 628 cm^{-1}, with a depolarisation ratio close to zero. At lower pH values they observed three lines (540, 625, and 830 cm^{-1}) and they found that the 830 cm^{-1} line is polarised. All these findings were confirmed (within measurement error) by other workers[40,41], who reported lines at 530, 620, 630, and 825 cm^{-1}. Some experimental data, together with the vibrations expected for the most likely symmetries with allowance for the selection rules and for line polarisation, are shown in Tables 1–4 and in Fig. 1.

Table 1. Raman and i.r. spectra of 4 M aluminate solutions (after Carreira and coworkers[39]).

pH	ν, cm^{-1} exper.	ν, cm^{-1} calc.	Depolarisation ratio	Line width $\Delta\nu$, cm^{-1}	Symmetry and activity of vibrations in Raman or i.r. spectra	
10.2	830	910	0	25	ν_1 (A_{1g} Raman)	O_h
	625	—	6/7	40	ν_2 (Eg Raman)	
	1240	1209	—	35	ν_3 (F_{1u} i.r.)	
	—	606	—	—	ν_4 (F_{1u} i.r.)	
	540	—	6/7	30	ν_5 (F_{2g} Raman)	
	—	—	—	—	ν_6 (F_{2u} i.r. inactive)	
13	628	—	0	35	ν_1 (A_1 Raman)	

The results given in Table 2 show a spontaneous change in the intensity of the Raman spectra, accompanied by a change in pH, if the pH of the solution is below 12.5–13.0. According to Tables 2 and 3, and Fig. 1, the bands at 530 and 825 cm^{-1} become weaker, and the band at 620 cm^{-1} becomes stronger, as the solution becomes progressively more alkaline. It is evident from Table 4 that in the pH region 8.3–13 the presence of three Raman lines cannot be reconciled with the $D_{\infty h}$ symmetry of the AlO_2^- ion for any of the models considered. Since none of the RS lines is found in the IRS (Table 1), we may assume that the aluminate ion is centrosymmetric[76,79]. Hence, the presence of $AlO_2^-(C_{2v})$ and $Al(OH)_4^-(Td)$ anions in solutions of pH $\leqslant$ 13 is not experimentally confirmed. The existence of aluminate ions having the O_h symmetry in weakly alkaline solutions is not eliminated by the spectra, but it is not confirmed by the vast majority of experimental results[23,24].

Thus, by comparing experimental results[31,39-41] with the calculated results of Table 4 we are led to the conclusion that solutions of pH $\leqslant$ 13 contain either $Al(OH)_4^-$ ions with the D_{4h} symmetry or polymeric associations, for which the linear group factor is isomorphous with the $D_{2h}(XY_4Z_2)$ or $D_{4h}(XY_4Z_2)$ point group. In the latter case the vibrations should be the same as in the octahedral $Al(OH)_6^{3-}(O_h)$ molecule if the transition from the octahedron to the polymer does not produce splitting of the degenerate vibrations or if the splitting is masked by solvent effects.

The presence of a planar $D_{4h}(XY_4Z_2)$ polymer in aluminate solutions seems unlikely. Therefore, the experimental results indicate an $Al(OH)_4^-$ structure, with D_{4h} symmetry, or an octahedral polymeric structure, $[Al(OH)_4]_n(OH)_2^{(n+2)-}$, with D_{2h} symmetry. However, the observed ageing of aluminate solutions accompanied by slow changes in pH,[30,31,48,49] and also the electrochemical measurements reported by Plumb and Swaine[78], convincingly point to the presence of polymeric aluminate ions in weakly alkaline solutions (pH $\leqslant$ 13).

Table 2. Raman spectra of 3 M aluminate solutions as a function of ageing time[40].

Time, h	pH	ν, cm^{-1}	I*
0.5	8.30	530	45
		825	20
		620	12
8.0	8.46	530	43
		825	18
		620	17
30	9.50	530	41
		825	12
		620	29
50	10.0	530	40
		825	10
		620	35
60	10.0	530	40
		825	10
		620	34

*Intensities relative to that of the 630 cm^{-1} line (taken as 100) for solutions of pH 13.0.

Table 3. Raman spectra of 3 M aluminate solutions[40].

pH	J_{530}	Line width $\Delta\nu$, cm^{-1}	J_{620}	Line width $\Delta\nu$, cm^{-1}	J_{630}	Line width $\Delta\nu$, cm^{-1}	J_{825}	Line width $\Delta\nu$, cm^{-1}
10.05	35	30	20	45	—	—	20	26
10.52	33	—	24	—	—	—	20	—
10.74	32	—	30	—	—	—	19	—
11.03	31	30	35	90	—	—	18	35
11.21	29	—	40	—	—	—	17	—
11.50	28	—	46	—	—	—	16	—
11.75	27	—	50	—	50	—	14	—
12.02	26	25	60	80	60	80	—	—
12.23	22	—	66	—	66	—	12	48
12.49	18	—	—	—	74	—	9	—
12.71	8	—	—	—	82	—	6	—
12.98	0	—	—	—	99	—	0	—
13.90	0	—	—	—	100	65	0	—

In the region of pH $\geqslant$ 13, the requirement of a single, polarised line at 630 cm^{-1} is satisfied only by the AlO_2^- structure with $D_{\infty h}$ symmetry (Tables 1 and 4, Fig. 1). This conclusion is confirmed by the absence of isotopic shifts in the spectra of deuteriated aluminate solutions at pH $\geqslant$ 13 (Fig. 1), which shows that in these solutions practically none of the protons are combined with aluminium through oxygen. On the other hand, the shift of the Raman bands towards lower frequencies following deuteriation at pH $\leqslant$ 13 (Fig. 1) justifies the conclusion[31,39-41] that under these conditions the Al ligands are hydroxyl ions.

The Raman spectra of potassium aluminate solutions [41] are practically indistinguishable from those of sodium aluminate. This suggests that the AlO_2^- and $[Al(OH)_4]_n(OH)_2^{(n+2)-}$ ions undergo only outer-spher interactions [80] with the alkali metal cations. Outer-sphere complex formation in aluminate solutions can be represented by the reactions

$$x\,M(H_2O)_y^+ + (OH)_2[Al(OH)_4]_n^{(n+2)-} \rightleftharpoons \{[M(H_2O)_y]_x(OH)_2[Al(OH)_4]_n^{x-n-2}\}, \quad (2)$$

$$M(H_2O)_y^+ + AlO_2^- \rightleftharpoons [M(H_2O)_y]AlO_2, \quad (3)$$

where M is an alkali metal cation.

Table 4. Symmetry and spectroscopic data according to the selection rules for structures similar to the aluminate ion [31,39].

Chemical formula	Точечная группа	I.r. active vibrations	Raman active vibrations	Inactive vibrations
AlO_2^-	C_{2v}	$\nu_1(A_1)$ $\nu_2(A_1)$ $\nu_3(B_2)$	$\nu_1(A_1)$ $\nu_2(A_1)$ $\nu_3(B_2)$	
	$D_{\infty h}$	$\nu_1(E1u)$ $\nu_3(A1u)$	$\nu_1(A1g)$	
$Al(OH)_4^-$	T_d	 $\nu_3(F_2)$ $\nu_4(F_2)$	$\nu_1(A_1)$ 615 cm^{-1}* $\nu_2(E)$ 310 cm^{-1} $\nu_3(F_2)$ 720 cm^{-1} $\nu_4(F_2)$ 300 cm^{-1}	
	D_{4h}	$\nu_4(A2u)$ $\nu_6(Eu)$ $\nu_7(Eu)$	$\nu_1(A1g)$ $\nu_3(B1g)$ $\nu_3(B2g)$	$\nu_5(B2u)$
$Al(OH)_6^{3-}$ (XY_4Z_2)	O_h	$\nu_3(F1u)$ $\nu_4(F1u)$	$\nu_1(A1g)$ $\nu_3(Eg)$ $\nu_5(F2g)$	$\nu_6(F2u)$
	D_{4h}	$\nu_3(A2u)+\nu_3'(Eu)$ $\nu_4(A2u)+\nu_4'(Eu)$	$\nu_1(A1g)$ $\nu_2(A1g)+\nu_2'(B1g)$ $\nu_5(B2g)+\nu_5'(Eg)$	$\nu_6(B2u)+\nu_6'(Eu)$
	D_{2h}	$\nu_3(B1u)$ $\nu_3'(B2u)$ $\nu_3''(B3u)$ $\nu_4(B1u)$ $\nu_4'(B2u)$ $\nu_4''(B3u)$	$\nu_1(Ag)$ $\nu_2(Ag)$ $\nu_2'(B1g)$ $\nu_5(Ag)$ $\nu_5'(B2g)$ $\nu_5''(B3g)$	$\nu_6(Au)$ $\nu_6'(B2u)$ $\nu_6''(B3u)$

*These lines were predicted by Lippincott and coworkers [52].

The large charge of the $[Al(OH)_4]_n(OH)_2^{(n+2)-}$ ion could lead to association of this anionic ligand with several cations. Hence, we could discuss these systems from the standpoint of polynuclear outer-sphere complex formation [81], possibly complicated by inner-sphere interactions in concentrated solutions, which may become significant when the system passes through the full solvation boundary [82].

Moolenaar and coworkers [63] also studied the state of aluminium in alkaline aqueous and deuteriated solutions by RS and IRS methods. They also examined the NMR spectra of ^{23}Na and ^{27}Al, covering the concentration range 0.5–6.0 g-ion litre^{-1} of Al. They were unable to prepare solutions containing appreciable quantities of aluminium at pH $\leqslant$ 13, such as had been prepared by earlier workers [39–41], and, therefore no comparison is possible outside the strongly

The RS and IRS results obtained [63] in aqueous and in deuteriated aluminate solutions at pH > 13 are summarised in Table 5. At aluminium concentrations below 1.5 g-ion litre^{-1} we find four vibrational bands, two of which correspond to infrared-active vibrations (950 and 725 cm^{-1}) and three to Raman-active vibrations (725, 625, 325 cm^{-1}). However, on raising the concentration of aluminate ions beyond 1.5 g-ion litre^{-1} new spectral bands are observed (900 cm^{-1} in the IRS and 705 and 540 cm^{-1} in the RS). The additional, weak Raman lines, which had not been observed by earlier workers [39–41,52], are ascribed [63] to the use of a more powerful source of radiation. None of the strongly alkaline aluminate solutions studied in this work [63] showed any significant ageing effects.

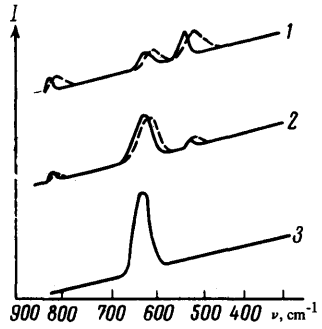


Figure 1. Raman spectra of 3 M aqueous solutions of sodium aluminate [41]: *1*) pH 10.5, *2*) pH 12.7, *3*) pH 12.9. The broken lines correspond to 80% deuteriated samples.

The Raman spectra of strongly alkaline aluminate solutions containing less than 1.5 g-ion litre^{-1} of aluminium are claimed [63] to be consistent with the tetrahedral model of the $Al(OH)_4^-$ ion predicted by Lippincott [52] (see Table 4). The IRS results only partly confirm this claim. According to Table 4, aluminate ions with T_d symmetry should give rise to two lines, both IRS and RS active. One line at 725 cm^{-1} (Table 5) satisfies this condition, but the second broad and weak IR line at 950 cm^{-1} is absent in the RS. This band cannot be seen in the deuteriated solutions because its new position (close to 700 cm^{-1}) is obscured by the strong line at 745 cm^{-1}. The R line at 950 cm^{-1} is assigned [63] to Al–O–H bending vibrations. The solvent isotope effect on the position of the spectral lines (Table 5) suggests that linear AlO_2^-, non-linear AlO_2^-, or indeed any solvated form of AlO_2^- containing the O–Al–O structural element cannot be present in significant amounts in aluminate solutions. NMR studies of ^{27}Al confirm that the aluminate ion has a tetrahedral configuration.

Additional evidence in favour of the T_d symmetry of the $Al(OH)_4^-$ anion in dilute solutions is obtained [63] by interpreting the spectra of concentrated aluminate solutions. Increasing the concentration of aluminate and of sodium hydroxide should favour the formation of ion pairs between $Al(OH)_4^-$ and hydrated sodium ions, with very little effect on the shape of the spectra [80]. However, this interaction could assist the formation in solution of mononuclear $AlO(OH)_2^-$ ions [29,30] or dinuclear dehydrated $Al_2O(OH)_6^{2-}$ ions. The latter were discovered and studied by Johansson [74] in crystalline potasium aluminate using X-ray diffraction spectroscopy. The $AlO(OH)_2^-$ and $Al_2O(OH)_6^{2-}$ ions have a lower symmetry than the T_d $Al(OH)_4^-$ ion, and therefore they could be responsible for the appearance of additional spectral lines in concentrated solutions (Table 5).

The monomeric, singly charged $AlO(OH)_2^-$ ion is probably the most convenient species for interpreting the vapour pressure, osmotic, and other properties of aluminate solutions [23]. However, Moolenaar and coworkers [63] prefer to discuss their results in terms of the dimeric, doubly charged $[(HO)_3Al-O-Al(OH)_3]^{2-}$ ion.

Table 5. Raman and i.r. spectra of aluminate solutions [63]*.

Composition of solution	Raman ν, cm^{-1}		I.r. ν, cm^{-1}	
	in H_2O	in D_2O	in H_2O	in D_2O
1 g-ion Al $litre^{-1}$	–	–	~950	–
1 mole $litre^{-1}$ NaOH (excess)	725 ± 5 vw, dp 625 ± 2 s, p 325 ± 10 vw, dp	745 ± 5 vw, dp 605 ± 2 s, p 320 ± 10 vw, dp	725 ± 5 s –	745 ± 5 s –
6 g-ion Al $litre^{-1}$	–	–	900 ± 5 s	895 ± 5 s
2.3 mole $litre^{-1}$ NaOH (excess)	705 ± 10 p –	725 ± 10 p –	– 725 ± 5 s	– 745 ± 5 s
	625 ± 2 s, p 540 ± 5 p 330 ± 10 w, dp	605 ± 2 s, p 534 ± 5 p 316 ± 10 w, dp	625 ± 3 v.w.	–

*s = strong, w = weak, vw = very weak, p = polarised line, dp = depolarised line.

Their only evidence for this choice is the similarity between the spectra of the solutions (Table 5) and the IR and Raman spectra of the dimeric ion in the solid state. A comparison of the spectra for the solid and the liquid phase, allowing for the spectral effects of the phase itself, has shown that all the bands found in concentrated solutions (Table 5) appear also in the spectra of the solid material. However, the latter contain additional bands at wavelengths which are obscured in aluminate solutions by strong bands from the solvent and from the $Al(OH)_4^-$ monomer. Hence, the conclusion [63] is that two types of ion coexist in concentrated aluminate solutions: $Al(OH)_4^-$ and $Al_2O(OH)_6^{2-}$, having T_d and C_s symmetry respectively.

Moolenaar and coworkers [63] also made another interesting observation: the IR, Raman, and NMR spectra of 2 M aluminate solutions containing ions of both types remain unchanged at temperatures up to 150°. Obviously, the equilibrium is relatively independent of temperature, or the concentration of dimeric ions is not large enough to influence the spectra significantly. If the first explanation is correct, the effect of temperature on the stability of metastable aluminate solutions cannot be ascribed to a structural rearrangement of the aluminate ion.

It should be noted that most of the concentrated aluminate solutions examined by Moolenaar and coworkers [63] were supersaturated with respect to aluminate ions, and therefore some caution is needed in extending their results and conclusions to the structure of unsaturated aluminate solutions. So far, the only (indirect) confirmation of the existence of polymeric ions with a single Al–O–Al oxygen bridge in supersaturated solutions of hydrated sodium aluminate comes from the work of Ni and coworkers [69,70], who also observed lines at 900, 740, 635, and 540 cm^{-1} in the IR spectra of their aqueous solutions. By comparing these spectra with those of the solid salt $K_2O.Al_2O_3.3H_2O$, whose lattice is known to consist of double $Al(OH)_4^-$ tetrahedra [83] joined by a single oxygen bridge, those workers concluded that a similar structure must be present in solution. Their Raman spectra [70] were not fully consistent with those of Moolenaar [63].

Thus, a search of the literature on the vibrational spectra of aluminate solutions suggests that monomeric aluminate ions with T_d symmetry are present in moderately concentrated solutions at pH > 13. The problem of polynuclear aluminium complexes, and of their existence regions, requires further study.

Studies of the NMR spectra of aluminate solutions also led a number of workers [51,60,61,63,71,72,84] to the conclusion that the aluminate ion has tetrahedral symmetry. The large negative chemical shift of ^{27}Al in alkaline solutions [51,60,61,63,71] as compared with the octahedrally hydrated Al ion in acid solutions [85–88] suggests that the coordination number of aluminium in the aluminate ion is less than six.

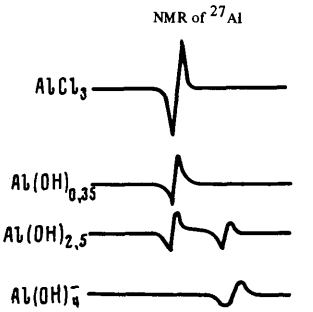


Figure 2. NMR spectra of ^{27}Al for solutions with different OH : Al ratios [51].

Fig. 2 shows the NMR spectrum of ^{27}Al in solutions with different OH : Al ratios [51]. In the acid solutions the resonance peaks are assigned to ^{27}Al in the AlO_6 group, whereas in alkaline solutions (OH/Al > 4) they are assigned to AlO_4. However, it appears from the spectra that both six- and four-coordinated aluminium ions can exist in solutions with an OH/Al ratio close to 3. This conclusion has been confirmed [89].

According to O'Reilly [60], the small width of the quadrupole line in aluminate solutions indicates a high degree of symmetry of the field surrounding the aluminium nuclei. The $Al(OH)_4^-$ ion has the required symmetry, whereas the AlO_2^- ion should give a broader line.

Mal'tsev and coworkers [30,90] used the NMR method (with ^1H and ^{23}Na) to study aluminate solutions containing up to 24% of Na_2O, and they observed a correlation between the chemical proton shift and the vapour pressure [29,30]. This work confirmed Dibrov's suggestion [29] that the tetrahydroxoaluminate ion becomes dehydrated at high concentrations according to reaction (1).

More recent work [63] also confirmed the dehydration of the $Al(OH)_4^-$ ion with increasing concentration of Na_2O and Al_2O_3, but to give the dimeric complex $Al_2O(OH)_6^{2-}$ rather than ions of the $AlO(OH)_2^-$ or AlO_2^- type. It is pointed out that the chemical shift of the ^{27}Al NMR line of the $[(HO)_3Al-O-Al(OH)_3]^{2-}$ ion should not differ significantly from that of $Al(OH)_4^-$, as is found in practice. If, on the other hand, a dehydrated ion of $AlO(OH)_2^-$ type had been

formed, no resonance would have been observed because of the line broadening caused by the asymmetric electric field gradient surrounding the nucleus of the aluminate ion. The insensitive dependence of the chemical shift of ^{27}Al on the concentration of alkali and of aluminate ions in solution can be ascribed[71] to the strong screening effect of the OH ions on the aluminium ion. Hence, the various interactions between the components of the solution and the $Al(OH)_4^-$ ion have only a minor effect on the electron density around the ^{27}Al ion.

The formation of ionic associations between sodium and aluminate ions has been convincingly demonstrated[30,63,71,90]. The increasing concentration of these associations with concentration of Na^+ ions in solution is revealed by a broadening of the ^{27}Al and ^{23}Na lines. This observation is consistent with analogous studies of the ^{23}Na line width in aqueous solutions of NaOH and certain salts[30,91,92]. Ion-pair formation significantly affects the time of half-exchange between free and associated ions in solution[30], and therefore the concentration dependence of the ^1H relaxation time observed in NMR cannot be ascribed wholly to polymerisation of the aluminate ions, as suggested by Romanov and Ni[72].

There is a single report[71], not supported by other published work[30,90,91], that the ^{23}Na resonance signal is shifted towards weaker fields in alkali as well as in aluminate solutions. The large changes in the chemical shift of ^{23}Na with Al concentration suggest that the interaction of the aluminate ions is stronger with sodium cations than with OH ions. It is important to take account of this interaction in any discussion of the bulk properties of the solution (electrical conductivity, viscosity[1,2]), and also when considering the dissociation mechanism of aluminate solutions.

The line widths and nuclear relaxation times of ^{23}Na and ^{27}Al, and also the results of ultrasonic and refractometric investigations[71], are consistent with the conclusions reached by analysing the chemical shifts of ^{23}Na and ^{27}Al. The NMR spectra indicate[71] the formation of dimeric complexes of the $Al_2O(OH)_6^{2-}$ type[63] at concentrations of aluminium above 1.5–2.0 g-ion litre^{-1}.

U.v. spectral studies of aluminate solutions over a wide range of concentrations[23,28,53,57,58,66] have identified two absorption bands at wave lengths 230 and 265 nm[32,66]. The overall absorption band[93] of aluminate solutions[32] is shown in Fig. 3 together with its expansion into two Gaussian components.

According to Taichi[66], the absorption bands at 230 and 265 nm are due to the presence of the ions $Al(H_2O)_6^{3+}$ and $Al(OH)_4.2H_2O^-$ in aluminate solutions. This assignment of the first absorption band to the hexa-aquo Al ion is not convincing, since optical studies of acid solutions of Al have shown that this ion does not absorb at wave lengths greater than 200 nm.[32,94] Equally, the presence of the $Al(OH)_4.2H_2O^-$ ion in aluminate solutions has not been confirmed experimentally[23]. Hence, we cannot accept Taichi's explanation of the anomalously high viscosity of aluminate solutions in terms of hydrogen-bond formation between these two non-existent species.

It can be seen from Fig. 3 that the relationship between optical density and concentration of the aluminate ion in solution follows the Lambert–Beer law[93]. The law is obeyed in solutions both undersaturated and supersaturated with respect to hydrargillite. This behaviour suggests that one particular type of aluminate ion (which could not be identified from u.v. spectra alone) is predominantly present in the solutions examined. Because of the low values of the extinction coefficients, structural rearrangements of the aluminate ion as between undersaturated and supersaturated solutions cannot be detected.

However, in supersaturated solutions a decrease in the concentration of alkali and aluminium (at a constant $Na_2O : Al_2O_3$ ratio of 2.0) produces a bathochromic shift of both u.v. bands by 3–5 nm. This effect is absent in undersaturated aluminate solutions. The bathochromic shift observed in supersaturated solutions could be due to the formation of small amounts of polymeric aluminate ions.

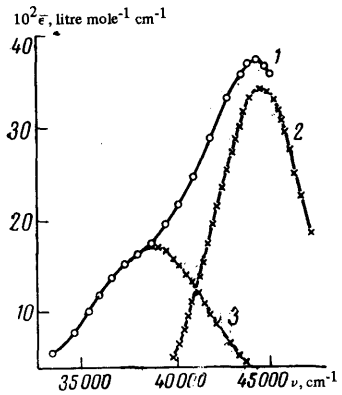


Figure 3. Absorption spectrum of aluminate solutions (*1*) resolved (*2*, *3*) according to Volokhov[32]: Na_2O concentration 0.5–2.51, alkalinity modulus α (Na_2O/Al_2O_3) 2–10.

Thus, some published work[31,39–41,78] suggests that polynuclear anions may be present in aluminate solutions of pH < 12–13, but when the pH is greater than 13 spectroscopic methods indicate that monomeric aluminate ions are predominant in concentrated solutions. Very accurate measurements of electrical conductivity and of diffusion coefficients[57,58], and also by the anion exchange method[84], have confirmed this conclusion, but unfortunately these measurements have been confined to aluminate solutions with a total electrolyte concentration not greater than 2 M.

III. ELECTROCHEMICAL INVESTIGATIONS

Studies of the chemistry of aluminium in aqueous solutions are complicated by the lack of simple and reliable methods for determining equilibrium concentrations of aluminium ions[78,95,96]. For this reason the Al–OH system has been studied by the very convenient pH method[97], which allows the composition of the aluminate ions to be determined from the measured concentration of hydroxyl ions[98]. However, the study of concentrated aluminate solutions in which the concentration of alkali is greater than 1 M is precluded by the large errors attending the use of glass or hydrogen electrodes in strongly alkaline solutions[97]. Not surprisingly, therefore, the solutions studied by the pH method have been more dilute, on the whole, than those studied by spectroscopic methods.

Brosset[48] reported, in 1952, one of the most important investigations of the chemistry of hydroxo-complexes of aluminium. He studied the hydrolysis of aluminium ions at concentrations between 2.21×10^{-3} and 1.11×10^{-2} g-ion litre^{-1} by a potentiometric method, using hydrogen electrodes. The measurements were made at a constant ionic strength of 2, maintained by sodium perchlorate[99,100]. Brosset concluded, from his results, that the main products of the hydrolysis of aluminium ions in alkaline solutions are polynuclear hydroxo complexes of $[Al(OH)_3]_n(OH)^-$ type.

However, a recalculation of these results by the method developed by Sillén to establish the mechanism of polynuclear hydrolysis[101-103] led to the conclusion[49] that the main hydrolysis product is the mononuclear $Al(OH)_4^-$ complex. The following reactions were suggested for the formation of these ions:

$$Al(OH)_{3(s)} + H_2O \overset{K'}{\rightleftharpoons} Al(OH)_4^- + H^+ , \quad (5)$$

or

$$Al(OH)_{3(s)} + OH^- \overset{K}{\rightleftharpoons} Al(OH)_4^- . \quad (6)$$

The logarithms of the constants for these equilibria are 12.5 ± 0.2 and 1.0 ± 0.2 respectively. Ageing of an $Al_2O_3 . xH_2O$ precipitate may result in the transformation of amorphous aluminium hydroxide into a more stable form, for which [according to Eqn. (6)] $\lg K = 0.5 \pm 0.2$.

It is stressed[49] that the precision of the measurements is relatively low, and there is no really convincing evidence of the absence of polynuclear anions in the solution.

After a more detailed analysis[51] of the data for these hydrolytic equilibria Sillèn concluded that alkaline aluminate solutions contain predominantly mononuclear anions with a tetrahedral $[Al(OH)_4^-]$ or octahedral $[Al(OH)_4 . 2H_2O^-]$ configuration.

Most of the published potentiometric investigations[24,26,55,65,104] confirm Sillèn's conclusion that the most abundant species in dilute aluminate solutions are mononuclear tetrahydroxo or dioxo complexes of aluminium.

Table 6 lists the published data for the equilibrium constant of reaction (5), assuming different modifications of aluminium hydroxide. It is evident that the equilibrium in the heterogeneous aluminate system depends very significantly on the structure of the solid aluminium hydroxide. The differences (Table 6) between the constants for a given modification of aluminium hydroxide suggest that in some of the work the crystalline form of the solid phase was not identified with sufficient care. In some cases the solid aluminium hydroxide was prepared under conditions different from those chosen for the equilibrium study. The criterion adopted as an indication of the establishment of equilibrium, and possibly also the presence of aluminate ions of composition other than $Al(OH)_4^-$, may have influenced the results.

Berecz and Szita[26] used as their equilibrium criterion for the dissolution of hydrargillite in alkali an electrochemical cell containing two mercury–oxide electrodes:

$$-Hg\,|\,HgO\,|\,OH^-,\ Na^+,\ Al(OH)_4^-\,|\,Al(OH)_3(s)\,HgO\,|\,Hg^+. \quad (7)$$

The electromotive force of this cell decreases with time as the $Al(OH)_3$ dissolves, and vanishes when equilibrium between the solution and the solid phase is established. This method has the advantage that the cell e.m.f. does not include a diffusion potential, and it gives reliable results with concentrated as well as with dilute NaOH solutions. Hence, the equilibrium constants can readily be extrapolated to zero ionic strength (Table 6).

These workers[26] did not observe a break in their plots of e.m.f. against time, and they showed that the rate of change of potential is practically independent of alkalinity, and hence of the concentration of aluminate ions. By combining this observation with other published data they concluded that the dissolution of hydrargillite in NaOH produces only $Al(OH)_4^-$ anions. However this conclusion[26] applies only to solutions with pH > 12.5.

Table 6. Thermodynamic equilibrium constants of reaction (5) for different modifications of aluminium hydroxide.

Solid phase	lg K'	t°C	References
Freshly precipitated hydroxide	−12.71	25	24
	−12.50*	40	49
Boehmite (AlOOH)	−12.45	25	55
Bayerite ($Al_2O_3.3H_2O$)	−13.84	25	55
	−13.95	25	24
	−14.52	25	56
Gibbsite ($Al_2O_3.3H_2O$) (hydrargillite)	−14.57	25	55
	−15.26	25	
	−14.72	35	26
	−14.04	50	
	−13.65	60	

*This value was obtained at a constant ionic strength of 2.

Except for the paper by Stefanowicz and Kiziak[65], there are no data on the stability of tetrahydroxoaluminate ions in aqueous solutions. These workers studied the state of the aluminate ions by potentiometric titration with a glass electrode, using an ionic strength of 0.1 and varying the pH from 1 to 10–11. They interpreted their results in terms of monomer hydrolysis only, to give complexes of the $Al(OH)_n^{3-n}$ type with $n = 1$, 3, and 4 and stability constant logarithms of 12.30 ± 0.3, 31.98 ± 0.3, and 36.58 ± 0.3 respectively.

The complex $Al(OH)_2^+$ does not appear to be formed in the solutions examined[65]. This fact is contrary to the principle of stepwise complex formation[105] and needs to be confirmed. Furthermore, the large difference between the stability constant of the $AlOH^{2+}$ ions and the values reported by other workers[25,32], and also the convincing evidence for the presence of polymeric associations in weakly acid solutions of aluminium salts[24,25,89,106,107], raise some doubts on the reliability of the stability constant obtained for the $Al(OH)_4^-$ ion.

Plum and Swaine[78] obtained some interesting results on the composition and structure of aluminate ions in their study of dilute aluminate solutions with a special electrode[108] reversible towards aluminium ions. They found[78] a definite relationship between the electrode potential and the concentration and pH of the aluminate solution. At pH > 12.4 the potential of the aluminium electrode against the saturated calomel electrode becomes independent of the concentration of aluminate ions and varies less steeply with pH. Under these conditions only four protons take part in the electrode reaction, and the experimental results are described by the empirical equation

$$E_{SCE} = 0.962 + {}^4/_3(0.059)\,pH . \quad (8)$$

However, in solutions of pH < 12.4 the potential depends on the concentration of aluminate ions, and is described by the equation

$$E_{SCE} = 0.5099 + \frac{0.059}{3} \lg [\text{aluminate}] + 2(0.059)\text{pH}. \quad (9)$$

The authors assumed the electrode reaction

$$Al + 4H_2O \rightleftharpoons Al(OH)_4^- + 4H^+ , \quad (10)$$

whose potential should be given by

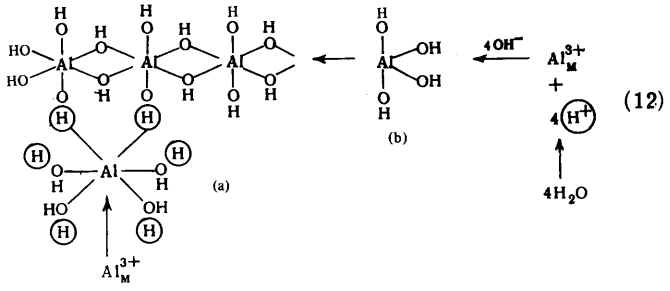
$$E = E^0 - \frac{0.059}{3} \lg [Al(OH)_4^-] + \frac{4}{3}(0.059)\,\text{pH} . \quad (11)$$

However, Eqn.(11) is inconsistent with the empirical equations (8) and (9). Hence, the hypothetical electrode reaction (10) cannot be correct. But if we assume that the formation of the products of the electrode reaction is independent of the total concentration of aluminate ions in solutions of pH > 12.4, and is determined only by the concentration of OH^- ions, Eqns.(8) and (11) become identical. Under these conditions, as can be seen from Eqn.(8), we have a direct reaction between four hydroxyl ions and one aluminium ion from the metal electrode.

In order to explain the dependence of the potential on the concentration of aluminate ions in solution of pH < 12.4 the authors assume that the aluminate ion takes part in the electrode reaction. In other words, the aluminium ion transferred to the solution from the metal electrode must react with aluminate ions to give some form of polynuclear association. It would appear from the experimental results [Eqn.(9)] that six protons are set free when an aluminium ion goes into solution.

Plumb and Swaine [78] considered the most probable structures of aluminate ions in which the Al can have a coordination number of four or six. By combining their own results with those of others [49,52] they concluded that the anion has a polymeric structure of the type $[Al(OH)_4]_n.(OH)_2^{(n+2)-}$. They assume, with little justification, that the same polymer must exist also in solutions of high pH, in which the monomeric ions are thought to be in equilibrium with the ends of polymer chains. If the chains are sufficiently long, the electrode potential will be independent of the total concentration of aluminate ions in solution.

According to Plumb and Swaine [78], the two reactions in solutions of low and high pH respectively can be described by the following scheme:



(12)

where the circles denote replaceable protons.

The reaction between active centres on the side of the polymer chain and an aluminium ion hydrated by four water molecules gives a branched structure in which bonding is by two adjacent oxygen bridges [Eqn.(12a)]. A linear polymer with n aluminium ions will have $(n-1)$ such positions, and therefore the electrode reaction leading to the formation of the branched polymer will depend on the concentration of aluminate ions in solution [see Eqn.(9)].

However, at high pH the concentration of OH ions exceeds the number of active centres in the polymer, and $Al(OH)_4^-$ ions are formed (probably in equilibrium with the ends of polymer chains). In this case, according to mechanism (12b), the coordination number of the aluminium should change from four to six. We can expect the branched polymer to be metastable with respect to the linear polymer, since the former should have a greater density of negative charges than the latter. A thermodynamic analysis of experimentally observed standard electrode potentials [78] has confirmed this expectation.

The polymeric model of the aluminate ions, $[Al(OH)_4]_n(OH)_2^{(n+2)-}$, is formally consistent with the observation [49] that the mean Bjerrum number $\bar{n}$ [105] in dilute aluminate solutions is slightly greater than four. Using published [49] values of $\bar{n}$ for different Al concentrations, Plumb and Swaine calculated that the number of monomer units (n) in the polymer chain increases with concentration and can reach a value of 100 at an Al concentration of 1.1×10^{-2} g-ion litre^{-1}. However, this calculation is possible only for the unlikely case of a solution containing only polymeric anions of uniform composition.

The reaction of the $Al(OH)_4^-$ ion with a polymer (mechanism 12b) does not explain the well known increase of pH with time in freshly prepared aluminate solutions [49]. The effect could be due to the migration of branches in a metastable (highly branched) polynuclear structure towards the ends of the chain, the oxygen bridges taking up a proton from the solution, or to mutual interaction of the polymer chains according to the equation

$$[Al(OH)_4]_n(OH)_2^{(n+2)-} + [Al(OH)_4]_m(OH)_2^{(m+2)-} \rightleftharpoons [Al(OH)_4]_{m+n}(OH)_2^{(n+m+2)-} + 2OH^- . \quad (13)$$

If the increase of pH with time is due to polymerisation of the aluminate anions, and each elementary step is accompanied by the generation of two free OH ions, it can easily be shown from Brosset's results [49] that in solutions with $\bar{n} > 4$ the amount of polymer does not exceed 2%. If this is so, the disagreement between the results of pH measurements [24,48,49] and those of electrochemical measurements [78] is not surprising.

Plumb and coworkers [39] have recently confirmed by spectroscopic methods that polymeric species are present also in concentrated aluminate solutions of pH < 13.

IV. MONONUCLEAR AND POLYNUCLEAR ALUMINATE IONS IN STRONGLY ALKALINE SOLUTIONS

The existence of polymeric aluminate ions in solutions of different concentrations but pH $\leqslant$ 12–13 has been proposed in a number of publications [31,39–41,78] discussed in the previous sections of this review. However, information on the presence of polynuclear structures in strongly alkaline solutions is controversial, and erroneous in parts.

The first report of the polymerisation of aluminate ions in alkaline solutions is due to Brintzinger [109], who concluded from dialysis results that the two polymeric structures $[Al_2(OH)_{10}]^{4-}$ and $[Al_2O_2(OH)_8]^{8-}$ were present in his solutions. Because of the difficulty of interpreting dialysis data correctly, the equivalent weights of the ions cannot be established with confidence [110]. In our system the problem is further complicated by the fact that the equivalent weights of the dimeric anions are almost identical. Brintzinger's results [109] are also inconsistent with more recent work which suggests that the formal

charge on the aluminate ion, at least in equilibrium solutions at high pH, is unity [22-26,29-31,33,66]. However, the former of the above ions, $[Al_2(OH)_{10}]^{4-}$, agree in composition with the general polymer formula $[Al(OH)_4]_n \cdot (OH)_2^{(n+2)-}$, with $n = 2$, proposed for solutions of pH < 12.5. [31,39-41,78]

Calvet and coworkers [12] have shown, by diffusion measurements, that the calculated apparent radius of the aluminate ions decreases by about a factor of two on raising the temperature of the solution from 20° to 50°. This effect could be due to dissociation of ion pairs and polymeric ions, or to the dehydration of aluminate ions, but the diffusion method lacks the power to distinguish between these processes.

Jahr and Plaetschke [53] also used the diffusion method to study aluminate solutions. By referring to some earlier and unconfirmed diffusion measurements they concluded that the size of the aluminate ion is determined mainly by the alkalinity of the solution. Weakly alkaline solutions contain polymeric aluminate ions whose size decreases with increasing concentration of OH^- ions according to the reaction

$$[(H_2O)_2(OH)_3Al{-}OH{-}Al(OH)_3(H_2O)_2]^- + OH^- \rightleftharpoons 2[Al(OH)_4 \cdot 2H_2O]^- , \quad (14)$$

The resulting mononuclear aquohydroxoaluminate ions are dehydrated if the concentration of OH^- ions is increased from 6.5 to 20 (expressed as OH : Al ratio), giving rise to water-free polymers of general formula $[Al_n(OH)_{3n+1}]^-$, for example by the reaction

$$2[Al(OH)_4^-] \rightleftharpoons [(HO)_3Al{-}OH{-}Al(OH)_3]^- + OH^- , \quad (15)$$

with an average degree of polymerisation not greater than four. Further increase in alkalinity leads to decomposition of the $[Al_n(OH)_{3n+1}]^-$ complexes, and $Al(OH)_4^-$ ions become the predominant species in solution.

The polymerisation scheme proposed by Jahr and Plaetschke [53] is in general agreement with other experimental results obtained at about the same time, and is not incompatible with the growing belief that the aluminate ion carries a unit charge. However, later work has not produced any convincing evidence in favour of the formation of polymers by reactions of the type of (14) and (15).

Indeed, Jahr and Pernoll [57,58] made a series of high-precision measurements in 1965 but they were unable to confirm the earlier conclusions [53]. Their measurements of OH^- ion activity [57] indicated that only monomeric $Al(OH)_4^-$ complexes are present in alkaline solutions of pH $\geqslant$ 11.5. Their measurements of diffusion coefficient and electrical conductivity [58] also suggested that the composition of the aluminate ions is independent of the OH : Al ratio, and that polymeric anions cannot exist in strongly alkaline solutions.

An improved anion exchange method [64] has been used to show that aluminate ions in 1 M NaOH solution are always present as the monomer $Al(OH)_4^-$. The composition of the ions is independent of the ageing time of the solution, and remains unchanged up to the onset of visible decomposition of the aluminate solutions. It should be noted that these conclusions [57,58,64] apply to solutions in which the overall concentration of the components is less than 2 M, i.e. to dilute and moderately concentrated solutions.

The work of Kuznetsov [2,20-22,111] has had a profound effect on the development of our views on the structure of alkaline solutions of aluminium. According to Kuznetsov, aluminate solutions with a high alkalinity modulus ($\alpha = \frac{Na_2O}{Al_2O_3}$) contain $Al(OH)_4^-$ ions, which can form polymeric groupings in low-modulus solutions containing less than 150–180 g litre^{-1} of Na_2O according to the scheme

$$Al(OH)_4^- \rightarrow Al_n(OH)_{4n}^{n-} \rightarrow Al_6(OH)_{24}^{6-} \rightarrow \underset{\text{(Gibbsite)}}{\text{hydrargillite}} . \quad (16)$$

The formation of hydrargillite from ring structures of the $Al_6(OH)_{24}^{6-}$ type is explained by assuming that aluminate ions in solution have the same structure as the elements of the crystal lattice of hydrargillite, and also from electrical conductivity and viscosity data [20-22,111].

At Na_2O concentrations greater than 150–180 g litre^{-1} Kuznetsov assumes [2,20-22,111] that dehydrated polymers of the $[AlO(OH)_2]_n^{n-}$ type are present in solution. He suggests that changes in size of the polymer are due to fluctuations in the solutions, leading to changes in local concentration, temperature, density, etc. Hence, "conditions favourable to polymerisation are created in some microscopic regions, giving rise to hetero-phase fluctuations" [22]. Kuznetsov has not attempted to confirm his hypothesis experimentally, particularly since the problem of homogeneity or microheterogeneity in supersaturated solutions in general is still highly controversial [112].

Measurements of the electrical conductivity and viscosity of aluminate solutions [20-22,111] indicate a strong dependence of structure on concentration. Thus, the specific conductance of the alkali decreases very markedly when aluminate ions are introduced into the solution, but the electrical conductivities of aluminate solutions and of NaOH have very similar concentration dependences, going through a maximum as the concentration increases. The decrease in conductivity with increase in concentration occurs when the system has crossed the full solvation boundary [82,113], and can be explained by the formation of ion pairs [30] or by polymerisation of the aluminate ions [111].

In dilute aluminate solutions the activation energies for viscous flow ($E\eta$) and for electrical conduction ($E\lambda$) are small (less than 1 kcal mole^{-1}), and approximately equal. This suggests the presence of mobile ions, small in size, in dilute solutions. In aluminate solutions containing more than 150 g litre^{-1} of Na_2O the quantity $E\eta$ increases much faster than $E\lambda$. According to Kuznetsov [21,111], this behaviour could be associated with the appearance of large aluminate ions in solution, since viscosity is more sensitive than electrical conductivity to the presence of low-mobility ions.

Kuznetsov has also pointed out [22] that at some particular concentrations the solution develops a quasi-crystalline structure due to the formation of hydrogen bonds between aluminate ions. This effect is favoured by low temperature and low alkalinity.

Starting from the hydrated model of the aluminate ion, $Al(OH)_4.2H_2O^-$ (O_h), Pearson [19] also finds a correlation between the hydrogen bonding of aluminate ions and the viscosity of the solution. However, other work [26,30,57-59,63,64] has failed to confirm the presence of these ions, in which the aluminium should have a coordination number of six.

Kuznetsov and coworkers [114] found additional evidence in favour of hydrogen bond formation between hydroxo complexes in aluminium solutions in their study of the rheological properties of these solutions [115]. The deviations from Newtonian behaviour in aluminate solutions suggest that these liquids are structured, becoming quasi-crystalline beyond the full solvation boundary. It is pointed out [114] that structural ordering is more marked in solutions with a high content of aluminate ions and at low OH : Al ratios. Hence, plots of the stability of the structure (said [114] to be related to the degree of polymerisation)

against the alkalinity modulus at constant Al_2O_3 concentration go through a maximum at a $Na_2O : Al_2O_3$ ratio of 1.6.

Unfortunately, the authors [114] do not comment on the similarity between the concentration dependences of electrical conductivity [111] and structural stability in aluminate solutions, and they offer no explanation for the appearance of a stability maximum at that particular value (1.6) of the alkalinity modulus. Furthermore, the interpretation of the rheological properties of aluminate solutions is complicated by the lack of data on the rheological properties of concentrated solutions of pure alkalies, which are also known [116,117] to have a quasi-crystalline structure.

Thus, Kuznetsov's views on the presence of polymeric aluminate ions formed by hydrogen bonding in alkaline solutions of aluminium salts are based essentially on measurements of electrical conductivity, viscosity, and rheological properties, although the concentration dependence of these parameters could equally well be explained by postulating the formation of ion pairs or associated ionic species with a more complex structure.

Firstly, the electrical conductivity of aluminate solutions varies with concentration in the same way as in pure alkali solutions [1,2,30,111]. The conductivity of NaOH solutions begins to decrease beyond the full solvation boundary as a result of a decrease in the concentration of Na^+ and OH^- ions, due to ion pair formation [29,30,117]. The analogous trend of the conductivity changes in aluminate solutions could also be due to the formation of ionic associations between aluminate and hydroxyl anions, on the one hand, and sodium cations [30,71]. Of course, hydrogen bonding between the water molecules of the hydration shell surrounding the Na^+ cations and the hydroxyl groups of the aluminate ions could assist the formation of ionic associations of the $[Na(H_2O)_x^*]_yAl(OH)_4$ type, where y cannot be greater than 4. But in this case the formation of significant amounts of large polynuclear aluminate ions is unlikely, because ion pairs held by strong hydrogen bonds do not readily polymerise [118]. The increase in the viscosity of alkali solutions following the addition of aluminate ions can be ascribed to the same interactions. Furthermore, electrostatic considerations suggest that aluminate anions in alkali solutions should more easily form bonds with the oppositely charged Na^+ cations than interact with each other. Only when the concentration of aluminate ions is not very different from the concentration of Na^+ ions are conditions favourable to the formation of polynuclear aluminate structures, particularly in supersaturated solutions.

Secondly, reactions leading to the formation of complicated polymeric structures are kinetically slower than simple hydrolysis reactions [32,68], because they involve a number of separate steps. However, equilibrium is established very rapidly both in the dissolution of metallic aluminium in NaOH solutions and in the dilution of aluminate solutions with solutions of alkali, and the properties of supersaturated aluminate solutions (electrical conductivity, density, viscosity, pH,[119] optical density [32,63], velocity of ultrasonic waves [71,120]) remain constant up to the onset of visible decomposition. If, on the other hand, mononuclear and polynuclear anions of different degree of condensation were present in aluminate solutions of high pH, and if their composition were changing with time during the ageing period of the solution, none of the above properties would remain constant during the period preceding the precipitation of aluminium hydroxide.

Thirdly, the stability of supersaturated and undersaturated aluminate solutions as a function of temperature, concentration, and alkalinity modulus [2,121] can be explained not only in terms of polynuclear complex formation but also by considering the formation of ionic associations between aluminate anions and sodium cations [28], particularly since these associations are fairly stable [71] and they appear to be of the outer-sphere complex type [122], whose formation in concentrated salt solutions is known to be endothermic. Hence, increase of temperature may produce not only a rearrangement of the structure of the aluminate ions but also a blocking of those ions by sodium cations, thus increasing the stability of the solutions. Differences in behaviour between potassium and sodium aluminate solutions [41,123] lend some support to these views.

Many other published results [26,29,30,39-41,57-61,63] are also inconsistent with the presence of significant amounts of highly complex polymeric aluminate ions in strongly alkaline and concentrated solutions. An analysis of data on polynuclear hydroxo complexes of various metal ions [25] suggests that the stability of these complexes is, in general, low, and therefore their concentration must be small. Evidently, aluminate solutions are not exceptional in this respect. To some extent, this is confirmed by the low intensities of the i.r. and Raman lines obtained [63] with supersaturated solutions. It seems likely that the formation of aluminium hydroxide from alkaline solutions does not require large numbers of large polynuclear aluminate ions to be formed during the induction period.

V. THERMODYNAMIC PROPERTIES

The fullest and most reliable thermodynamic data on alkaline and aluminate solutions of composition $NaOH-H_2O$, $KOH-H_2O$, $Na_2O-Al_2O_3-H_2O$, $K_2O-Al_2O_3-H_2O$, and also $Na_2O-K_2O-Al_2O_3-H_2O$, were obtained in the Physical Chemistry Department of the Lensovet Leningrad Technical Institute. Measurements of density, equilibrium water vapour pressure, and specific heat were made over a wide range of concentrations and at temperatures between 25° and 300°. Details of the apparatus, procedures, and results obtained have already been given [29,30,33,90,117,124-140]. Most of the results relate to stable aluminate solutions. Only one publication [141] deals with the saturated vapour pressure and relative partial molar enthalpy of water in a small range of metastability. Some workers have calculated the thermodynamic characteristics of aluminate solutions by taking the aqueous solutions of pure alkali (NaOH or KOH) as the solvent [142], since their thermodynamic properties are known with sufficient precision [143-145]. The validity of this approach has been demonstrated by Karapet'yants [146].

Mal'tsev and Mashovets [30,128] obtained a large amount of valuable experimental data on the specific heat of alkali and aluminate solutions in the temperature range 25-90°. They showed that the specific heat is fairly high at low temperatures, and decreases with increasing temperature. This effect is more marked in aluminate solutions than in pure alkali solutions. The decrease in heat capacity observed on adding aluminium to a solution of sodium hydroxide is ascribed [128] to the formation of polymers or complex ions.

The theoretical interpretation of the results is extremely difficult, because of the complexity of the processes which can take place in aluminate solutions. Negative deviations from additivity of the specific heat may arise through changes in the structure of water under the influence of the dissolved ions and their hydration processes, since water is known to have a lower specific heat when in

a bound state. Positive deviations from additivity indicate predominantly interionic interactions (formation of ion pairs or polymeric associations). Using this type of argument, Mal'tsev and Mashovets [128] ascribed the small changes in specific heat at 75–90° to decomposition or dehydration of polymeric aluminate ions. Increase in concentration is also thought [128] to assist the degradation of polymeric structures at all temperatures.

More recently, Mal'tsev and coworkers [30,90] have tried to explain the measured specific heats of aluminate solutions by postulating monomeric aluminate ions of different degree of hydration. Positive deviations of the measured specific heats from the linearly interpolated values are ascribed to the formation of ionic association or ion pairs by the reactions

$$Na^+ + Al(OH)_4^- \rightleftharpoons Na^+[Al(OH)_4^-] \rightleftharpoons Na^+\left[O{-}Al\begin{matrix}OH\\OH\end{matrix}\right]^- + H_2O \rightleftharpoons Na^+AlO_2^- + 2H_2O \quad (17)$$

This equilibrium should be shifted towards the right by increasing the concentration. In addition to the heat capacity measurement, data on the electrical conductivity of aluminate solutions [30,90] and the NMR spectra of ^{23}Na [30,90] provide indirect support for the suggested interionic interactions [Eqn.(17)]. Direct proof of the very strong interaction of aluminate ions with sodium cations is given in Ref. 71. Other workers [130,139–141] have critically assessed the experimental vapour pressure data, and have proposed new formulae and graphical methods for determining the vapour pressure of sodium and potassium aluminate solutions over a wide range of concentrations and temperatures. Mal'tsev [30] concludes from the dependence of vapour pressure on Al content that the total number of ions in a sodium aluminate solution is almost the same as in the corresponding solution of pure alkali, and that the two solutions have very similar structures. The dehydration mechanism of aluminate ions is consistent with the observed increase in water vapour pressure with concentration of aluminate ions [29,30]. Eqn.(17) predicts a sharp decrease in the symmetry of the aluminate ion after dehydration: the prediction is not borne out by the NMR spectra of ^{27}Al [51,60,61,63,71] or by other spectroscopic observations [52,62,63,71]. This discrepancy between the vapour pressure data and the NMR spectra of ^{27}Al can be resolved [63] by postulating the presence of partly dehydrated anions (e.g. $[Al_2O(OH)_6]^{2-}$) in concentrated solutions, since in these anions the tetrahedral configuration of the aluminate point group is distorted to a negligibly small extent.

Chakhal'yan [141] has carried out a thermodynamic assessment of the structure of aluminate solutions and of various models of the aluminate ion by combining thermochemical data with vapour pressure data for the stable and the metastable regions of these solutions. Using specially designed apparatus, he obtained some important experimental results:

1. The relative partial molar and specific enthalpies of water and of the defined solvent [aqueous alkali with a constant $(Na_2O)/(Na_2O + H_2O)$ ratio] were measured in sodium and potassium aluminate solutions at 25°, and also the heats of dilution of these solutions with solutions of pure alkali.

2. The differential heats of dissolution of hydrargillite in $R_2O–Al_2O_3–H_2O$ systems (where $R = Na^+$ or K^+) and in pure alkali solutions with a ratio $(R_2O)/(R_2O + H_2O) = 0.23243$ by weight were measured at 85°.

3. The saturated water vapour pressure was measured only over sodium aluminate solutions, for nine values of the alkalinity modulus [$\alpha = (Na_2O)/(Al_2O_3)$] in the Na_2O concentration range 5–25 wt.% and at two temperatures (25° and 75°).

From his experimental results he calculated the integral heats of dissolution of hydrargillite at three constant $(Na_2O)/(Na_2O + H_2O)$ ratios, the relative partial molar entropic terms of water in sodium and potassium aluminate solutions at 25°, and some other parameters, and he compiled an enthalpy–concentration diagram for the $Na_2O–Al_2O_3–H_2O$ ternary system.

Because of the profound influence of water on the behaviour of aluminate solutions, Chakhal'yan [141] calculated the activity of water as a function of $1/\alpha$ at various concentrations of R_2O, using vapour pressure data for solutions of sodium and potassium aluminates, and of pure alkalies. The data for 300° and for the $K_2O–Al_2O_3–H_2O$ system, were taken from the work of Mashovets and coworkers [126,130,140]. As an example, the activity of water in the $Na_2O–Al_2O_3–H_2O$ system (a_{AR}) is compared in Fig.4 with the same parameter for a pure alkali solution (a_R) as a function of the alkalinity modulus and of the Na_2O content at 25°.

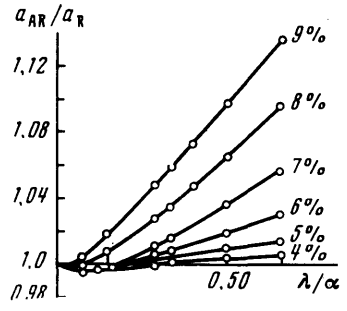


Figure 4. Ratio of the activities of water in sodium aluminate solutions (a_{AR}) and in alkali solutions (a_R) against $1/\alpha$ at 25°.[141] The numbers against each curve denote mol.% of Na_2O.

It is evident from the Figure that the activity of water in aluminate solutions with a high alkalinity modulus drops below the value for solutions of pure alkali at first, but it then crosses the horizontal axis and begins to increase at a rate depending on the Na_2O content. This type of curve is believed [141] to indicate the existence of two regions in which the structure of the aluminate ion is different, and therefore the degree of hydration is also different: for example, $Al(OH)_4^-$ and $AlO(OH)_2^-$. However, no allowance was made for the possible formation of hydrates such as $[Al(OH)_4^-](H_2O)_X$.

In order to investigate further the structure of the aluminate ion, the $a_{AR}/a_R = f(1/\alpha)$ curves (Fig.4) were compared with $n_{AR}/n_R = f(1/\alpha)$ curves (where n_{AR} and n_R are the mole fractions of water in the aluminate and the pure alkali solutions respectively) calculated for

various proposed models of the aluminate ion. The calculations showed that the mole fraction of water decreases with increase in $1/\alpha$ in the following sequence:

$$[AlO(OH)_2]_n^{n-} > [AlO(OH)_2]_6^{6-} > Al(OH)_4^{3-} > [Al(OH)_4]_6(OH)_2^{8-} >$$
$$> AlO_2^- = [Al(OH)_4]_n^{n-} = [Al(OH)_4]_n(OH)_2^{(n+2)-} > [Al(OH)_4]_6^{6-} =$$
$$= [Al_6(OH)_{24}]^{6-} > AlO(OH)_2^- > [Al_6(OH)_{18}](OH)_6^{6-} >$$
$$> Al(OH)_4^- = [Al_6(OH)_{18}]_n(OH)_6^{6-} \quad (\text{for } n \gg 6).$$

The mole fractions of water in aluminate and in pure alkali solutions become the same if the aluminate solution is assumed to contain only monomeric AlO_2^- ions or polymeric $[Al(OH)_4]_n^{n-}$ and $[Al(OH)_4]_n(OH)_2^{(n+2)-}$ ions. In other words, these calculations[141] suggest that the hydration properties of Al_2O^- and OH^- ions are identical. This surprising result can be explained by the failure to take account, in the calculation of n_{AR} and n_R, of the water molecules in the hydration shells of the components of the solution, and also of the trans-solvation effects accompanying the formation of various ion pairs or ionic associations between sodium cations and hydroxyl or aluminate anions[30,71,90,117]. Furthermore, it is not easy to distinguish "physical" from "chemical" phenomena in these solutions without *a priori* knowledge of the final result[147], though some allowance for the "chemical" contribution to the phenomenon can be made by choosing the correct model for the aluminate ion.

Evidently, still greater complications can be expected in the calculation of the mole fraction of water in concentrated solutions, where the composition of the aluminate ions can be even more complex. In particular, the increase in the activity of water with concentration (Fig. 4) could be due not only to dehydration and polymerisation of the aluminate ion[141], but also to interactions between aluminate anions and sodium cations stronger than the corresponding interactions between Na^+ and OH^-.[71] Hence, the real composition of the aluminate ion cannot readily be inferred from integral properties of the system such as the activity of water.

From his comparison of the $a_{AR}/a_R = f(1/\alpha)$ plots (Fig. 4) with calculated plots of $n_{AR}/n_R = f(1/\alpha)$ Chakhal'yan concludes[141] that $Al(OH)_4^-$ ions are present in solutions with a high concentration of Na_2O (>8 mol.%) but a low concentration of aluminium. Increasing concentration apparently leads to dehydration of these anions and formation of polymers of the $[AlO(OH)_2]_n^{n-}$ type, or even $[AlO_2]_n^{n-}$. The existence of these polymers is not inconsistent with the thermodynamic measurements carried out by the author, or with his calculations[141] of the equilibrium constants of aluminate solutions saturated with hydrargillite at 25°. But his analysis of the equilibrium constants involve the doubtful assumption that ions of the same charge have the same activity coefficient in a given solution, although quite different numerical values have been reported for concentrated electrolytes of the same type[148].

Chakhal'yan's model[141] resembles Kuznetsov's theory[2,21,22] most closely. However, the presence of polymers of composition $[AlO(OH)_2]_n^{n-}$ and $[AlO_2]_n^{n-}$ is not confirmed by the spectroscopic results[5,52,60-63,71], or by the very low heats of dilution of aluminate solutions by solutions of alkali[141], since the degradation of these polymers should require a fairly large expenditure of energy.

A comparison of the relative partial molar entropies of water in solutions of aluminates and of pure alkalies respectively has shown[141] that water is more strongly bound in aluminate solutions (containing not more than 8 mol.% of Na_2O) than in solutions of sodium hydroxide. This finding agrees with conclusions reached by other methods[19,71], but it is given a different interpretation: some assume[19,141] that the water is built into the "intrinsic" structure of the aluminate ion ($[Al(OH)_4^-]$ (T_d)[141] or $[Al(OH)_4 \cdot 2H_2O]^-$ (O_h)[19]), whereas others[71] believe that the aluminate ion itself can form hydrates of the $[Al(OH)_4^-](H_2O)_X$ type, in which the tetrahedral (T_d) configuration is retained.

VI. KINETIC DATA ON THE BEHAVIOUR OF THE $Na_2O-Al_2O_3-H_2O$ SYSTEM

In contrast to the hydrolysis of Al ions in acid solutions, the hydrolysis of this metal in the alkaline region usually produces an increase of pH with time[48]. The decomposition of aluminate solutions is an autocatalytic process in which the resulting aluminium hydroxide (and various salt additives[1,2]) can act as catalysts[22].

Brosset[48] studied the rate of hydrolysis of aluminium ions in alkaline solutions, but he was unable to obtain reproducible results. He ascribed the varying rates to the slow establishment of equilibrium potentials on the hydrogen electrode. The errors in the measured pH were particularly serious during the first hour after mixing of the Al and alkali solutions.

This problem was avoided[32,149] by using glass electrodes, whose equilibrium potentials are developed almost instantaneously[97]. Mironov[81] monitored the hydrolysis of Al in alkaline solutions by pH measurements at a constant ionic strength of 3, maintained by adding sodium perchlorate, at 40°. The total concentration of aluminium was varied between 10^{-3} and 10^{-1} g-ion litre^{-1}, but most of the measurements were made at an aluminium concentration of 1×10^{-2} g-ion litre^{-1}.

Measurements of pH, combined with Raman spectral studies, have shown[149] that the ratio of the total concentrations of alkali and aluminium (OH : Al) has a profound effect on the hydrolytic reactions. We can distinguish three regions of OH : Al values, corresponding to different hydrolysis rates and mechanisms.

Region No. 1 (OH : Al $\simeq$ 4.4, pH $\geqslant$ 13.0) is a region of stable solutions, where equilibrium is established very rapidly.

Region No. 2 (OH : Al $\simeq$ 3.3–4.4, pH $\simeq$ 9.3–12.8) gives pH–time curves of the type shown as curve *a* in Fig. 5).

Region No. 3 (OH : Al $\simeq$ 3.01–3.3, pH $\simeq$ 8.2–9.3, curves *b* and *c* of Fig. 5). There seems to be general agreement[24-26,29-31,33-65] that monomeric aluminate ions are the predominant species in solutions within region No. 1.

In region No. 2, polymers of composition $[Al(OH)_4]_n \cdot (OH)_2^{(n+2)-}$ are formed as soon as sodium hydroxide is added to the solutions[31,39-41,78]. Migration of the polymer chains leads to gradual chain breaking and formation of hydroxyl ions, so that the pH of the solution increases with time.

Solutions prepared within region No. 3 show a rapid formation of a mixture of aluminium hydroxide and polymers of the $[Al(OH)_3]_n(OH)^-$ and $[Al(OH)_4]_n(OH)_2^{(n+2)-}$ type (sections *1* and *2* of the curves in Fig. 5*b* and 5*c*), the former consisting of fine colloidal particles. The transformation of these polymers into aluminium hydroxide (sections *2–3–4–5* in Fig. 5*b* and 5*c*) causes a gradual release of OH^- ions into the solution.

The apparent first-order rate constants for the generation or disappearance (region No. 3) of OH^- ions, calculated for sections *1* and *2*, are $(5.5 \pm 0.7) \times 10^{-2}$, $(3.0 \pm 0.5) \times 10^{-2}$, and $(3.6 \pm 0.4) \times 10^{-2}$ min^{-1} respectively. The rate constants calculated from Figs. 5*b* and 5*c* are the same within experimental error: this is not surprising, since the two curves refer to systems within the same region.

Scotford and Glastonbury [150] studied the effect of temperature on the rate of dissolution of gibbsite and boehmite in NaOH solutions at temperatures between 25° and 100°. They assumed the following reactions

$$\underset{\text{(gibbsite)}}{Al(OH)_3} + OH^- \rightleftarrows Al(OH)_4^- \qquad (18)$$

$$\underset{\text{(boehmite)}}{AlOOH} + OH + H_2O \rightleftarrows Al(OH)_4^- \ . \qquad (19)$$

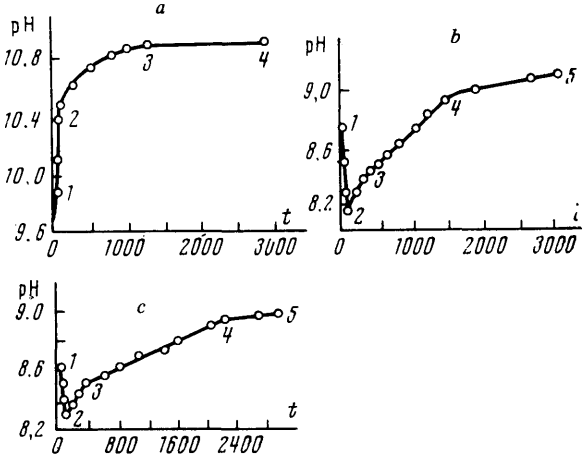


Figure 5. Changes of pH with time [149] t, min, for different OH : Al ratios: *a*) 3.5, *b*) 3.1, *c*) 3.01.

The activation energies, calculated from the initial rates of dissolution, were found to be (30.6 ± 0.9) and (29.4 ± 1.3) kcal $mole^{-1}$ respectively.

The heat of reaction (18), according to Sato [151], lies between 5.88 and 7.34 kcal $mole^{-1}$. However, most workers prefer to use the higher value (approximately 7.3 kcal $mole^{-1}$) obtained by Russell and coworkers [37], who also estimated the heat of dissolution of boehmite as ~4.8 kcal $mole^{-1}$. By combining these values with the activation energies obtained for the forward reaction (18) and (19), Scotford and Glastonbury [150] calculated the activation energies for the reverse reactions (23 and 25 kcal $mole^{-1}$ for gibbsite and boehmite respectively).

The high activation energies obtained for both the forward and the reverse reactions suggest that the lixiviation of alumina and the decomposition of aluminate solutions are both activation controlled. Herrmann [13] on the other hand concludes that these reactions are diffusion controlled, but his views on the nature of aluminate solutions have been severely criticised, in particular by Kuznetsov [22].

The calculation [150] of the activation energy from the initial rates of dissolution of alumina avoids the difficulties arising from the reversibility of reactions (18) and (19) and from the need to find the true rate constants, particularly since the latter cannot be determined unless the correct kinetic equations and the complex mechanisms of the dissolution and precipitation of alumina are known. Furthermore, activation energies obtained from the temperature dependence of rate constants are valid only on the assumption of constant composition of the components of the solution, and of the solid phase, at different temperatures. This condition, of course, is not fulfilled in the present system, since both the composition and the structure of the aluminate ions may vary with temperature [23,30]. An incorrect value of the activation energy will be obtained from the temperature dependence of the rate of reaction also if the surface area of the precipitate after a given time is different at different temperatures.

The latter effect is probably responsible for the low activation energy attending the dissolution of gibbsite in alkali, previously reported [152,153] as 23.8 kcal $mole^{-1}$, determined from the temperature dependence of the reaction rate measured over long time intervals (and therefore possibly affected by changes in the specific surface area of the alumina).

Elson and coworkers [154] reported an even lower value of the activation energy (19.6 kcal $mole^{-1}$). This value was calculated from the following empirical kinetic equations, which relate the reaction rate to the surface area of the solid phase and the composition of the aluminate solution:

$$\frac{dx}{dt} = k_2 A_t \left(\frac{x_\infty - x_t}{a_\infty + x_\infty} \right)^2 \qquad (20)$$

$$\frac{dx}{dt} = k_1 A_t (x_\infty - x_t)^2 \ , \qquad (21)$$

where $k_2 = k_1(a_\infty + x_\infty)^2$; x_t and x_∞ are the molar concentrations of aluminium at time t and at equilibrium; a_∞ is the molar concentration of sodium expressed as NaOH at equilibrium; A_t is the surface area of the solid phase at time t; k_1 and k_2 are the rate constants.

These workers [154] did not attempt to justify theoretically their choice of Eqns. (20) and (21): some of the arguments against the use of these equations are discussed briefly above, and in greater detail by Scotford and Glastonbury [150]. The latter recalculated previous results [152–154] by the initial dissolution rate method, and they showed that the resulting value of the activation energy for the dissolution of gibbsite in alkali is close to their value of (30.6 ± 0.9) kcal $mole^{-1}$. Hence the activation energy is essentially independent of the initial particle size of the solid phase (20–120 μm) and of the concentration of alkali (30–210 g $litre^{-1}$ of Na_2O).

In spite of the fairly large effort devoted to the study of the kinetics of the lixiviation of alumina and of the decomposition of aluminate solutions [1,2], the mechanism of these processes is still far from clear. A full understanding of the processes taking place in metastable aluminate solutions must await the final resolution of the structural problem presented by aluminate ions under different conditions.

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Conformational Analysis of Sulphur-containing Six-membered Heterocycles

N.S.Zefirov and I.V.Kazimirchik

The review deals with one of the problems of dynamic stereochemistry—the conformational analysis of six-membered heterocycles containing bivalent sulphur. The general conformation characteristics of the above class of compounds are reviewed.
The bibliography includes 115 references.

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5. Heterocycles with several sulphur atoms
6. Sulphur-containing heterocycles with a multiple bond in the ring

I. INTRODUCTION

The extensive use of conformational concepts in the interpretation of various transformations of organic compounds is due to the relative simplicity and largely universal applicability of the main postulates of conformational analysis. On the one hand, it involves (at least in its commonest form) taking into account the steric interaction of non-bonded groups of atoms (usually repulsion), from which the most stable conformation is deduced, and, on the other, the steric hindrance in various conformations to the approach of the attacking agent. However, it is quite evident that the presence of a powerful additional non-steric interaction between two or more groups in the molecule could allow the relative stability to be determined precisely by this factor. Such additional interactions (usually regarded as "effects" specific to the given group) are associated mainly with the introduction of polar functional groups and heteroatoms. Hence the unusual conformational behaviour of heterocyclic compounds in relation to their alicyclic analogues becomes understandable.

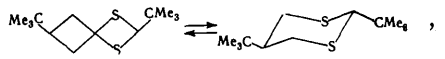
The replacement of a carbon atom in an alicyclic system by a heteroatom can lead to a change both of molecular geometry and of electronic structure. Although the influence of a change in geometry is to a rough approximation often insignificant, particularly in a purely qualitative treatment, nevertheless on passing to a quantitative treatment this inevitably leads to the conformational non-equivalence of the individual positions in the molecule and hence to a wide variety of conformational behaviour of these systems. Sometimes such geometrical changes are shown also on a qualitative level. The change in electronic structure leads to a change in the electric moments, polarity, and degree of solvation, etc. of heterocyclic systems compared with their alicyclic analogues, which is also bound to have an effect on their conformational properties.

The aim of the present review is to examine the conformational behaviour of six-membered systems containing a bivalent sulphur atom. Fairly extensive experimental data have now accumulated, demonstrating the fundamental difference between the conformational behaviour of sulphur-containing heterocycles and not only the corresponding alicyclic compounds but also the analogous oxygen-containing heterocycles. This is why we thought it useful to review the available literature data on the conformational behaviour of six-membered heterocycles containing a bivalent sulphur atom and to formulate its characteristic.

II. GENERAL PROBLEMS IN THE CONFORMATIONAL ANALYSIS OF SULPHUR-CONTAINING COMPOUNDS

The chair conformation of cyclohexane is the most stable and the difference between the energies of the boat and chair forms is estimated as 5–7 kcal mole^{-1} (Table 1) [1-3]. On passing to heterocyclic compounds, the fundamental problem is the change in the energy difference between the chair and flexible conformations (twist-boat). This difference may be related to a change in the barrier to rotation about the C-heteroatom bond compared with the C–C bond. The barrier to rotation about the C–S bond (2.1 kcal mole^{-1} in dimethyl sulphide [4]) is smaller than that to rotation about the C–C bond (3.4 kcal mole^{-1} in propane [5]). Thus, since the eclipsed conformations of sulphur-containing heterocycles are energetically less favourable than those of carbocyclic compounds, presumably compounds of the first kind will show a greater tendency towards existence in the boat conformations. We may note also that the flagstaff–flagstaff interaction, which destabilises the boat conformation, is likewise weakened by virtue of the greater length of the C–S bond. For example, in 1,3-dithiane this distance is 2.4 Å, while in 1,3-dioxane it is 1.46 Å. [6]

Numerous experimental data on the geometry of sulphur-containing heterocycles (derivatives of oxathiane [7,8] and dithianes [9-12]) show that they exist in the chair conformation, which is the main, most stable conformation. However, there are reliable experimental data showing a decrease of the energy difference between the chair and flexible forms. For example, the study of the epimerisation of 2,5-di-t-butyl-1,3-dithiane showed that the difference between the enthalpies of these conformations,



is 3.4 kcal mole^{-1} (Table 1). [13,14]

Table 1. Thermodynamic parameters of the conformational equilibria of the chair/twist type.

System	$\Delta G_{25°}$, kcal mole^{-1}	ΔH, kcal mole^{-1}	ΔS, cal mole^{-1} deg^{-1}	References
Cyclohexane	4.9	5.9	3.5	2
1,3-Dioxane	5.7	7.1	4.8	14,27,28
1,3-Dithiane	1.8	3.4	5.3	13,14

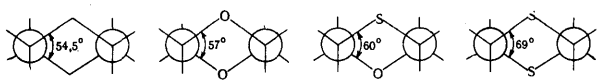
Cyclohexene exists in the stable half-chair conformation [15-17] and the "sofa" conformation is in many instances more stable only for polycyclic compounds [18]. There is also evidence that this conformation predominates for certain sulphur-containing heterocycles [19] (see Section III, 6).

Here special emphasis must be laid on the fundamental difference between sulphur-containing heterocycles and their oxygen analogues. Bearing in mind that the barrier to rotation about the C–O bond is greater than for the C–S bond [20] (2.7 kcal mole^{-1} in methyl ether [21]), the energy difference between the chair and boat conformations of oxygen-containing systems is presumably the same as for cyclohexane. There has been a fairly lively discussion of this problem in the literature; however, the evidence in support of the dominance of boat conformations is frequently based on incorrect theoretical postulates or an incorrect interpretation of experimental data. (See, for example, the discussion concerning 1,4-dioxane derivatives [22-24].) The theoretical estimates of the enthalpy differences between the two conformations of tetrahydropyran [25] (3.9 kcal mole^{-1}) and 1,3-dioxane [26] (2.2 kcal mole^{-1}) evidently cannot be regarded as satisfactory because they were derived taking into account the barrier in methanol, whereas it would be more logical to employ the barriers to rotation in ethers†. Reliable experimental data on the thermodynamics of epimerisation and the heats of formation of 1,3-dioxane derivatives yield 7.1 kcal mole^{-1} for the difference between the enthalpies of the chair and boat forms [14,27-29]. The thermodynamic parameters of the conformational equilibrium of the chair–twist type for the cyclic compounds under consideration are compiled in Table 1.

Thus the specific features of sulphur-containing heterocycles should be revealed in a tendency towards an increased fraction of boat conformations in conformational equilibrium; this should be particularly true of heterocycles with several heteroatoms.

Next, the replacement of a carbon atom by a sulphur atom in a six-membered alicyclic compound should lead to an appreciable distortion of the geometry of the ring, since the length of the C–S bond (1.81 Å) [30] is much greater than that of the C–C bond (1.52 Å) and the C–S–C angle (about 100°) [7-12] differs appreciably from the tetrahedral value. This should lead to an increase of the degree of puckering of the ring and a change in the magnitude of the 1,3-diaxial repulsion.

We shall consider the effect of these factors on the conformational characteristics. An increase in the degree of puckering should lead to an increase of the dihedral angles in the ring.



(I) (II) (III) (IV)

The dihedral angles for cyclohexane [31] (see Buys and Geise [32] for a compilation of data on cyclohexane), dioxane [31], oxathiane [33,34], and dithiane [34,35] are shown in diagrams (I)–(IV). The "average dihedral angle" has been introduced [34] as a parameter characterising the puckering or flattening of the ring. For the above compounds, the values of this parameter are 54.5°, 57.9° (Romers et al. [34]), 58.3° (Schultz et al. [33]), and 65° (Schultz et al. [33]) respectively, which also confirms the above view. Thus, whereas the cyclohexane ring is flattened, the introduction of a sulphur atom leads to an appreciable increase of the dihedral angles.

Table 2. The parameters R for certain six-membered compounds of type X⬡Y.

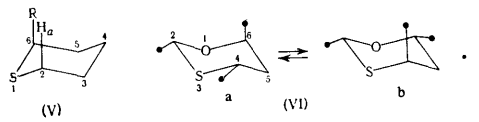
X	Y	I_{trans}, Hz	I_{cis}, Hz	R	Refs.	X	Y	I_{trans}, Hz	I_{cis}, Hz	R	Refs.
CD_2	CD_2	8.04	3.65	2.20	40	S	S	8.11	2.40	3.38	36
O	O	6.11	2.78	2.20	36	O	CD_2	7.41	3.87	1.9	37
O	S	7.35	2.65	2.77	36	S	CD_2	8.54	3.26	2.61	37

Analogous data were obtained in a study of the conformations in solution by ^{1}H NMR. The protons of adjacent methylene groups of 1,4-heterocyclic systems give rise to the AA'BB' signal in the spectrum, from which one can obtain experimental values of I_{cis} and I_{trans}. The first is equal to I_{ae} and the second to $\frac{1}{2}(I_{aa} + I_{ee})$. Their ratio $R = I_{trans}/I_{cis}$ is a parameter characterising the distortion of the chair conformation [36-39]. For a normal chair, $R \simeq 2.2$, while for a puckered chair the parameter should be greater [36-40]. Table 2 lists the values of I_{trans}, I_{cis}, and R for a series of six-membered rings. Evidently all the sulphur-containing compounds have significantly higher values of the parameter R, reaching 3.38, which is evidence of a very marked increase of the dihedral angle in the ring.

We shall examine the variation of the 1,3-*syn*-axial interaction in sulphur-containing rings. The $C_{(2)}$–$C_{(6)}$ distance in tetrahydrothiopyran (V) is greater than in

†The conclusion that the energy difference between the above conformations of 1,3-dioxane is reduced [6] is likewise unsatisfactory owing to the neglect of the eclipsed butane conformations.

cyclohexane, because the smaller C–S–C valence angle compared with C–C–C does not compensate the increased C–S bond length. For example, the $C_{(2)}$–$C_{(6)}$ distance in dithiane is 2.8 Å,[9-12,34] while in cyclohexane the distance is 2.5 Å.[31,32,41] Consequently this should lead to an increase of the distance between R and H_a in tetrahydrothiopyran and hence to decreased 1,3-*syn*-axial repulsion. Consequently the quantity ΔGR, characterising the difference between the free energies of the equatorial and axial conformers[42], will have a smaller absolute magnitude in a series of sulphur-containing heterocycles than in the cyclohexane series, as has been confirmed experimentally[43-47]. In this connection it is important to emphasise also that the reverse situation obtains with oxygen-containing compounds: since the $C_{(2)}$–$C_{(6)}$ distance in this case is 2.3 Å, the steric interaction between R and H_a is much more pronounced[14,29]. This can be clearly illustrated for the isomerisation of trimethyloxathianes (VI, a and b):



(V) a (VI) b

It has been found that for this equilibrium $-\Delta H = 1.15$ kcal mole^{-1}, $-\Delta S = 0.04$ e.u., and $-\Delta G_{25^\circ} = 1.16$ kcal mole^{-1}.[44] Thus the methyl group in the axial position is located "preferentially" next to the sulphur atom at $C_{(4)}$. Pihlaja and Pasanen[44-46] calculated by an additive procedure the contributions of the individual interactions in 1,3-heterocyclic six-membered systems, the relevant data being presented in Table 3.

Table 3. The contributions of the 1,3-interactions for heterocycles with heteroatoms in the 1,3-positions[44].

Heteroatom		Interaction energy, kcal mole^{-1}				
1	3	$H_{(2)}$-$Me_{(6)}$ or $H_{(6)}$-$Me_{(2)}$	$H_{(2)}$-$Me_{(4)}$ or $H_{(4)}$-$Me_{(2)}$	$H_{(4)}$-$Me_{(6)}$ or $H_{(6)}$-$Me_{(4)}$	$Me_{(5)}$-1	($Me_{(5)}$-3
O	O	2.035	2.035	0.885	0.46	0.46
S	S	0.885	0.885	0.805	0.52	0.52
O	S	2.20	1.05	0.73	0.74*	

*The sum $Me_{(5)} - 1 + Me_{(5)} - 3$.

Table 3 shows that the energies of the *syn*-axial interaction of the methyl group and the hydrogen atom in the 2- and 6-positions in dioxane and dithiane are 2.035 and 0.885 kcal mole^{-1}, i.e. differ by a factor of 2.3. We may mention for comparison that ΔG for methylcyclohexane is 1.7 kcal mole^{-1}.[42]

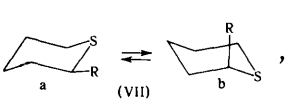
The introduction into the ring of a heteroatom with a lone pair of electrons gives rise to the problem of their interaction with the axial substituent. The problem of the existence of the "steric volume" of the electron pair of the heteroatom as an effective conformational parameter is controversial[13,48-55]. Table 3 shows that the repulsion of the axial methyl group in the 5-position from the oxygen atom (0.46 kcal mole^{-1}) is weaker than its repulsion from the sulphur atom (0.52 kcal mole^{-1}), which may be attributed to the increase of the van der Waals radius. However, both these values are fairly low, which is the reason for the possible existence of axial conformers.

The most striking example is provided by 2,5-*cis*-disubstituted derivatives of 1,3-dioxane and 1,3-dithiane[52-55] in which even the t-butyl group can assume the axial conformation[52]. However, in the presence of a polar substituent the situation becomes more complicated. Dipole–dipole repulsion or attraction between the substituent and the heteroatom[44] as well as interaction between the orbitals of the lone electron pairs of the ring heteroatom and the substituent become possible ("the hockey-stick effect")[29,56,57]; see Section III, 4). However, *a priori* estimates for dipole interactions in sulphur-containing compounds are difficult. On the other hand, the overlapping of the orbitals should become more marked on passing from oxygen to sulphur by virtue of the greater spread of the 3*p* orbital of sulphur compared with the 2*p* orbital of the oxygen atom. Possibly one should also consider the difference between the degrees of hybridisation of oxygen and sulphur atoms (the C–O–C and C–S–C valence angles should be compared) and consequently the difference between the steric directions of the orbital axes of the lone electron pairs[13]. We may also note that the most striking effect of the conformational characteristics of heterocyclic compounds is probably the anomeric effect[58-60]. Bearing in mind the polar nature of this effect, it should be expected also for sulphur-containing compounds[59]. Finally the sulphur atom can be formally quadrivalent and sexivalent and hence tricoordinate and tetracoordinate respectively. Such compounds have many interesting conformational characteristics (see, for example, Refs. 61–63); but their discussion is outside the scope of the present review.

III. CONFORMATIONS OF SIX-MEMBERED SULPHUR-CONTAINING HETEROCYCLES

1. Derivatives of Tetrahydrothiopyran

There are no data on the geometry of tetrahydrothiopyran (thiane), but ^{1}H NMR spectroscopic data[36-38] (Table 2) show that the compound exists in the puckered chair form. The experimental barrier to the inversion of tetrahydrothiopyran is 11.7 kcal mole^{-1} [37] (cf. 10.7 kcal mole^{-1} for tetrahydropyran[37]) and is therefore close to the value for cyclohexane derivatives[64]. Systematic conformational studies on functional derivatives of tetrahydrothiopyran have not been made either. In stereochemical studies on compounds of this series attention was concentrated on the problem of the anomeric effect. The equilibrium (VII) has been investigated[43,47,65] for a wide range of 2-substituted tetrahydrothiopyrans and the presence of a distinct anomeric effect was demonstrated [the predominance of conformer (VIIb) in the conformational equilibrium]:

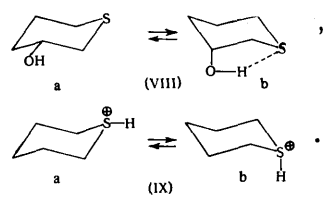


a (VII) b

where R = Cl,[47] OH,[66] OR,[43,47] SAlk,[43,47] SAr,[43] or $SP(S)(OR)_2$.[43]

The effect of the solvent on the position of conformational equilibrium is consistent with the polar nature of the anomeric effect: on passing from CCl_4 to CH_3CN, the contribution of conformer (VIIb) diminishes. The anomeric effect is shown to a greater extent with the

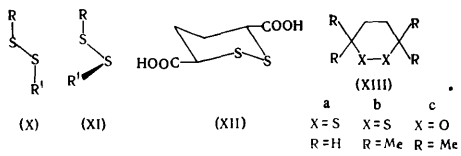
C–S–C–OR fragment than with C–O–C–SR.[59] This behaviour was explained by the weakening of the 1,3-*syn*-axial repulsion in tetrahydrothiopyran (see Section II). It must be emphasised that the anomeric effect has been found for the C–S–C–SR fragment and therefore the repulsion between the two sulphur atoms is fairly strong and must be taken into account as one of the factors in conformational equilibrium (0.7 kcal mole^{-1} in carbon tetrachloride[43]). As expected, the anomeric effect for 2-chlorotetrahydrothiopyran is fairly pronounced (1.75 kcal mole^{-1}).[47] We may also note that an appreciable "benzene effect" has been found for 2-alkoxytetrahydrothiopyrans[34,47]. An interesting conformational features has been noted for 3-hydroxytetrahydrothiopyrans[67]. Infrared spectroscopy revealed the presence of an intramolecular hydrogen bond in this compound, but the existence of the latter is possible only for the axial conformation (VIIIb). We may also note that the axial conformer (IXb) predominates in the conformational equilibrium of the protonated form (IX)[37]:



^{1}H NMR data have shown that the geometries of the rings of tetrahydrothiopyran and its *S*-methylsulphonium salt are almost identical and *R* is in the range 2.3–2.6.[68]

2. Derivatives of 1,2-Dithiane

For aliphatic disulphides, the transoid conformation (X) is not the most stable, as might have been expected on the basis of elementary stereochemical considerations. The disulphide molecule has the zig-zag shape (XI),[69–72] as shown by quantum-mechanical calculations of the potential curves for barriers to rotation about the S–S bond, and is consistent with the concept of the so called "*gauche*-effect"[73,74]. It is important to emphasise in this connection that such geometry of the disulphide bridge makes it possible to incorporate it without much strain in the chair conformation of the six-membered ring.



There are few experimental data for 1,2-dithianes. X-Ray diffraction analysis of *trans*-1,2-dithiane-3,6-dicarboxylic acid (XII) showed that the compound exists in the chair conformation with the carboxy-groups in the equatorial positions[75,76].

A study of the temperature variation of the ^{1}H NMR spectra of 1,2-dithiane (XIIIa) showed that the free energy of the inversion of the chair form is 11.6 kcal mole^{-1}.[77] Similarly $\Delta G^{\neq}_{-20^\circ C}$ for the tetramethyl derivative (XIIIb) is 13.8 kcal mole^{-1} ($\Delta S^{\neq}$ = 6.7 e.u.)[77]. This value is smaller than for the corresponding oxygen-containing analogue (XIIIc), where $\Delta G^{\neq}_{12^\circ} = 14.6$ kcal mole^{-1} ($\Delta S^{\neq} = 14.4$ e.u.).

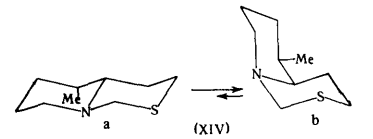
It is particularly interesting that the curves giving the energy as a function of the coordinate for the conformational transition of the last two compounds differ appreciably from one another[77]. The authors attribute this to different transition states in the inversion of these compounds. Compound (XIIIc) undergoes inversion via an asymmetric boat form (minimum) with two maxima corresponding to conformations with planar five-atom fragments. The maximum for the sulphur-containing compound (XIIIb) corresponds to the symmetrical boat conformation. This conformation is impossible for compound (XIIIc) owing to the powerful repulsion of the methyl group in the "flagstaff" position; such repulsion for the sulphur-containing compound (XIIIb) is much weaker owing to the increase of the C–S distance.

3. Derivatives of 1,3-Oxathiane and 1,3-Dithiane

Six-membered systems with heteroatoms in the 1,3-positions have recently been studied extremely vigorously. The results of these investigations have been described in several reviews[6,13,14,29,44]. Therefore we shall confine ourselves to an examination of the general relations formulated in Section II. The preferential conformation of 1,3-dithiane is the chair form with an inversion barrier of 10.4 kcal mole^{-1}.[78]

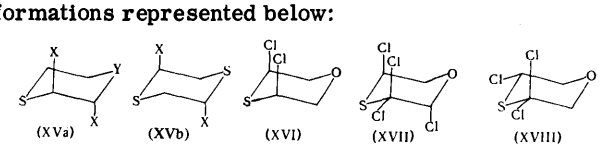
The powerful influence of hydrogen bonds on the relative stabilities of the conformations may also be noted. Thus the axial isomer of 5-hydroxy-1,3-dithiane is more stable than the equatorial isomer [ΔG = 0.5 kcal mole^{-1} (Luttringhaus et al.[79]) and 0.8 kcal mole^{-1} (Abraham and Thomas[80])].

Derivatives of 1-aza-3-thiabicyclo[4,4,0]decane exist in the chair conformation, like *trans*-decalin[81]. However, in the presence of the axial methyl group in the 7-position of compound (XIV) the conformation with the *trans*-junction becomes less stable and conformer (XIVb) with the *cis*-junction of the rings predominates in the conformational equilibrium[81]:

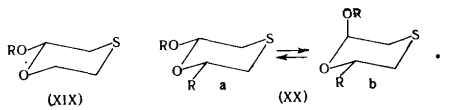


4. Derivatives of 1,4-Oxathiane and 1,4-Dithiane

Numerous studies on the geometries of oxathiane[7,8,34,82,83] and dithiane[9–12,34,35,84,85] showed that these compounds exist in the chair conformation. The inversion barrier for 1,4-dithiane itself is unknown; however it amounts to 10.05 kcal mole^{-1} for the perfluoro-derivative[86]. A distinct anomeric effect has been found for the *trans*-2,3- and *trans*-2,5-dihalogeno-derivatives (XV, a and b), since the halogen atoms occupy the axial positions[7,9,10]. Judging from the infrared spectra and the dipole moments, the same conformation exists also in solution. It has been found[82] that *trans*-3,5-dichloro-oxathiane (XVI) and also polychloro-oxathianes (XVII) and (XVIII) have the conformations represented below:



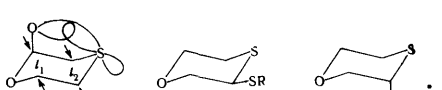
However, we may note that these assignments are based on the spin–spin interaction constants which sometimes had an "intermediate" value of the order of 6 Hz. Possibly this indicates the occurrence of conformational equilibria. Although the anomeric effect has been found for the majority of the compounds, for example (XV) and (XVI), certain questions remain obscure. For example, it is not clear why the diaxial repulsion between two chlorine atoms leads to the predominance of conformation (XVIII) but is not found in compound (XVII). The anomeric effect has been found also for a series of polyfluoro-derivatives of oxathianes and dithianes [87,88].



(XIX) (XX)

Unusual results were obtained in a study of the alkoxy-derivatives of oxathiane. Detailed studies of various 2-alkoxyoxathianes by ^{1}H NMR showed that the equatorial conformer (XIX) predominates in the conformational equilibrium [56], in sharp contrast to 2-alkoxy-derivatives of tetrahydropyran, tetrahydrothiopyran, and 1,4-dioxane [59]. For example, at least 50% of the equatorial form is present in conformation equilibrium for 2-methoxy- and 2-butoxy-1,4-oxathianes, These data were confirmed by a study of the epimerisation of 2-alkoxy-6-methyl-, 2-alkoxy-6-hydroxymethyl-, and 6-acetoxymethyl-2-alkoxy-1,4-oxathianes (XX) [89–92]. Epimerisation leads to an equilibrium in which the diequatorial isomer (XXa) (67%) predominates, in sharp contrast to the behaviour of tetrahydropyrans[59].

A possible explanation of this phenomenon was based on the "hockey-stick" effect [56,57]. The overlapping of the orbitals of the substituent and the sulphur atom leads to repulsion, because the two orbitals are populated by four electrons. Such repulsion probably depends on the nature of the heteroatoms (S > O) and fine geometrical details [for example, the relative distances l_1 and l_2 in compound (XXI)]:

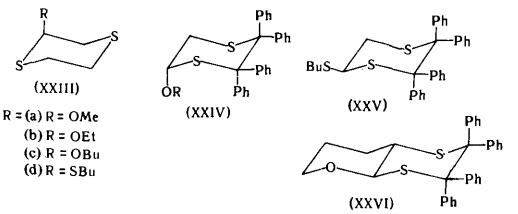


(XXI) (XXIIa) (XXIIb)

The position of conformational equilibrium for 3-propylthio- and 3-butylthio-1,3-oxathianes [93,94] depends on the solvent. In acetonitrile these compounds exist almost entirely in the equatorial conformation (XXIIa). An increased content of the axial conformer (XXIIb) (25–40%) is observed in carbon tetrachloride.

The data on the conformational behaviour of dithiane derivatives are non-systematic. The anomeric effect has been discovered for a series of 2-alkoxy- and 2-alkylthio-1,4-dithianes by ^{1}H NMR, [94] i.e. the axial conformation (XXIII) predominates. However, as noted by the authors themselves, these data are based on arbitrarily selected standard values of Iaa, Iae, and Iee and in the absence of a large set of data for model compounds this conclusion must be treated with caution. A distinct predominance of the axial conformer was found for the tetraphenyl derivative (XXIV). [95] However, the corresponding butylthio-derivative (XXV) exists in the equatorial conformation [95]. Possibly as a result of the large bulk of the sulphur atom, the 1,3-repulsion between the butylthio-substituent and the axial phenyl group predominates in this case over the anomeric effect. The axial conformation (XXIV) is possible owing to the weakening of the 1,3-repulsion (see Section II).

The reaction of thiobenzophenone with dihydropyran leads to the bicyclic compound (XXVI) having the *trans*-configuration [95,96]. In this connection it is interesting to investigate its epimerisation and to compare its stability with that of the *cis*-isomer.



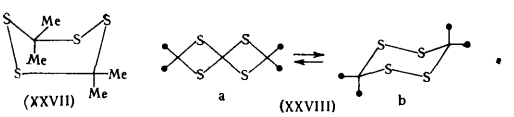
(XXIII) (XXIV) (XXV)

R = (a) R = OMe
(b) R = OEt
(c) R = OBu
(d) R = SBu

(XXVI)

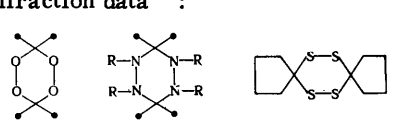
5. Heterocycles with Several Sulphur Atoms

As early as 1937, it was shown by X-ray diffraction that 1,3,5-trithiane exists in the chair conformation [97,98]. The inversion barrier is 11.0 kcal mole^{-1}. [99] However, X-ray diffraction analysis of 3,3,6,6-tetramethyl-1,2,4,5-tetrathiane (XXVII) showed that in the crystal lattice this compound has the true boat conformation (XXVII), the sulphur atoms being displaced from the plane [100]:



(XXVII) a (XXVIII) b

The study of the conformations of this compound in solution by ^{1}H NMR demonstrated the presence in the equilibrium mixture of two conformers: the more stable twist-form (XXVIIIa) and the less stable chair conformation (XXVIIIb). [101] At −15°C the (XXVIIIa)/(XXVIIIb) ratio in carbon disulphide is 2.6 and $\Delta G^{\neq}_{50}{}^{\circ} = 16$ kcal mole^{-1}. It must be emphasised that the oxygen analogue (XXIX) [102] and the nitrogen analogue (XXX) [103] of compound (XXVII) exist in the chair conformations. We may also note that the inversion barrier for the thia-derivative (XXVIII) is higher than for compounds (XXIX) ($\Delta G^{\neq}_{30}{}^{\circ} = 15.4$ kcal mole^{-1}) and (XXX) ($\Delta G^{\neq} = 11.7$ kcal mole^{-1}). An equilibrium between the chair and twist conformations, with the former predominating (80%) was observed also for the bistetramethylene derivative (XXXI). [101] The stability of the chair conformation of (XXXI) was also demonstrated by X-ray diffraction data [101]:



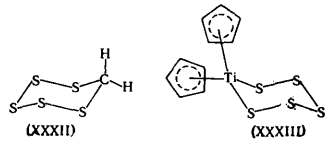
(XXIX) (XXX) (XXXI)

It is interesting that, when crystals of tetrathiane (XXVIII) are cooled to −80°C and dissolved at this temperature in carbon disulphide, a solution of the pure twist form is formed. Bearing in mind the above X-ray diffraction data, this finding implies that the boat/twist transition (XXVII) → (XXVIIIa) has an extremely low potential barrier [101].

Thus a minimal difference between the energies of the twist and chair conformations (0.49–0.6 kcale mole^{-1}) is characteristic of tetrathiane (XXVIII). This finding can be explained both by the factors discussed in section (II) and

by additional factors among which mention may be made of the *syn*-axial interaction of the electron pairs ("the rabbit ear effect"[104]) and the influence of the *gem*-dialkyl groups (the Thorpe–Ingold hypothesis concerning the deviation of the valence angles[105,106]).

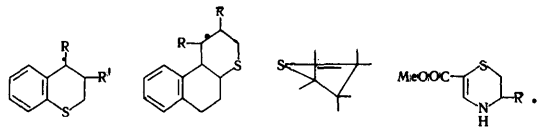
Pentathiane exists in an exceptionally stable chair conformation (XXXII).[107] The ^{1}H NMR spectrum at room temperature shows the signal of the AB-system of the equatorial and axial protons. The authors point out the possibility of inversion at elevated temperatures but do not quote experimental details. The separate signals of the two cyclopentadienyl rings are also shown for the analogous cyclic pentathia-compound (XXXIII) at +30°C. However, coalescence is observed at 90°C and at 120°C the spectrum consists of a sharp singlet, which indicates rapid (on the NMR time scale) inversion of the six-membered ring of compound (XXXIII)[108].



(XXXII) (XXXIII)

6. Sulphur-containing Heterocycles with a Multiple Bond in the Ring

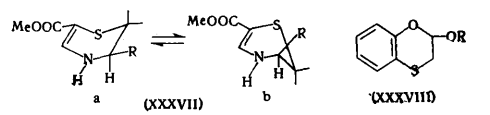
As stated above (section II), the half-chair conformation is the most stable for cyclohexene[15–17]. The "sofa" conformation is encountered in isolated cases[18]. The data concerning the most stable conformations of unsaturated sulphur-containing systems are unfortunately limited. The "sofa" conformation (XXXVI) has been adopted for a series of thiachromans (XXXIV) and dihydronaphthothiapyrans (XXXV):[19]



(XXXIV) (XXXV) (XXXVI) (XXXVII)

However, this conclusion was based only on the spin–spin interaction constants using the Karplus equation and cannot be regarded as very reliable. The "sofa" conformation was also postulated for derivatives of 2,3-dihydro-6-methoxycarbonyl-1,4-thiazine (XXXVII)[109–111], but the evidence supporting this is doubtful too.

A number of studies have been made on the conformations of functional derivatives. A distinct anomeric effect was found for 2-alkoxybenzoxathianes (XXXVIII):[112]



a (XXXVII) b (XXXVIII)

The content of the axial conformer is in excess of 80% and is almost independent of the nature of the alkoxy-group. Interesting data were obtained for compounds of type (XXXVII)[109–111]. The methyl derivative (XXXVII) (R = CH_3) contains equal amounts of the equatorial and axial forms, (XXXVIIa) and (XXXVIIc), in conformational equilibrium. The axial conformers (XXXVIIb) of compounds (XXXVII, R = OH, OAc, CH_2Cl, and CH_2I) predominate in the conformational equilibrium. The equilibrium position for the methoxycarbonyl derivative (XXXVII, R = $COOCH_3$) depends on the solvent: the conformer (XXXVIIa) predominates in non-polar solvents, while in polar solvents the equilibrium is displaced towards the axial form (XXXVIIb). Evidently a detailed interpretation of these results is fairly difficult.

The numerous "exceptions" found in conformational studies on heterocyclic compounds clearly show that the introduction of heteroatoms with lone electron pairs, which cause an appreciable change in the geometrical relations in the molecule, leads to the appearance of a new set of properties, the understanding of which requires a development of the principles of conformational analysis. Although experimental studies have clearly demonstrated the inadequacy of the theoretical concepts in the field of conformational analysis, nevertheless it is already possible to discover in broad outline the principal characteristics of the conformational behaviour of heterocycles. As shown by the present review, sulphur-containing compounds exhibit interesting and even unique conformational features, the further study of which will undoubtedly promote a general progress in this branch of stereochemistry.

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Further reports were published[113–115] during the period when the review was considered by the editors.

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The Mode of Cyclisation of the Arylhydrazones and *O*-Phenyl Ethers of the Oximes of Asymmetric Ketones Under the Conditions of the Fischer Reaction

I.I.Grandberg and V.I.Sorokin

Both the Fischer synthesis of indoles and the recently discovered rearrangement of *O*-phenyl ethers of oximes, which takes place under similar conditions and leads to the formation of benzofurans, are assessed in the review from the same standpoint. A number of studies published recently altered the ideas held for a long time concerning the mode of cyclisation of the arylhydrazones of asymmetric ketones into indoles. It was believed previously that CH_3, CH_2, and CH groups in the α-position in the carbonyl fragment constitute a series in which the capacity for cyclisation increases. However, it has been found that the acidity of the medium plays a very significant role in determining the mode of cyclisation and can actually reverse it. The concepts put forward to account for this finding are examined critically and general ideas are developed which, in the author's view, explain satisfactorily the influence of the pH of the medium and of certain other factors on the mode of cyclisation of both arylhydrazones and *O*-aryloximes.
The bibliography includes 109 references.

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1. GENERAL POSTULATES OF THE MECHANISM OF THE FISCHER REACTION

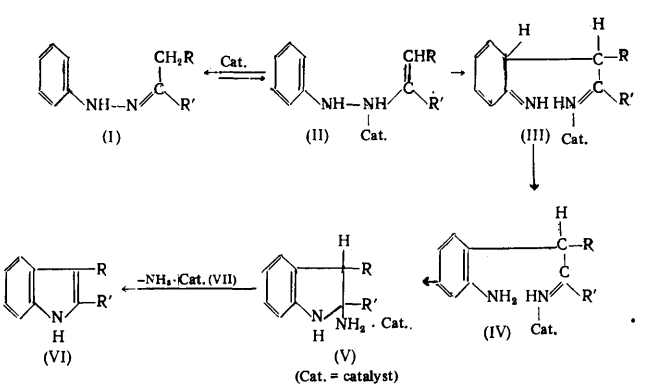
The cyclisation of arylhydrazones into indole derivatives in acid media, discovered by Fischer in 1883,[1] still continues to attract attention. This reaction has become the basis for a general, convenient, and easy preparative method for synthesising a wide variety of indole derivatives. Several mechanisms have been proposed at different times for this reaction, but those put forward by Reddelin[2] and Wieland[3], Bamberger and Landau[4], Neber et al.,[5] and Pausacker and Schubert[6] failed to pass experimental tests.

The generally accepted mechanism of the Fischer indole synthesis, to which a number of reviews have been devoted[7-12], is now that proposed by G. M. and R. Robinson[13,14] supplemented and additionally elucidated by Allen and Wilson[15], Carlin and Fischer[16], Arbuzov and Kitaev[17], and Suvorov et al.[18]

The elucidation of the mechanism of the synthesis of tryptamines from arylhydrazones and γ-chloroketones in a number of studies by Grandberg and coworkers[19-22] also made a definite contribution to the Robinson mechanism.

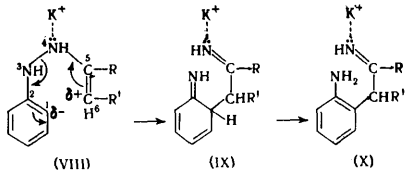
According to the Robinson mechanism, the reaction proceeds via the following main stages: (1) tautomeric conversion of the hydrazone (I) into the enehydrazine (II); (2) formation of a new C–C bond [(II) → (III)]; (3) cyclisation with subsequent elimination of an ammonia molecule and the formation of the indole structure [(III) → (IV) → (V) → (VI)].

The first and second stages of the reaction [(I) → (II) and (II) → (III)] are of greatest theoretical interest, while the last stage [(III) → (IV)] permits different ways of indole ring closure, depending on the conditions under which the indole is formed.



The most important stage of the process—the formation of a new C–C bond [(II) → (III)]—was regarded until recently as involving intramolecular electrophilic attack by the ene fragment on the aromatic ring[9-12]. On the basis of the concepts of the general theory of conjugation[23,24], Arbuzov and Kitaev[17] suggested that this stage be regarded as an intramolecular rearrangement of the activated 1,6-conjugated system. In an acid medium or on formation of a complex with the catalyst, this conjugated system is activated: bond polarisation is enhanced as a result of which the atoms in the 1- and 6-positions receive excess charges which are of opposite sign. When these atoms are in significantly close proximity, the formation of a bond between them, leading to a redistribution of

electron density in the system and the rearrangement (VIII) → (X) with dissociation of the 3–4 linkage, becomes quite probable.

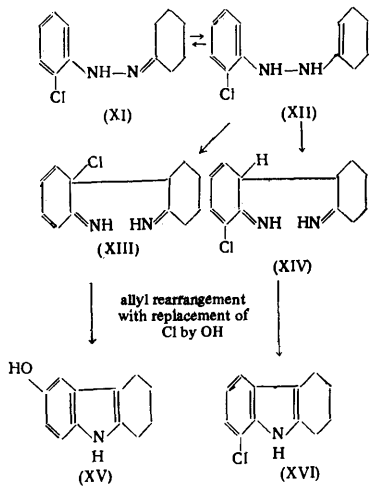


(VIII) (IX) (X)

However, it is noteworthy that there is virtually no direct experimental evidence for the electrophilic attack.

The evidence supporting the electrophilic attack, which explains the influence of substituents in the aromatic ring of arylhydrazones on the reaction, quoted by a number of workers[25–28] is based on two unproved hypotheses, namely that the stage involving the formation of a new C–C bond [(II) → (III)] determines the rate of the entire reaction and that the yield of the indole derivative is directly proportional to the rate of the stage. Moreover, the ideas according to which the formation of the C–C bond involves a carbon atom in the aromatic ring already occupied by a substituent are inconsistent with the general theory of electrophilic substitution. It is well known that as a rule an electrophilic species is directed to the position without a substituent even in those cases where the substituent is an electron-donating group. This is because the abstraction of a proton from the resulting σ-complex is more favourable on energy grounds than the abstraction of another positively charged group. Exceptions are observed only in the case of non-concerted orientation, severe process conditions, and marked electrophilicity of the attacking species (NO_2^+, SO_3H^+).[29]

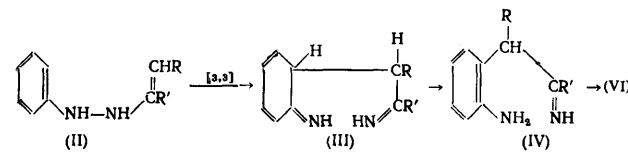
As an example one may quote the data of Barnes et al.,[30] who observed the formation of a mixture of two products [(XV) and (XVI)] on conversion of the *o*-chlorophenylhydrazone of cyclohexanone (XI) into an indole derivative. It was found that, together with the normal product 8-hydroxytetrahydrocarbazole (XVII), the reaction involves also the formation of 6-hydroxytetrahydrocarbazole (XVI), the structure of which was subsequently proved[31], i.e. the formation of the C–C bond involves also a position occupied by a substituent even though a free position is present in the aromatic ring.



(XI) (XII) (XIII) (XIV) (XV) (XVI)

Indole structure syntheses of this kind, in which the C–C bond is formed with a carbon atom of the aromatic ring occupied by a substituent with subsequent migration or elimination of the substituent, are fairly numerous[16,32–42]. These results led to doubts being cast in one of the recent studies on the electrophilic mechanism of the formation of the C–C bond in the second reaction stage[43] and it was suggested that the formation of the C–C bond in the Fischer reaction occurs as a result of a sigmatropic [3,3] rearrangement.

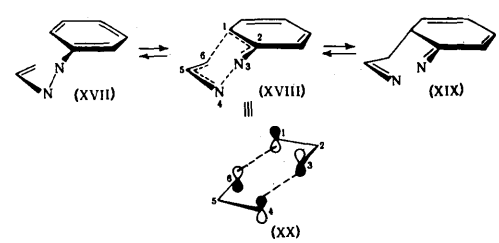
A similar approach was previously justified in the discussion of the mechanism of the Claisen rearrangement[44,45]. Other reactions related to the Fischer indole synthesis (for example the benzidine rearrangements) were also regarded in the above study as sigmatropic rearrangements[43].



(II) (III) (IV) →(VI)

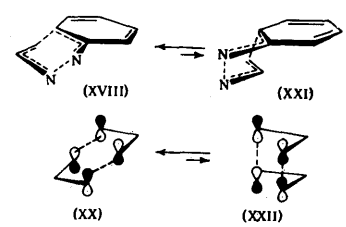
Cautious attempts to regard the Fischer reaction as a sigmatropic rearrangement were described in the literature even earlier. Thus Schmid and coworkers[46] suggested that the acid-catalysed Fischer reaction may be a sigmatropic process and Robinson suggested, using a more cautious form of words[10], that a process of this kind is possible only in the thermal indole-formation reaction.

In the study quoted above[43] an attempt was made to explain the available experimental literature data for the Fischer reaction and similar processes from the standpoint of the principle of the conservation of orbital symmetry. In this treatment the formation of a new C–C bond in the reaction proceeds via a four-centre transition state [the chair conformation (XVIII)], which consists of two highest occupied molecular orbitals of allyl radicals in which the 3–4 linkage has still not been finally ruptured and the 1–6 linkage has not been finally formed [formula (XX)].



(XVII) (XVIII) (XIX) (XX)

The interaction of the central parts of the non-bonding molecular orbitals does in fact occur in the chair conformation[47], which is the reason for its advantage over the boat conformation of the transition state (XXII).

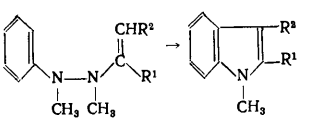


(XVIII) (XXI) (XX) (XXII)

In this approach to the process the nitrogen atoms in the 3- and 4-positions, in the system of atoms in the positions ranging from 1 to 6 which are directly involved in the rearrangement, are formally treated as carbon atoms; hence it is assumed that their n electrons are not involved in the process[43]. The recently described syntheses of 1-acylindoles can probably be regarded as experimental confirmation of this postulate[48-50].

Sigmatropic rearrangements are known to be non-catalysed intramolecular thermal processes. Therefore the question of the validity of the extension of the theory of sigmatropic reactions to the Fischer cyclisation of phenylhydrazones, which are classified as acid-catalysed processes[7-12], may seem to arise at first sight. However, it has recently been suggested in a number of studies that the involvement of acid catalysts in the Fischer reaction is not obligatory[51,52]. Moreover it has been shown that, when the enehydrazine formed is reduced in the synthesis of the arylhydrazone, it is readily converted into an indole derivative on heating both with and without a catalyst[43].

Chiess and Grieder[53] investigated the behaviour of enehydrazines on heating in the absence of a catalyst and established that the enehydrazines (XXIII) give rise in this case to a 25–74% yield of the corresponding indoles (XXIV) in decalin at 110°C. This cyclisation was also achieved in absolute acetonitrile in the presence of 0.5 N dichloroacetic acid:



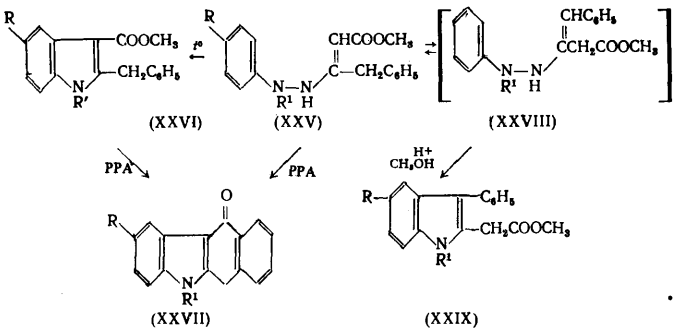
(XXIII) (XXIV)

In most cases the use of an acid catalyst accelerates the process and lowers the reaction temperature.

Kelly et al. investigated the thermal conversion of phenylhydrazones into indoles without using acid catalysts, which proved to be successful[54] (this study is described in detail below).

In a study of the behaviour of methyl γ-phenylacetoacetate in the Fischer indole synthesis, Grinev and coworkers[55,56] established that compound (XXV) is converted in a thermal process into 2-benzylindole derivatives (XXVI). When compound (XXV) was treated with polyphosphoric acid, derivatives of 6,11-dihydro-11-hydroxybenzo[b]carbazole (XXVII) were isolated. The reaction probably proceeded via a stage involving the formation of methyl esters of 2-benzylindole-3-carboxylic acids (XXVI) with subsequent intramolecular cyclisation, since on heating with polyphosphoric acid compound (XXVI) yielded compound (XXVII). When compound (XXV) was treated with sulphuric acid in methanol at room temperature, methyl esters of 3-phenylindole-2-acetic acid (XXIX) were isolated.

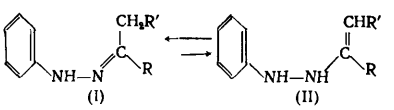
Thus experimental data show that, contrary to the generally accepted view, the Fischer reaction can occur also in the absence of acid catalysts. It is well known that, for compounds containing atoms with different electronegativities in the tautomeric triad (for example, in the keto–enol, lactim–lactam, and thione–thiol tautomerism), the tautomeric equilibrium is usually displaced towards the form in which the proton is linked to the less electronegative atom.



(XXVI) (XXV) (XXVIII)

(XXVII) (XXIX)

For arylhydrazones of the usual carbonyl compounds (I), the shift of the equilibrium towards the hydrazone should be enhanced also in consequence of the electronegative influence of the C_6H_5NH residue on the main tautomeric fragment, since electron-accepting substituents at the nitrogen atom in potentially tautomeric systems are known to shift the tautomeric equilibrium in this particular direction[57]:



(I) (II)

Calculations by the LCAO-MO method in terms of the Hückel approximation of the molecular energies of the tautomeric forms of acetophenone phenylhydrazone confirmed that arylhydrazones exist in the hydrazone and not the enehydrazine form—the latter is less favourable to the extent of approximately 4 kcal mole^{-1} even for acetophenone hydrazone, where it is stabilised by conjugation[58].

This can explain the finding that the existence of the enehydrazine form (II) in solutions of arylhydrazones of aliphatic aldehydes and ketones has not so far been observed by physicochemical methods[10]. The 23 kcal mole^{-1} energy gain for the protonated hydrazine molecule in relation to the enamine is evidence that acid agents displace the equilibrium towards the hydrazone form but at the same time they should increase also the rate of the tautomeric transformation by taking part in proton transfer[43].

However, insufficient attention has been devoted to the mechanism of the tautomeric transformation, particularly bearing in mind that, according to kinetic studies[59-62], this is in fact the rate-determining stage in the Fischer reaction. Pausacker and Schubert[59] made the first attempt to investigate the kinetics of the Fischer reaction. They established that in glacial acetic acid the reaction is of first order. Subsequently this was confirmed by other investigators[60,61], although the cyclisation conditions were different. The reaction was performed in glacial acetic acid[60] and in alcoholic solutions of hydrochloric acid[62], while Grandberg and Przheval'skii[61] studied the kinetics of the conversion of cyclohexanone phenylhydrazone into an indole derivative on treatment with allyl bromide.

Scheltus determined the rate constants for the cyclisation of cyclohexanone phenylhydrazone in an aqueous alcoholic solution of hydrochloric acid[62]. Measurements were

also made of the rate constants for the conversion of the phenylhydrazones of various cyclic ketones into indole derivatives, which were compared with the pK_a values for these compounds[62]. Moreover it has been noted[59-62] that, following the addition of water to the solvent, the rate of reaction increases. Thus Pausacker and Schubert[59] established that, on diluting glacial acetic acid by the addition of 6.3 and 16.0 mole % of water, the rate constant increases from 6.18×10^{-5} to 7.68×10^{-5} and 9.37×10^{-5} respectively.

In a study of the effect of the acidity of the medium on the rate of the Fischer reaction it was established[62] that the values of $\lg k$ are satisfactorily correlated with the acidity functions H_0 (Fig. 1).

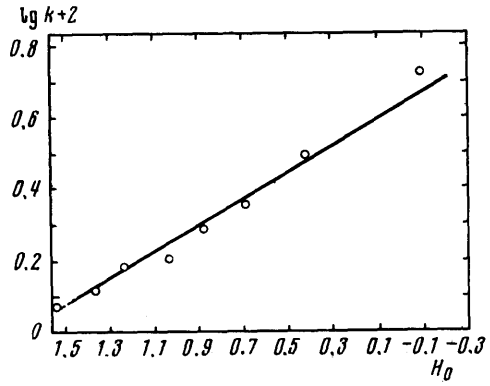


Figure 1. Variation of the logarithm of the rate constant for the reaction of cyclohexanone phenylhydrazone with the acidity function H_0 in 60% methanol as the solvent.

The problem arises of which stage of the conversion of the arylhydrazone into an indole should be regarded as the slowest. If one assumes that this stage is the formation of a new C–C bond as a result of electrophilic attack on the aromatic ring, it is difficult to explain from this standpoint the marked acceleration of the reaction by the p-CH_3O group in relation to the m-CH_3O group (from the standpoint of electrophilic substitution, the opposite effect should have been observed). Moreover, it is well known that electrophilic substitution in the aromatic series is accelerated by the introduction of electron-donating substituents into the ring, but it has been observed that the introduction of the m-CH_3O group leads to a decrease of the rate of reaction compared with the unsubstituted product.

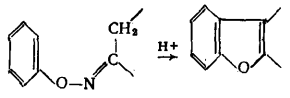
Thus experimental facts suggest that the stage involving the formation of a new C–C bond is hardly rate-limiting in the Fischer reaction and throw doubt on its electrophilic nature.

These kinetic data can be satisfactorily accounted for from another standpoint, namely that the slowest stage is the tautomeric conversion of the hydrazone into the enehydrazine [(I) ⇌ (II)].

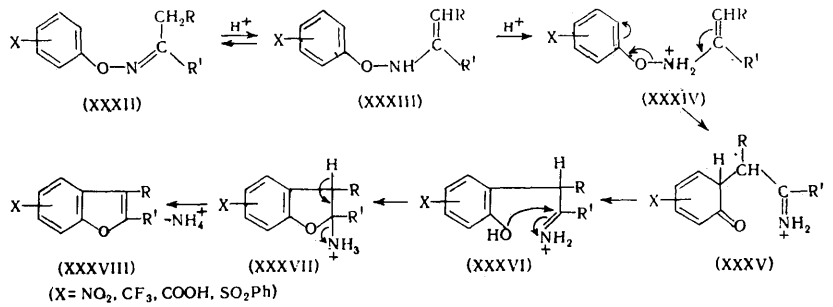
The following facts confirm this view: (1) on cyclisation of the phenylhydrazone of α-deuterated cyclohexanone, a kinetic isotope effect was observed ($K_D/K_H = 1.8$)[62]: (2) in the D_2O–CH_3OH–HCl solution cyclohexanone phenylhydrazone reacts twice as fast as in the H_2O–CH_3OH–HCl system[62]; (3) the rate constants for the phenylhydrazones of cyclic ketones are satisfactorily correlated with the basicities of these compounds[62]; (4) a methyl group introduced into the 2-position of the cyclohexane ring of cyclohexanone phenylhydrazone accelerates the reaction approximately by a factor of eight compared with the unsubstituted hydrazone[60]; an increase of the acidity of the medium leads to an increase of the rate of reaction[62].

In addition it is possible to explain from this standpoint the effect of substituents in the aromatic ring on the rate of reaction. Electron-donating substituents in the p- and o-positions in the aromatic ring of arylhydrazones increase the basicity of the β-N atom (protonation is probably the initial stage of the tautomeric transformation), in contrast to the substituents in the m-position. This is also indicated by the finding[63,64] that the basicity of the three isomeric methoxyphenylhydrazones decreases in the sequence 4 > 2 > 3.

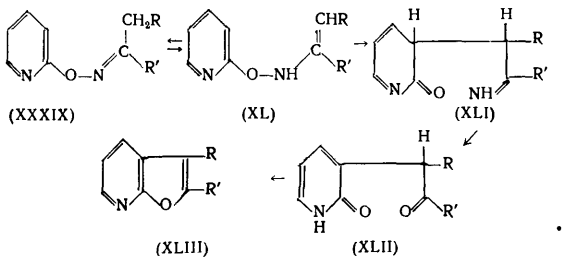
Thus, on the basis of data for the kinetics of the Fischer reaction, one can probably assume that the rate-limiting stage is the tautomeric conversion of the hydrazone into the enehydrazine [(I) ⇌ (II)]. In 1966 Sheradsky reported the acid-catalysed rearrangement of phenyl ethers of oximes (XXX) into benzofuran derivatives (XXXI), which he discovered[65]:



This report was followed by several communications in which it was suggested that the mechanism of this reaction is analogous to that of the Fischer indole synthesis[66-76]:



It is interesting to note that the introduction of two powerful electron-accepting groups, such as two NO_2 groups or a CF_3 and an NO_2 group, into the *o*- and *p*-positions in the aromatic ring does not prevent the closure of the benzofuran ring (39% yield for derivatives with *o*-CF_3 and *p*-NO_2 groups and 20% yield for derivatives with NO_2 groups in *o*- and *p*-positions)[68,72]. The initial attempt to carry out this rearrangement under thermal conditions did not lead to the required result, since on heating the product charred markedly[67]. However, subsequently the thermal rearrangement (XXXIX) → (XLII) was achieved using *O*-(2-pyridyl) oximes of carbonyl compounds[74]:



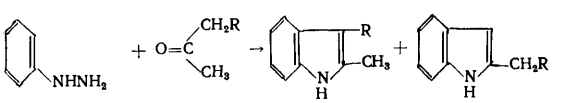
(XXXIX) (XL) (XLI) (XLIII) (XLII)

It has been suggested[43,52] that, in the stage involving the formation of a new C–C bond, this rearrangement should also be regarded as a sigmatropic [3,3] shift and not electrophilic substitution.

2. THE MODE OF CYCLISATION OF ARYLHYDRAZONES OF ASYMMETRIC KETONES

a. The Mode of Conversion of the Arylhydrazones of Alkyl Methyl Ketones into Indoles

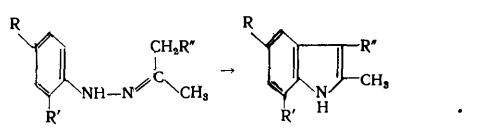
In 1886 Fischer stated that two isomeric indoles, the products of cyclisation involving both alkyl groups, can be formed in the reaction of phenylhydrazine and asymmetric ketones[77]:



(XLIV) (XLV) (XLVI) (XLVII)

However, until recently the entire vast experimental data on the Fischer reaction indicated that only one compound (XLVI) is formed in this process.

Thus Buu-Hoi and Reyer[79] showed that, when a methyl and a methylene group adjoin the carbonyl group, indoles are formed only via the methylene group. Schofield and Theobald[80] demonstrated chromatographically that there is no second substance in the product isolated after the cyclisation of the *o*- and *p*-nitrophenylhydrazones of 2-pentanone (XLVIII, a and b) and *o*- and *p*-nitrophenylhydrazones of phenylacetone (XLVIII, c and d).

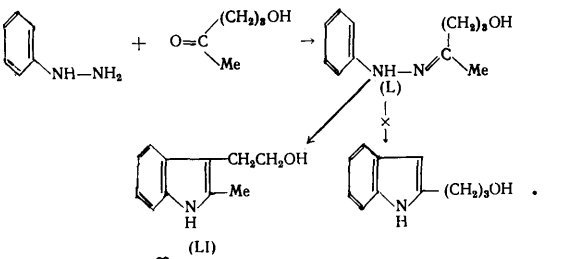


(XLVIII) XLIX

(a) R=NO_2 R′=H R″=Et
(b) R=H R′=NO_2 R″=Et
(c) R=NO_2 R′=H R″=Ph
(d) R=H R′=NO_2 R″=Ph

Later a very small amount of a dark tarry product, the structure of which was not established, was isolated in the chromatographic separation on alumina of the cyclisation products of the phenylhydrazone of phenylacetone (XLVIII, R = R′ = H, R″ = Ph). However, it was suggested that this consisted of traces of 2-benzylindole.

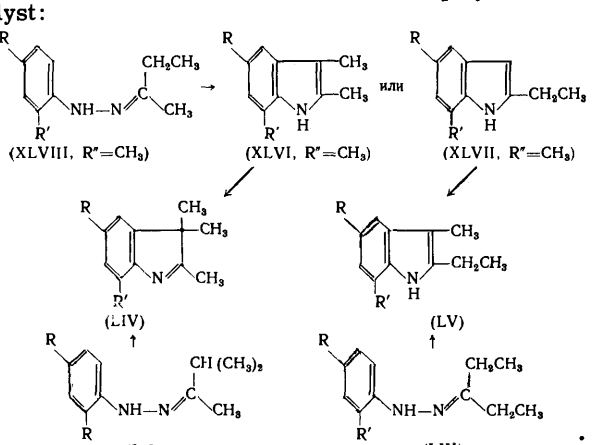
Grandberg et al.[82] established that the reaction of phenylhydrazine (XLIV) and 1-hydroxypentan-4-one yields the hydrazone (L); they cyclised it under the conditions of the Fischer reaction using zinc chloride and copper(I) chloride as catalysts. In both cases 3-(β-hydroxyethyl)-2-methylindole (LI) was isolated in a pure form and 2-(γ-hydroxypropyl)indole, the possible second product, was not detected:



(L) (LI)

Deorha and Joshi[83] confirmed that the methylene group is exclusively involved in the Fischer conversion of the phenylhydrazones of asymmetric ketones into indoles. The structures of the compounds isolated were established by methylation. Thus the methylation product of the indole obtained from the arylhydrazone of 2-butanone (XLVIII) is either compound (LIV) or (LV), since the indole has either the structure (XLVI) or (XLVII). It was established that compound (LIV) is identical with the compound obtained in the cyclisation of the arylhydrazone of 3-methylbutan-2-one (LII) and compound (LV) is identical with the product of the cyclisation of the arylhydrazone of 3-pentanone (LIII). Thus the indole obtained from compound (XLVIII) is 2,3-dimethylindole formed as a result of the cyclisation involving the methylene group [compound (XLVI)].

The formation of two isomers was noted only in a study by Korczynski et al.[78]; having discovered that *p*-diazonitrobenzene reacts with 2-monosubstituted indoles but not with 2,3-disubstituted derivatives, the authors established that the phenylhydrazone of ethyl methyl ketone yields a mixture of products as a result of the Fischer reaction, containing 20% of ethylindole and 80% of 2,3-dimethylindole, when an excess of zinc chloride is employed as the catalyst:



(XLVIII, R″=CH_3) (XLVI, R″=CH_3) (XLVII, R″=CH_3)
(LIV) (LV)
(LII) (LIII)

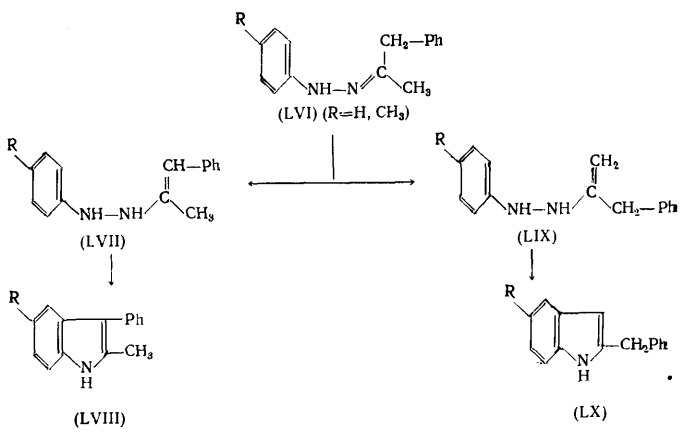
(a) R=NO_2, R′=H; (b) R=H, R′=NO_2; (c) R=Cl, R′=NO_2; (d) R=NO_2, R′=Cl; (e) R=I, R′=NO_2; (f) R=NO_2, R′=I

Thus numerous examples of the synthesis of 3-substituted 2-methylindoles by the Fischer reaction using various catalysts, which have been described in the literature[7-12], suggest that the arylhydrazones of asymmetric ketones yield exclusively 3-substituted 2-methylindoles as a result of the Fischer reaction.

Against the background of the numerous investigations published in 1965, the study by Buu-Hoi et al.[84] appeared to be an exception to this rule. When polyphosphoric acid (PPA) was used as the catalyst in the cyclisation of the arylhydrazone of phenylacetone (LVI), it was found that the product of the cyclisation involving the methyl group (LX) is formed together with the usual product (LVIII) in proportions of 1 : 5.

Earlier they showed that the Fischer reaction of this compound under the influence of gaseous hydrogen chloride in glacial acetic acid leads to cyclisation involving the methylene group, yielding indoles which do not contain any traces of 2-substituted isomers[85].

It was suggested that the action of the catalyst in the Fischer reaction involves the tautomeric conversion of the phenylhydrazone (LVI) into two intermediate enehydrazines (LVII) and (LIX), (LVII) being formed when zinc chloride, boron trifluoride, and hydrogen chloride in acetic acid are employed as catalysts and compound (LIX) is formed in the presence of polyphosphoric acid[84].



Yamamoto's data[49] confirm these results: for example, it was shown that, when R = Ph, the ratio of the two isomeric indoles (XLVII)/(XLVI) increases with increase of the concentration of phosphorus pentoxide in the orthophosphoric acid employed as the catalyst.

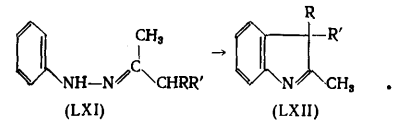
The selective action of the catalysts was investigated in greater detail by Palmer and McIntyre[86]. It was established by ^{1}H NMR that the reaction yields a mixture of isomeric indoles in which the (XLVI) : (XLVII) ratio depends on the catalyst employed. The following catalysts were investigated: boron trifluoride-ether in acetic acid, sulphuric acid at different concentrations in 1 : 1 aqueous ethanol, 90% orthophosphoric acid, and various polyphosphoric acids.

When boron trifluoride-ether in acetic acid was employed as the cyclising agent, only one product (XLVI, R = CH_3, C_6H_5, or p-$NO_2C_6H_4$), formed as a result of the cyclisation involving the methylene group, was isolated. The use of other catalysts led to the formation of a mixture of indoles, the ratio of the isomers depending on the concentration of phosphorus pentoxide in orthophosphoric acid. In all the reactions the fraction of the 2-substituted indole (XLVII, R = CH_3, C_6H_5, or p-$NO_2C_6H_4$), the product of the cyclisation involving the methyl group, increases from O when 90% H_3PO_4 or 40% H_2SO_4 is employed to a level which makes it the main component in 70% sulphuric acid or 83% solution of phosphorus pentoxide in 90% orthophosphoric acid.

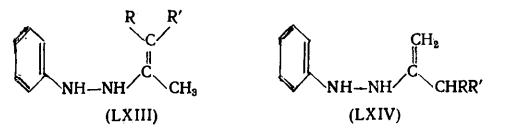
It was shown[86] that the formation of two isomeric indoles is not a consequence of an intramolecular rearrangement, which might have been postulated by analogy with the familiar migrations of substituents in indole systems[87], since the indoles isolated remain unchanged on heating under conditions where mixtures of two isomeric compounds are formed.

b. The Mode of Conversion of Arylhydrazones of 3-Substituted Alkyl Methyl Ketones into Indoles

For arylhydrazones of ketones with an α-branched alkyl chain, there is a rule[88] according to which these compounds cyclise exclusively via the third carbon atom, yielding 2-methylindolenines:

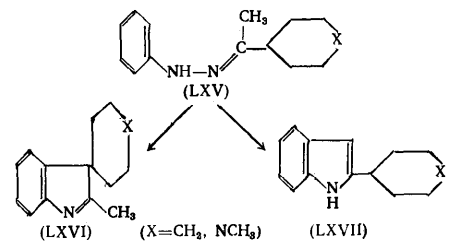


This mode of cyclisation was explained by the fact that the enehydrazine (LXIII), which has the greatest number of substituents at the double bond, is more stable than compound (LXIV).



Numerous examples of this type of cyclisation have been compiled[7-12].

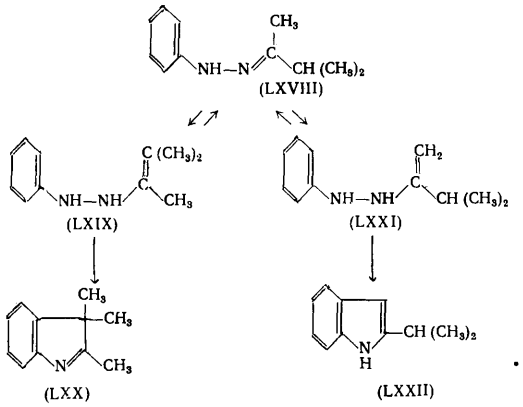
However, it is striking that the cyclisation of the phenylhydrazone of cyclohexyl methyl ketone (LXV, X = CH_2) resulted in an 18% yield of 2-cyclohexylindole (LXVII)[89], an excess of zinc chloride being used as the catalyst. Spiro-3*H*-indole (LXVI), expected as the product of the main reaction pathway, was not isolated, although it had been shown previously that the reaction does in fact follow this pathway[90]:



Later Lyle and Skarlos reinvestigated this reaction[91]. They converted into indoles the phenylhydrazones of cyclohexyl methyl and methyl 1-methyl-4-piperidyl ketones (LXV, X = CH_2 or NCH_3) and established that the Fischer indole synthesis catalysed by polyphosphoric acid yields mainly the products of the cyclisation via the methyl group (LXVII), while the use of an excess of zinc chloride or acetic acid as the catalyst makes it possible to obtain the corresponding spiro-3*H*-indoles (LXVI) alone.

The authors suggested[91] that the mode of cyclisation leading to two products is associated with the stability of the transition states for two different cyclisation pathways. (The cyclisation mechanism is discussed in greater detail below.)

In a study of the cyclisation of the phenylhydrazone of isopropyl methyl ketone (LXVIII), Illy and Funderburk concluded that the pathway followed in the indole formation reaction depends on the acidity of the medium[92]:



Zinc chloride, acetic acid, the hydrogen sulphate ion, and aqueous phosphoric acid always give rise to 2,3,3-trimethyl-3*H*-indole (LXX), the product of the cyclisation involving the more branched chain of the ketone. Polyphosphoric acid and concentrated sulphuric and hydrochloric acids give rise to a mixture of products, the yield of 2-isopropylindole, the product of the cyclisation involving the methyl group, increasing with the acidity of the medium (Fig. 2).

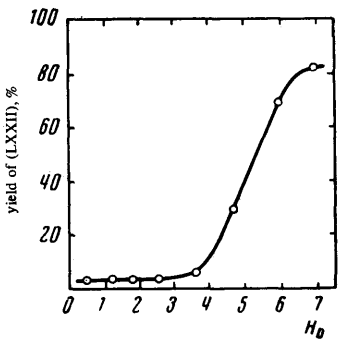


Figure 2. Variation of the yield of 2-isopropylindol (LXXII) with the acidity function H_0 in the cyclisation of compound (LXVIII) for the molar ratio catalyst : hydrazone = 5 : 1.

Palmer and McIntyre[86] also investigated the cyclisation of the phenylhydrazone of isopropyl methyl ketone (LXVIII) as a function of the concentration of the acids employed as catalysts. Their results agree satisfactorily with those of Illy and Funderburk[92]. At relatively low catalyst concentrations the cyclisation involves the more branched chain of the ketone, but, on increasing the concentration, the cyclisation involves the less branched chain[86].

c. The Mode of Conversion of the Phenylhydrazones of 2-Substituted Cyclohexanones into Indoles

The cyclisation of the phenylhydrazones of 2-substituted cyclohexanones (LXXIII) leads to two products: 1,2,3,4-tetrahydrocarbazole (LXXIV) and 1,2,3,4-tetrahydro-4a*H*-carbazole(LXXV)[9,10,12]:

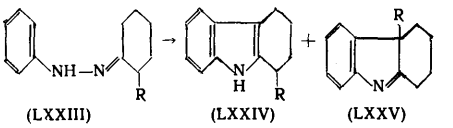


Table 1.

R in phenylhydrazone (LXXIII)	(LXXIV):(LXXV)		
	catalyst		thermal cyclisation
	20% H_2SO_4	CH_3COOH	
CH_3	45:21	6:61	49:51
C_2H_5	44:28	13:76	—
n-C_3H_7	—	—	72:28
i-C_3H_7	44:18	16:70	—
cyclo-C_6H_{11}	29:17	9:79	94: 4
C_6H_5	54:19	27:69	87:13

Hughes and Lions[90] and subsequently Pausacker and Schubert[93,94], established that the ratio of the isomers formed depends on the catalyst employed and the substituent R (Table 1).

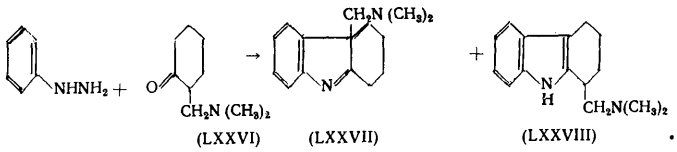
Table 2.

Catalyst	Solvent	Yield of (LXXIV), %	Yield of (LXXV), %
CH_3COOH	CH_3COOH	6	61
CH_3COOH	H_2O	—	56—40*
CCF_3COOH	H_2O	—	53
HCL(gas)	C_6H_6	4	65
HCL(gas)	C_2H_5OH	19	44
HCl(conc.)	H_2O	40	38
H_2SO_4(conc.)	C_2H_5OH	33	36
H_2SO_4(conc.)	H_2O	45	21

*The yields varied with the concentration of acetic acid in water.

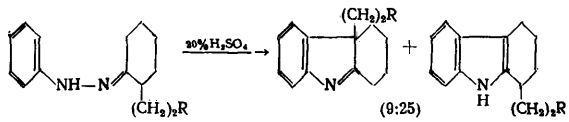
Pausacker showed[94] for 2-methylcyclohexanone phenylhydrazone that the ratio of the products formed is influenced by the nature of the acid catalyst and the solvent employed (Table 2). However, in a later study[95] on the behaviour of compounds (LXXIII) (R = CH_3, C_2H_5, C_3H_7, C_4H_9, C_6H_{11}, and C_8H_{17}) products other than (LXXV) were not detected. Concentrated hydrochloric acid in glacial acetic acid was used as the catalyst. The absence of the second isomer (LXXIV) when the reaction was carried out under these conditions appears strange, since subsequent studies on these lines demonstrated the formation of two products.

Thus Grandberg et al.[96] established that the reaction of phenylhydrazine and the ketone (LXXVI) yields two products (LXXVII) and (LXXVIII):



(LXXVI) (LXXVII) (LXXVIII)

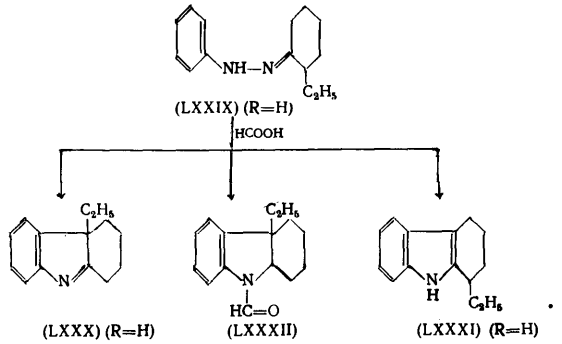
Two products are formed also on cyclisation of the phenylhydrazone of 2-(2-cyanoethyl)cyclohexanone (LXXIX)[97]:



(LXXIX) (LXXX) (9:25) (LXXXI) (R=CN)

A tetrahydrocarbazole was obtained together with compound (LXXXI) on heating compound (LXXIX) with a catalytic amount of zinc chloride at 170–190°C. The appearance of the tetrahydrocarbazole among the reaction products was explained by the elimination of the cyanoethyl group from compound (LXXXI). However, one cannot rule out the possibility that the cyanoethyl group can be eliminated not only from compound (LXXXI) but also from compound (LXXX) and reaction intermediates. On the basis of these findings, the authors concluded[96,97] that, when there is competition between the methylene and methyl groups, the Fischer reaction proceeds via both pathways.

However, when 98–100% formic acid is used as the catalyst, the cyclisation of (LXXIX) leads mainly to 4a-ethyl-1,2,3,4-tetrahydro-4a*H*-carbazole (LXXX), although it was isolated in only a low yield, since it reacts with formic acid under the process conditions, yielding 4a-ethyl-9-formyl-1,2,4,4a,9a-hexahydrocarbazole (LXXXII). The ultraviolet spectra of the product also indicate the formation of a small amount of 1-ethyl-1,2,3,4-tetrahydrocarbazole (LXXXI)[98]:

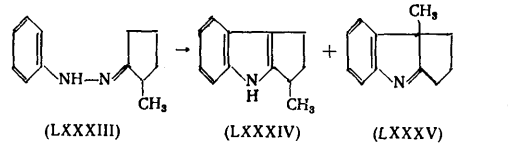


(LXXIX) (R=H)

(LXXX) (R=H) (LXXXII) (LXXXI) (R=H)

Kelly et al.[54] carried out the thermal conversion of compound (LXXIII) into an indole. They found that here too a mixture of indoles (LXXIV) and (LXXV) is formed. The ratio of the isomers is given in Table 1, where it is compared with the results of other studies[93,94].

In addition the phenylhydrazone of 2-methylcyclopentanone (LXXXIII) was converted into indoles by the thermal reaction[54], since the previous attempt to carry out this reaction with the aid of acid catalysis failed[95]. The authors report that in this case two products are also formed, but do not quote their proportions:

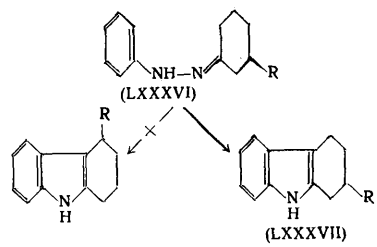


(LXXXIII) (LXXXIV) (LXXXV)

According to the results of Berlin et al.,[99] when equimolar amounts of phenylhydrazine and 2-cyclohexylcyclohexanone are refluxed in glacial acetic acid, 1-cyclohexyl-1,2,3,4-tetrahydrocarbazole (LXXIV, R = C_6H_{11}) is formed in 28.5% yield.

d. The Mode of Conversion of Phenylhydrazones of 3-Substituted Cyclanones

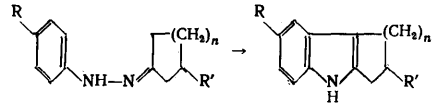
It has been reported[100] that 3-methylcyclohexanone phenylhydrazone (LXXXVI, R = CH_3) gives rise to one product, the structure of which was not established. Later, it was shown[101] that it is a tetrahydrocarbazole (LXXXVII, R = CH_3), since its dehydrogenation yields 2-methylcarbazole. An admixture of 4-methylcarbazole was not detected.



(LXXXVI) (LXXXVII)

In one of the earlier studies it was stated[102] that the cyclisation of the phenylhydrazones of 3-oxocyclohexanecarboxylic acid (LXXXVI, R = COOH) yields one isomer of unknown structure. Later Allen[103] took up the study of this problem and established that the product is 1,2,3,4-tetrahydrocarbazole-2-carboxylic acid (LXXXVII, R = COOH).

A similar study was made recently on the phenylhydrazones of cyclopentanone and cycloheptanone[104]. The structures of the compounds formed under the conditions of the Fischer reaction were established on the basis of their ^{1}H NMR spectra using Eu(DPM)$_3$. In both cases the formation of only one isomer was demonstrated.

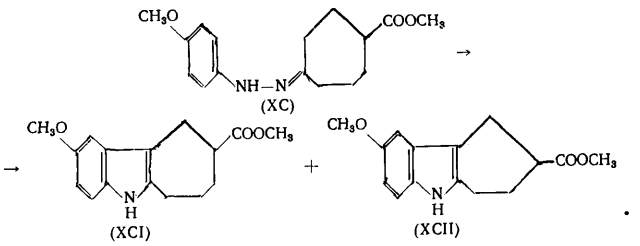


(LXXXVIII) (LXXXIX)

n=1, R=H, OCH_3 R′=COOH, $COOCH_3$

n=3, R=H, OCH_3 R′=CN, COOH, $COOCH_3$

As expected, the cyclisation of the phenylhydrazone of a 4-substituted cycloheptanone yields a mixture of two isomeric compounds (XCI) and (XCII):



(XC) → (XCI) + (XCII)

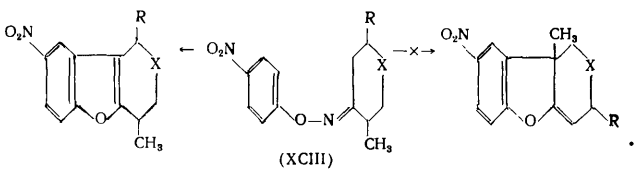
Calculations by the LCAO-MO method in terms of the Hückel approximation for model compounds showed that the equatorial 4-methylcyclohexene is more stable than the pseudoequatorial 3-methylhexene to the extent of 0.8 kcal mole^{-1}. [104] The authors used this fact in an attempt to explain the high selectivity of the Fischer reaction for the phenylhydrazones of 3-substituted cyclanones, although such a small difference can hardly exert a large influence under fairly severe reaction conditions. It is much more likely that steric factors operate in the transition state in the formation of the carbon–carbon bond.

3. THE MODE OF REARRANGEMENT OF *O*-PHENYL ETHERS OF THE OXIMES AND ASYMMETRIC KETONES

Mainly the aryl ethers of the oximes of symmetrical carbonyl compounds or compounds capable of rearranging in one specific position were investigated in rearrangements of the type (XXX) → (XXXI). However, the rearrangement of the oximes of asymmetric ketones was studied in several investigations.

Mooradian noted initially that a mixture of two benzofurans may be formed in the rearrangement of the *p*-nitrophenyl ether of the oxime of 2-butanone, as shown by the ^{1}H NMR spectrum of the unpurified reaction product [68]. However, the product of the rearrangement involving the methyl group could not be isolated.

On cyclisation of aryl ethers of the oximes of 2-methylcyclohexanone (XCIIIa) [69] and 1,2,5-trimethylpiperidin-4-one (XCIIIb) [76] in dilute acid solutions, compounds were formed as a result of a rearrangement involving exclusively the methylene group [compound (XCIVb)] and not the methine group [compound (XCV)]:

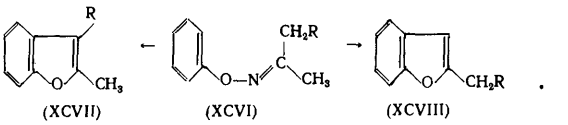


(XCIV) ← (XCIII) → (XCV)

(a) X=CH$_2$, R=H
(b) X=NCH$_3$, R=CH$_3$

The authors noted that, under analogous steric conditions, the closure of the indole ring in the Fischer reaction of the arylhydrazones of the same ketones involves exclusively the α-methine group. However, no explanation of this phenomenon has been put forward [68,76].

The mode of rearrangement of compounds of this kind was investigated in greater detail in other studies [52,105]. It was established that the cyclisation of compound (XCVI) (for R = alkyl) involves both the α-methylene and the α-methyl groups with formation of a mixture of isomeric benzofurans. The reaction was carried out in a dilute alcoholic solution of hydrochloric acid. However, when the substituent was a powerful electron-accepting group, only one compound (XCVII) was formed. The ratio of the isomers formed was determined by ^{1}H NMR and by gas-liquid chromatography (Table 3).



(XCVII) ← (XCVI) → (XCVIII)

It has also been shown [52] that the ratio of the products [(XCVIII) : (XCVII), R = CH$_3$] is determined by the reaction conditions (Table 4).

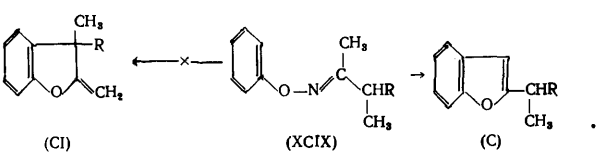
Table 3.

R in compound (XCVI)	Isomer ratio (XCVIII): (XCVII)	R in compound (XCVI)	Isomer ratio (XCVIII): (XCVII)	R in compound (XCVI)	Isomer ratio (XCVIII): (XCVII)
CH_3	55:45	C_6H_5	40:60	$COCH_3$	0:100
C_2H_5	65:35	$CH_2C_6H_5$	60:40	$COOC_2H_5$	0:100
n-C_3H_7	70:30	C_2H_4OH	70:30	CN	0:100
i-C_3H_7	85:15				

Table 4.

Reaction conditions (t = 100°C)		Isomer ratio (XCVIII): (XCVII)
acid catalyst [acid : (XCVI) = 1 : 1]	solvent	
HCl	methanol	78:22
—	2-propanol	55:45
—	t-butyl alcohol	37:63
—	nitromethane	33:67
—	DMSO	30:70
—	DMF	25:75
—	dioxane	12:88
—	THF	8:92
—	benzene	22:78
H_2SO_4	methanol	82:18
—	2-propanol	75:15
—	dioxane	58:42
$CH_3C_6H_4SO_3H$	2-propanol	65:35
$HClO_4$		81:19

^{1}H NMR and gas-liquid chromatography [52] have shown that the products of the rearrangement of the *O*-phenyl ethers of the oximes of branched alkyl methyl ketones are benzofurans (C). This is evidence that the closure of the benzofuran ring involves only the α-methyl group:



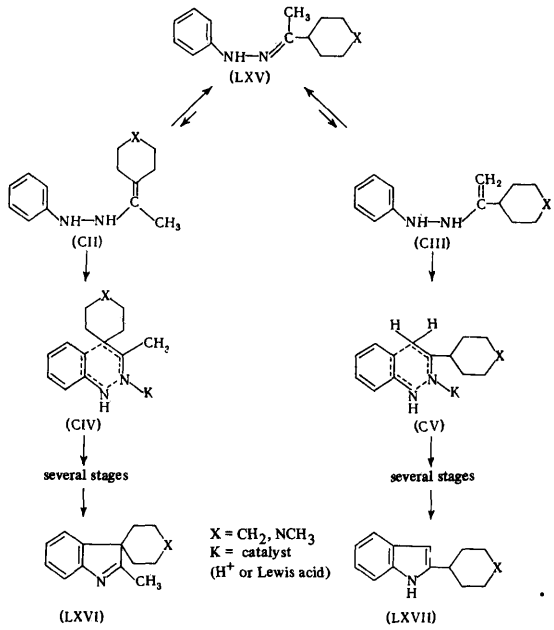
(CI) ← (XCIX) → (C)

4. FACTORS DETERMINING THE MODE OF CYCLISATION

The first attempt to explain the formation of two isomeric products in the Fischer reaction was made by Lyle and Skarlos [91]. In their discussion of the reaction mechanism they suggested that the mode of cyclisation of phenylhydrazones of asymmetric ketones should be related to the

energy of the transition state for two different cyclisation pathways.

For phenylhydrazones of cyclohexyl methyl ketones (LXV), there is a possibility of the formation of two enehydrazines (CII) and (CIII), which should subsequently cyclise via the transition states (CIV) and (CV) respectively. For the formation of a new C–C bond, the benzene ring must approach the π electrons of the double bond. Conformational analysis of the molecules of the enehydrazines (CII) and (CIII) showed that such approach is prevented by the 2- and 6-axial hydrogen atoms on approach from one side and the 3- and 5-axial hydrogen atoms on approach from the other side (cyclisation involving the methine group) [Fig. 3, compounds (CII, a and b)].



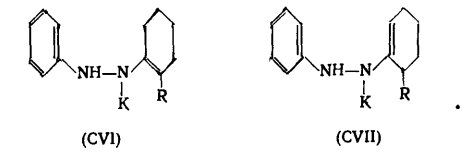
In cyclisation involving the methyl group, the steric interaction between the cyclohexane ring and the catalyst is enhanced [Fig. 3, compound (CIII)].

Therefore in the presence of "small" catalysts "K", such as a proton derived from polyphosphoric acid, cyclisation should proceed via the energetically more favourable transition state (CV) in which there is no interaction between the benzene ring and the axial hydrogen atoms of the cyclohexane ring. In the presence of "large" catalysts "K" such as zinc chloride or an acyl group (the authors apparently find it more convenient to assume that acetic acid behaves not as a protic acid but as an acylating agent[91]), the energy of the transition state (CV) increases in consequence of the interaction between the bulky catalyst and the cyclohexane ring. In this case the reaction proceeds via the transition state (CIV), since the enehydrazine (CII) is energetically more favourable.

Ultimately, when the cyclisation proceeds via the transition state (CIV), the products are 3*H*-indoles (LXVI), while cyclisation via the transition state (CV) gives rise to 2-substituted indoles (LXVII).

Lyle and Skarlos suggest that the ratio of the isomers (LXXIV) and (LXXV) formed from the phenylhydrazones of 2-substituted cyclohexanones (LXXIII) should be correlated with the steric $A^{(1,2)}$ strain (Johnson and Malhotra[106])

in the corresponding pairs of intermediate enehydrazines (CVI) and (CVII)[91]:



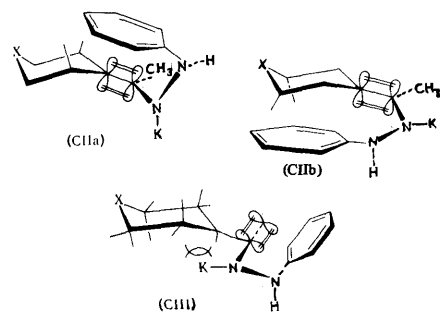


Figure 3. Conformation of the molecules of the enehydrazines (CII, a and b) and (CIII) (Dreiding models).

The authors believe that the transition state in the cyclisation of the enehydrazine (CVII) is preferable when a protic acid is employed as a catalyst or in a thermal rearrangement. Lewis acids or acetic acid should lead to an unfavourable steric interaction between K and the substituent R in the tautomer (CVII) and should favour the formation of the transition state from the enehydrazine (CVI) (Fig. 4).

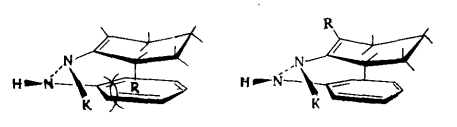
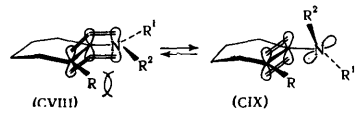
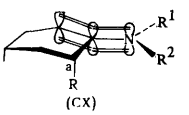


Figure 4. Conformations of the molecules of the enehydrazines (CVI) and (CVII) (Dreiding models).

These considerations are based on the following factors. The enamines obtained from 2-substituted ketones are known to exist as a mixture of isomers[107,108]. The isomer ratio is determined by different steric and electronic factors, which influence the conjugation of the n-electron pair of the nitrogen and the C=C double bond. Complete conjugation requires the coplanarity of the substituent at the nitrogen atom and the olefinic groups:

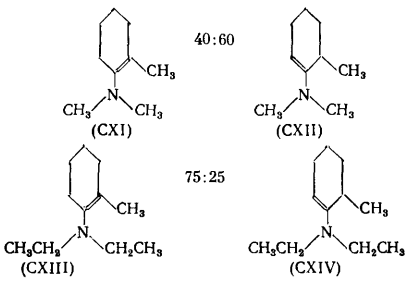


Steric interaction between the groups and the nitrogen atom (R^1 or R^2) on the one hand and the substituent R in the cyclohexane ring of (CVIII) on the other hinders the coplanarity of the substituents and a high degree of overlapping. Therefore the groups are displaced from coplanarity with a consequent weakening of their steric interaction and a simultaneous decrease of the degree of conjugation of the n-electron pair of the nitrogen with the C=C double bond of compound (CIX). The isomer (CX) with an axial R group is free from such steric interaction and therefore it can remain coplanar with a high degree of overlapping[109]:



(CX)

However, with increase of the size of the substituent R^1 or R^2 (in phenylhydrazones of ketones one of the substituents is the "large" NHC_6H_5 group), the relative degree of conjugation may prove to be low in any of the three structures quoted [(CVIII), (CIX), and (CX)]. Even the isomer (CX) does not have an energetically favourable structure in consequence of the increase of the steric interactions between the substituents at the nitrogen atom (R^1 or R^2) and the substituent R in the cyclohexane ring, regardless of whether R is an axial, equatorial, or vicinal substituent. It has been shown[108] that the isomer ratio (CXI) : (CXII) differs markedly from (CXIII) : (CXIV). The authors suggested that, with increase of the intensity of the steric interactions, the isomer (CXIV) with an axial methyl group is not energetically more favourable[108]. In order to weaken these interactions, the groups are displaced from coplanarity and the factors determining the stability of the normal (not conjugated) double bond operate independently—the more substituted double bond is preferred.



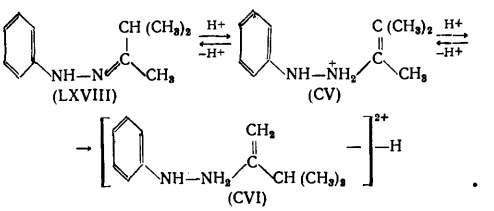
(CXI) (CXII) (CXIII) (CXIV)

Consequently, as suggested by Lyle and Skarlos, when an attempt is made to predict the mode of conversion of the phenylhydrazones of asymmetric ketones into indoles, account must be taken of the fact that the two possible intermediate enehydrazines are sterically hindered to different extents and the stabilisation due to the polyalkyl substitution of the C=C bond in the enehydrazine tautomer[91]. Robinson adheres to this view in his latest review[10].

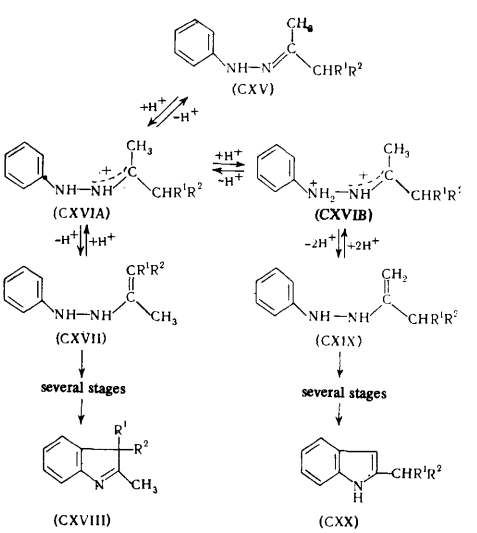
However, this concept is inconsistent with Pausacker's experimental data[94] and those of Canadian workers[54] (Table 1). The steric interactions between the substituents and the catalyst K in structure (CVII) should be greater the greater the bulk of the substituent R and hence the formation of the transition state from the other enehydrazine (CVI) should be favoured. On the other hand, experimental data show that the opposite situation obtains, i.e. that the isomer (LXXIV), formed from the sterically hindered isomer (CVII), predominates in the mixture of indole products isolated (particularly in a thermal rearrangement). Thus the explanation proposed for the formation of two isomers in the cyclisation of the phenylhydrazones of asymmetric ketones[91], based on the correlation between the steric strain of the $A^{(1,2)}$ type in the intermediate enehydrazines (CVI) and (CVII) and the ratio of the isomeric indoles (LXXIV) and (LXXV), does not take into account all the factors which determine this ratio.

Moreover, it is difficult to explain by the steric influence alone the formation of two products from the phenylhydrazones of ethyl methyl and isopropyl ethyl ketones in which there is no strain of the $A^{(1,2)}$ type. Nor is there any answer to the question concerning the influence of the concentration of the catalyst on the isomer ratio.

The approach to the consideration of the possible formation of two isomers in the Fischer reaction from other standpoints proved to be more promising. In an endeavour to account for the influence of the acidity of the medium on the proportions of the products of the Fischer reaction of the phenylhydrazone of isopropyl methyl ketone (LXVIII), Illy and Funderburk[92] suggested that an increase of the acidity of the medium (Fig. 2) entails double protonation of the molecule of the hydrazone (LXVIII), which causes the process to proceed via a different mechanism, leading to the formation of compound (CVI):


(LXVIII) (CV) (CVI)

This hypothesis was confirmed by the formation of 2-isopropylindole (LXXII) only when more than two moles of hydrochloric or sulphuric acid are involved in the reaction. Weak acids do not result in double protonation, because the acidity H_0 does not increase to the required value with increase of the concentration of the acid. Palmer and McIntyre also suggest that at a low concentration of the acid catalyst monoprotonation takes place, while on increase of the acidity of the medium to $H_0 \simeq -4.40$ the hydrazone molecule may be doubly protonated[86].

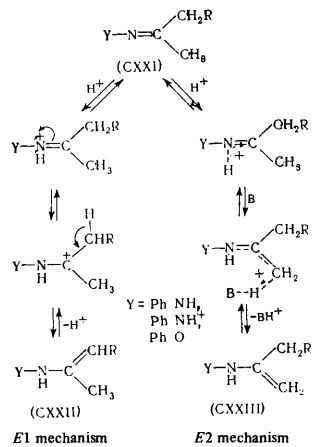

(CXV) (CXVIA) (CXVIB) (CXVII) (CXIX) (CXVIII) (CXX)

The authors believe that in solutions of weak acids the formation of the enehydrazines (CXVII) or (CXIX) from the cation (CXVI) is the slow stage in the sequence (CXV) → (CXVI, A) → (CXVII) or (CXIX). This is analogous to an

$E1$ elimination reaction where the product in which the C=C double bond is substituted by alkyl groups to the maximum extent should predominate. In very acidic solutions, there is an additional inductive withdrawal of electrons from the alkyl groups in the diprotonated molecule of compound (CXVIB), which increases the probability of the attack of the C–H bond by the anion. This is analogous to an $E2$ elimination reaction.

In a study of the rearrangement of the O-phenyl ethers of ketone oximes (XCVI) to benzofurans (XCVII) and (XCVIII), the authors concluded that the reaction constitutes a satisfactory model of the Fischer synthesis of indoles in highly acidic media[52,105]. Comparison of the pK_a values for the phenylhydrazones of the same ketones shows that the basicity of O-phenyloximes is smaller by factor of approximately 10^3 than the basicity of the corresponding phenylhydrazones.

The formation of two isomeric benzofurans (XCVII) and (XCVIII) is evidently associated with two possible modes of "migration" of the double bond in the tautomeric transformation caused by different mechanisms, analogous to the mechanisms of $E1$ and $E2$ elimination. It is clearly seen when one examines the fragment responsible for the pathway followed in the β-elimination reaction.



The double bond $N{=}\overset{|}{C}{-}\overset{|}{C}{-}H$, which dissociates on protonation, plays the role of the group X split off on β-elimination from $X{-}\overset{|}{C}{-}\overset{|}{C}{-}H$. The lower the basicity of the nitrogen atom the more difficult it is to protonate it, which in turn makes it more difficult to dissociate the N=C bond. This is analogous to the hindrance of the dissociation of the substituent X, which always leads to the $E2$ mechanisms becoming predominant.

In the usual Fischer reaction carried out in a weakly acid medium (Y = PhNH), the enehydrazine is formed via the $E1$ mechanism. After protonation of the β-N atom, there is a rapid shift of π-electrons with formation of a carbonium ion stabilised by the ejection of a proton with transformation into the thermodynamically favourable structure in which there is a maximum degree of branching at the double bond (cyclisation involving the CH_2 group).

As a result of the formation of the diprotonated structure (Y = $\overset{+}{P}h\overset{+}{N}H_2$), in an acid medium the fragment $Ph\overset{+}{N}H_2\overset{+}{N}H{=}$ becomes such a weak acceptor ($-I$ effect) that the hydrogen atoms in the α-alkyl groups become much more acidic. The α-hydrogen atoms are then split off from the most "acidic" CH_3 group via a synchronous mechanism under the influence of the nucleophilic agents present in the reaction medium.

If Y is a fairly strong acceptor (Y = PhO) with a high $-I$ effect, its electron-accepting activity favours the tautomeric transformation via the $E2$ mechanism even in a weakly acid medium. Naturally the kinetically more favourable isomer is then formed under the influence of solvent molecules (cyclisation involving the CH_3 group). Thus the mode of conversion of the phenylhydrazones of asymmetric ketones into indoles and the mode of cyclisation of the O-phenyl ethers of the oximes of the ketones are determined by the ratio of the probable intermediate enehydrazines and vinylhydroxylamines formed on tautomeric transformation of the initial compounds under acid conditions. The ratio depends on the probability of the tautomeric transformation via one of the possible β-elimination mechanisms.

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Rearrangements of Biradicals With Migration of an Alkyl Group or Hydrogen

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Studies published during the last decade on the rearrangement of biradicals are reviewed. In contrast to monoradicals for which reliably established examples of rearrangements with 1,2-migration of an alkyl group or hydrogen are unknown, such rearrangements have been observed with biradicals. Data on the types of rearrangements of biradicals with 1,2-migration of an alkyl group and 1,2-, 1,4-, and 1,5-migrations of hydrogen from carbon to carbon or from carbon to oxygen are reviewed. The available data on the mechanisms of the rearrangements are discussed.
The bibliography includes 65 references.

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I. INTRODUCTION

The study of the rearrangements of organic radicals constitutes a comparatively new branch of chemistry, The results obtained in this field have been described in a number of reviews[1-4]. As far as we are aware, no single review has been specially devoted to the rearrangements of biradicals. Nevertheless such somewhat exotic compounds can yield unique results[5]. Indeed, the study of the rearrangements of biradicals yielded results of fundamental importance both for synthetic organic chemistry and particularly for the understanding of the chemical properties of biradicals and for their comparison with those of monoradicals. We believe that the most interesting and newest feature in this field is the observation of rearrangements of biradicals with 1,2-migration of an alkyl group and hydrogen. Such rearrangements are unknown in the chemistry of monoradicals, although 1,2-migrations of hydrogen or the methyl group have been postulated in many investigations. However, the reactions usually described in such reports can be given an alternative interpretation which does not involve the above rearrangements[1-4,6,7]. Unusual types of rearrangements were described for the first time for biradicals generated photochemically but subsequently they were also noted in biradicals obtained by thermal and other procedures. Thus the ability of biradicals to undergo a rearrangement is probably a general property.

The field of rearrangements is still very new and a significant proportion of the known examples have been described only in "Letters to the Editor" and in brief communications. There are very few experimental data concerning the mechanisms of the observed reactions. Nevertheless the ability of biradicals to undergo rearrangements unknown in the chemistry of monoradicals must apparently be regarded as established.

In contrast to the rearrangements in monoradicals, which proceed according to the formal mechanism[4]

$$\underset{(I)}{\dot{A}-(B)_n-\overset{X}{\overset{|}{C}}} \xrightarrow{\text{rearrang.}} \underset{(II)}{A-(B)_n-\dot{\overset{X}{\overset{|}{C}}}} , \qquad (1)$$

where the migrating species (X = phenyl, halogen, hydrogen, etc.) forms a bond with the atom having an unpaired electron and therefore radical (I) isomerises to radical (II), which is usually more stable, the rearrangements of biradicals proceed in many cases in such a way that all the electrons in the product may be paired, for example in accordance with the following formal mechanism:

$$\cdot O-\overset{CH_3}{\overset{|}{C}}-CR'=CR''-O\cdot \xrightarrow{\text{rearrang.}} O=\overset{CH_3}{\overset{|}{C}}-CR'-C=O . \qquad (2)$$

It has been suggested in some studies that the formation of compounds of this kind constitutes one of the driving forces of the rearrangement of biradicals.

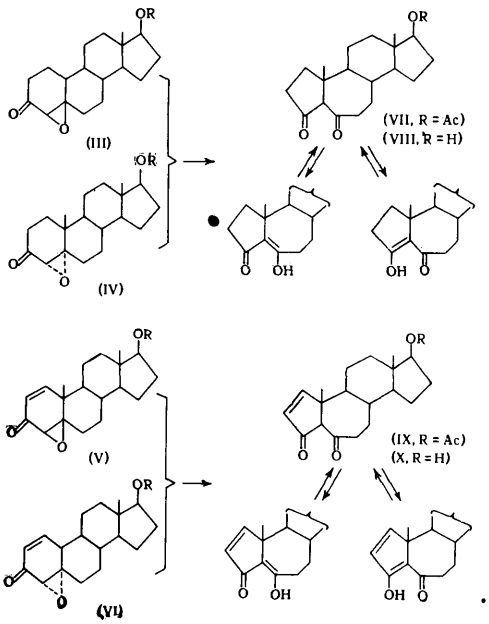
II. REARRANGEMENTS WITH 1,2-MIGRATION OF AN ALKYL GROUP

Rearrangements with 1,2-migration of an alkyl group have been observed in biradicals generated photochemically in systems with both $n-\pi^*$-excitation ($\alpha\beta$-epoxyketones) and with $\pi-\pi^*$-excitation (arylethylenes), thermally by the decomposition of the peroxides of substituted lactones, and also by the addition of triplet methylene to olefins.

a. Photochemical Rearrangement of $\alpha\beta$-Epoxyketones

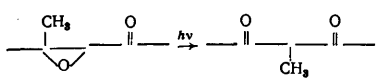
A photochemical rearrangement with 1,2-migration of an alkyl group was first described in 1962 for steroid epoxyketones[6]. Thus saturated and unsaturated diastereomeric 4,5-epoxy-3-oxosteroids (III)–(VI) isomerise in

high yields to compounds (VII)—(X) respectively on irradiation with ultraviolet light regardless of the configuration of the epoxy-ring in the molecule (see Scheme 3).



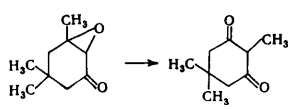
(3)

Soon a similar rearrangement was established in simpler examples: 3,4-epoxy-4-methyl-2-pentanone, isophorone oxide, and the stereoisomeric pulegone oxides[8]. In all cases products of isomerisation with 1,2-migration were accompanied by other compounds which can be described by the following formal scheme in the simplest instance:



(4)

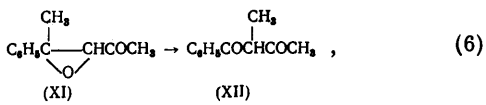
The reaction mechanism was not discussed in these first studies. However, the unusual sequence of groups in terms of their capacity for migration was pointed out[8], namely it was found that the methyl group migrates more readily in these systems than does the phenyl group. Thus isophorone oxide undergoes photochemical isomerisation, with 1,2-migration of the methyl group, to 2,5,5-trimethylcyclohexa-1,3-dione:



(5)

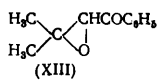
On the other hand, on prolonged irradiation with ultraviolet light, 2,3-epoxy-5,5-dimethyl-3-phenylcyclohexanone, which is an analogue of isophorone oxide, did not yield the isomerisation product 5,5-dimethyl-2-phenylcyclohexa-1,3-dione with 1,2-migration of the phenyl group. A similar difference between the capacities for migration of the methyl and phenyl groups was subsequently observed in a number of other instances[9]. This increase of capacity for migration, $C_6H_5 \ll CH_3$, conflicts with the rules observed in the rearrangements of radicals[3,4]. A molecular orbital calculation showed a decrease of the ease of 1,2-migration from carbon to carbon in the series carbonium ion > free radical > carbanion, the energy barrier being higher for the migration of an alkyl group than for the migration of an aryl group[10].

Zimmerman et al.[9] were the first to express the view in 1964 that the photochemical conversion of $\alpha\beta$-epoxyketones into β-diketones involves a rearrangement of the biradicals with 1,2-migration of an alkyl group. According to their data[9], 3,4-epoxy-4-phenyl-2-pentanone (XI) isomerises photochemically with 1,2-migration of the methyl group, forming 3-benzoyl-2-butanone (XII) as the main product (yield 25%):

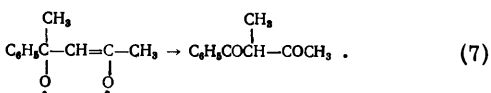


(6)

while the isomeric compound

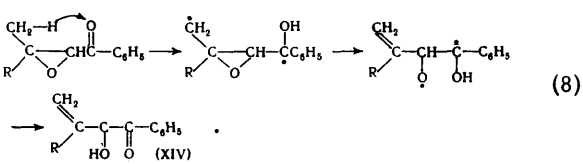


does not isomerise with 1,2-migration of the methyl group. The author suggested that in both cases there is $n-\pi^*$ excitation of the carbonyl group but in compound (XI) there is a greater localisation of the excited electron (π^*) in the carbonyl group and hence a greater probability of β-elimination with homolytic dissociation of the epoxy-ring at the C_α—O bond with the ultimate formation of a biradical, which isomerises:



(7)

In compound (XIII) the excited electron is delocalised over both the phenyl and carbonyl groups and is less accessible. 1,5- and 1,4-migration of hydrogen with formation of compound (XIV) then takes place intramolecularly†:

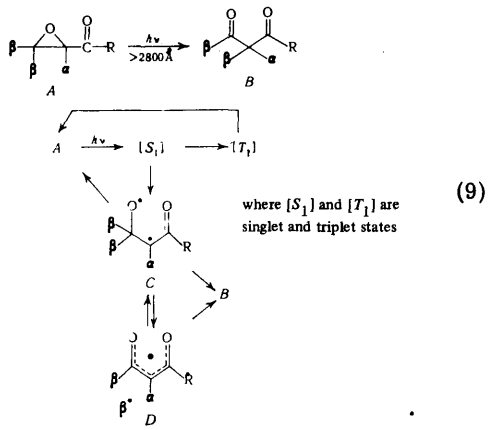


(8)

The homolytic mechanism of the photochemical rearrangement of $\alpha\beta$-epoxyketones to β-diketones is now widely recognised[11,12]. Zimmerman et al.[9] did not put forward any views concerning the mechanism of the methyl migration stage itself. This problem was discussed by other workers[11,12]. Markos and Reusch[11] considered the general case of the rearrangement of the $\alpha\beta$-epoxyketone *A* to the β-diketone *B* and described the mechanism of this rearrangement in terms of Scheme 9. Since the rearrangement of epoxyketones is not sensitive to the presence of oxygen or to a change in the nature of the solvent and since the addition of known triplet state quenching agents (piperylene and 2,5-dimethylhexa-2,4-diene) does not affect the rate or mode of the rearrangement, one may conclude that the intermediate biradical species *C* is formed preferentially from the singlet state $[S_1]$. The low quantum yield of this rearrangement, for example 0.03 for the conversion of 3,4-epoxy-4-methyl-2-pentanone into 3-methylpenta-2,4-dione, indicates either a low efficiency of the $[S_1] \rightarrow C$ transition or the competitive formation of the oxiran ring from *C*, which is unfavourable for the isomerisation. The authors believe that the

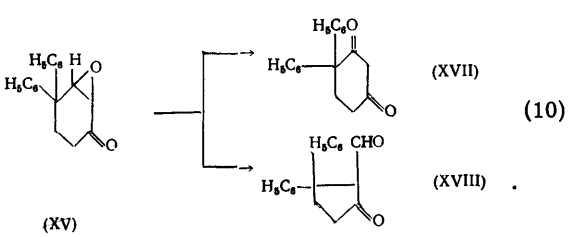
† For the formulation in terms of the symbols employed by the authors, see the Scheme in Ref. 9.

migrating group is of a radical type and that the migration can proceed either via a fragmentation (two-stage) mechanism with formation of a radical pair *D* in a solvent cage or via a synchronous (single-stage) mechanism with a transition state close to *D*. By experimental study of a number of rearrangements, the authors obtained evidence in support of both the intermediate formation of a radical pair and of the synchronous mechanism:



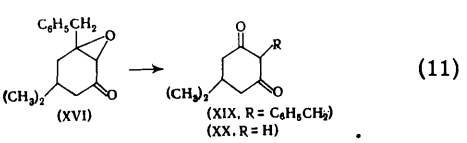
(9)

The above view concerning the rearrangement led the authors to the hypothesis that a particularly high capacity for migration should be observed for the benzyl and diphenylmethyl groups as β-substituents. This was confirmed by studying the rearrangement of 2,3-epoxy-4,4-diphenylcyclohexanone (XV) and 3-benzyl-2,3-epoxy-5,5-dimethylcyclohexanone (XVI). Thus irradiation of a solution of (XV) in ether for 3.5 h led to 50% conversion of the initial compound and the formation of a high yield of a mixture of (XVII) (1,2-migration of hydrogen in the intermediate biradical) and (XVIII) (1,2-migration of the alkyl-substituted diphenylmethyl group) in proportions of 1 : 4:



(10)

Irradiation of (XVI) yields the rearranged compound (XIX) as the main product (20%), but the reaction is accompanied by the formation of a significant amount of decomposition products [(XX), dibenzyl, and other products].

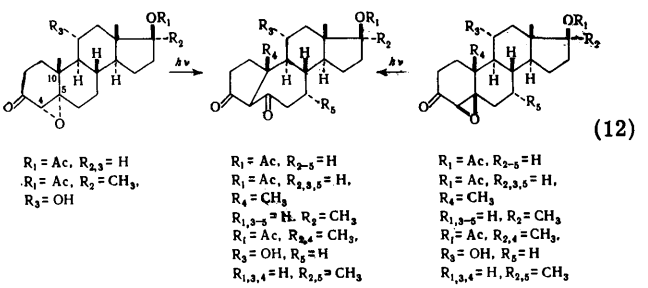


(11)

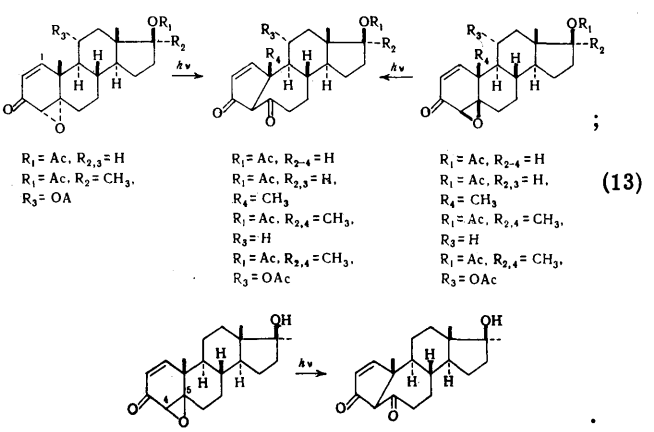
The formation of at least some fragmentation products is attributed to the conversion of *C* (Scheme 9) into the radical pair *D* and the liberation of the comparatively stable benzyl radical from the cage. By comparing their own results with data already available[8,9,12], the authors obtained the following sequence of groups in terms of their capacity for migration: diphenylmethyl and benzyl > hydrogen > methylene > methyl ≫ phenyl. The authors believe that the position of hydrogen in this series is evidence against the mechanism with fragmentation and formation of radical pairs, since a hydrogen atom is usually harder to form than an alkyl radical. Thus the migration capacity series of the groups is best explained by the synchronous mechanism of their migration in the biradical.

A team of investigators[12] who studied the photochemical conversion of a wide variety of steroid epoxyketones into β-diketones believe that this is a widely used and elegant method of synthesising β-diketones (see the references in the paper of Werli et al.[12] to other papers and reports by the authors).

These workers studied the conversion of epoxyketones with a saturated chromophoric keto-group (Scheme 12) into β-diketones on illumination with the unfiltered light of a mercury lamp ($n-\pi^*$-excitation). Unsaturated Δ^1-epoxyketones rearrange to β-diketones only on illumination with monochromatic light at λ = 253.7 ($\pi-\pi^*$ excitation) (Scheme 13).



(12)



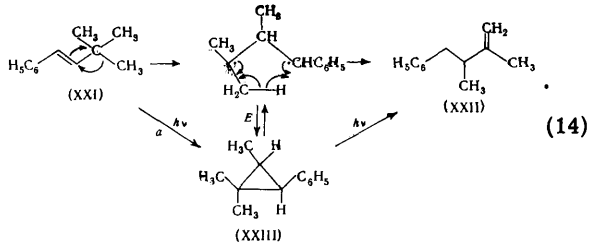
(13)

Werli et al.[12] noted that, although the rearrangement of saturated epoxyketones via Scheme 12, which involves the $n-\pi^*$ excitation, differs from the rearrangement of unsaturated epoxyketones which are unaffected by the $n-\pi^*$ excitation, selective $\pi-\pi^*$ excitation leads to an analogous rearrangement to β-diketones via Scheme 13.

The authors prefer the synchronous mechanism of the migration of an alkyl group in the biradical and note that the migrating group can be an alkyl group or hydrogen but not phenyl.

b. Photochemical Rearrangement of 3,3-Dimethyl-1-phenylbutene

The photochemical rearrangement of 3,3-dimethyl-1-phenylbutene (XXI) to 2,3-dimethyl-4-phenylbutene (XXII) via Scheme 14 was investigated[13]:



(14)

The authors noted[13] that they were first to observe the light-induced 1,2-migration of the methyl group in a hydrocarbon. The importance of this example of a rearrangement is that, whereas the $n-\pi^*$ excitation of epoxyketones can lead to the development of both heterolytic and homolytic processes[14,15], the comparatively low amount of the "ionic" character of the $\pi-\pi^*$ singlet or triplet states of alkyl- and aryl-substituted propenes is to a large extent responsible for the possibility of a homolytic process. In this case synchronous migration of the methyl group and cyclisation with formation of compound (XXIII) (pathway *a*) is possible. Indeed the *cis*- and *trans*-isomers of (XXIII) are readily converted into compound (XXII) by a photochemical reaction. The mechanism involving the formation of a common transition species, probably of type *E*, is also not ruled out. This hypothesis concerning the rearrangement entails the assumption of 1,4-migration of hydrogen in the transition state *E*. The possibility of such migration of the hydrogen atom in the related $n-\pi^*$- and $\pi-\pi^*$-states has been assumed in a number of investigations (see Section III of the present review).

c. Interaction of Tritium-labelled Methylene with *trans*-But-2-ene

The reaction of the photolytically generated methylene with *trans*-but-2-ene in the gas phase leads to the formation of various compounds containing five carbon atoms, among them a number of pentenes and 1,2-dimethylcyclopropane[6]. At higher pressures pentenes are also detected, which cannot be explained by the reaction with singlet methylene[17]. The formation of *cis*-pent-2-ene, 2-methylbut-1-ene, and 3-methylbut-1-ene is therefore attributed to the reaction with triplet methylene. It has been suggested that the first reaction step is the addition of methylene to the double bond according to the following scheme:

$$CH_2{:} + CH_3CH{=}CH{-}CH_3 \rightarrow CH_3\underset{\cdot}{C}H{-}\underset{\cdot}{C}HCH_3 \quad (15)$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\quad CH_2$$

followed by a rearrangement of the biradical.

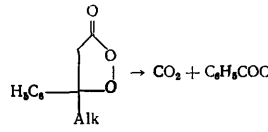
In order to investigate the mechanism of this rearrangement, the interaction of tritium-labelled methylene with *trans*-but-2-ene was studied[16]. In this case the biradical formed via Scheme 15 has the structure $CH_3-\underset{\cdot}{C}HT-\underset{\cdot}{C}HCH_3$ and the different modes of rearrangement should lead to different locations of tritium in the reaction products. The authors investigated the structures of two products important for the determination of the rearrangement mechanism: 3-methylbut-1-ene and *cis*-pent-2-ene. 1,2-Migration of the methyl group in the triplet biradical should lead to the formation of $(CH_3)_2CHCH{=}CHT$ and *cis*-$CH_3CHTCH{=}CHCH_3$, while $CH_3\underset{|}{C}H{=}CH_2$ might have been formed by 1,4-migration of hydrogen. The authors also examined the possible structures of the product generated by other reaction mechanisms (the closure of the three-membered ring and its subsequent opening at other bonds, the abstraction of hydrogen from but-2-ene by methylene, and subsequent recombination of the radicals). It was found that 3-methylbut-1-ene contained tritium in the alkyl and olefinic parts of the molecule, which indicates the operation of more than one mechanism in its formation. The presence of tritium-containing moieties in the olefinic part of the molecule suggests that the 1,2-migration of methyl plays an important role in the formation of 3-methylbut-1-ene. The authors believe that the formation of a double bond in this case provides an additional driving force for the rearrangement in the 1,3-biradical. Under the conditions investigated, *cis*-pent-2-ene did not contain tritium in the olefinic part of the molecule. This can be accounted for both by the mechanism involving 1,2-migration of the methyl group and by the hypothesis of the recombination of radicals. According to the authors, the fact that 3-methylbut-1-ene is not formed in the presence of oxygen and the product is propene constitutes additional evidence for the formation of the biradical. The propene obtained in the reaction of triplet CHT with *cis*- and *trans*-but-2-enes has the structure $CH_3CH{=}CHT$, which is consistent with the product expected via Scheme 16:

$$CH_3\underset{\cdot CHT}{C}HCH_3 + O_2 \rightarrow CH_3{-}\underset{\cdot CHT}{C}H\underset{O_2\cdot}{C}HCH_3 \rightarrow CH_3CH{=}CHT + \text{oxidation products.} \quad (16)$$

d. Rearrangement with 1,2-Migration of an Alkyl Group in Biradicals Generated by the Thermolysis of Organic Compounds

A series of publications appeared very recently[18-21] on the 1,2-migration of alkyl groups in biradicals which were not generated photochemically but by the thermolysis of β-alkyl-β-phenyl-β-peroxypropiolactones[18-20] and also 4,4,6,6-tetramethyl-1-oxaspiro[2,3]hexan-5-one[21].

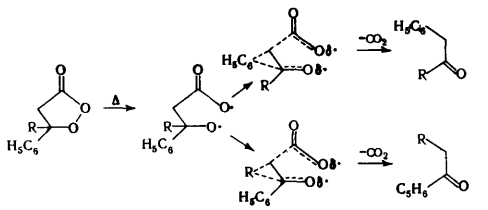
It has been shown[18] that CO_2 is evolved and ketones are formed with 1,2-migration of the alkyl or phenyl group in the thermolysis of β-alkyl-β-phenyl-β-peroxypropiolactones:



$$\rightarrow CO_2 + C_6H_5COCH_2Alk + C_6H_5CH_2COAlk\ . \quad (17)$$

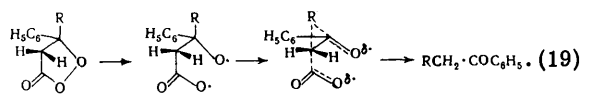
Comparison of a number of examples showed that the substituents can be arranged in the following sequence in terms of decreasing capacity for migration: isopropyl > benzyl > ethyl > methyl > phenyl. The authors drew attention to the fact that there are no instances in the literature of the preferred migration of the alkyl group compared with the phenyl group in thermally generated radicals. On the other hand, such

preference was observed in the 1,2-migration of a substituent in the photolysis of $\alpha\beta$-epoxyketones. The study of the kinetics of the thermal decomposition of β-alkyl-β-phenyl-β-peroxypropiolactones showed that the reaction is described by equations for first-order kinetics and the activation parameters are independent of the nature of the β-alkyl group. The authors put forward the following mechanism for this reaction:



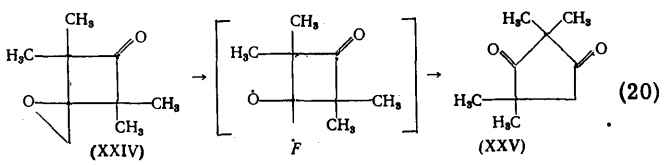
(18)

In subsequent studies[19,20] stereochemical investigations confirmed the hypothesis of the formation of non-classical bridge-type radicals. In particular, it was shown[20] in 1971 that the thermolysis of the optically active peroxide where R = $CH(CH_3)CH_2C_6H_5$ yields the optically active ketone $RCH_2COC_6H_5$ with complete retention of the configuration of the migrating group. The authors represent the stereochemical mechanism of this rearrangement as follows:



(19)

The thermolysis of 4,4,6,6-tetramethyl-1-oxaspiro-[2,3]hexan-5-one (XXIV) was carried out in a quartz tube at 650°C; the main reaction product was 2,2,4,4-tetramethylcyclopentane-1,3-dione (XXV):

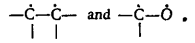


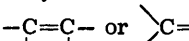
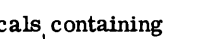
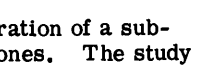
(20)

The authors suggest[21] that the reaction proceeds via the homolytic opening of the oxiran ring with formation of the biradical F the rearrangement of which with 1,2-migration of the alkyl group leads to the formation of the diketone (XXV).

III. REARRANGEMENTS WITH MIGRATION OF HYDROGEN

The migration of hydrogen was studied in biradicals with different relative positions of the radical centres: (a) $\alpha\beta$-homobiradicals and $\alpha\beta$-heterobiradicals with radical centres at adjacent atoms; these are biradicals incorporating the groups



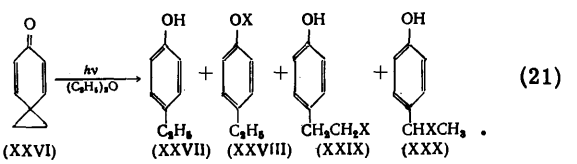
They are formed in the photolysis of the double bonds  or ; (b) $\alpha\gamma$-homobiradicals containing radical centres in the 1,3-positions:  ; biradicals of this type are usually formed in the photolysis of compounds incorporating the cyclopropane ring; (c) $\alpha\omega$-heterobiradicals incorporating, for example, the group  ; such biradicals are formed in the photochemical decomposition of *endo*-peroxides.

We shall examine the available data in the following sequence: instances of 1,2-migration of hydrogen first and then examples of migration from the fourth and fifth carbon atoms to a radical centre at a carbon or oxygen atom.

1. MIGRATION OF HYDROGEN FROM CARBON TO CARBON

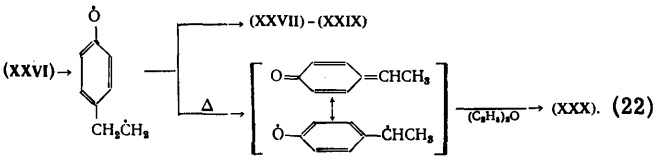
a. 1,2-Migration of Hydrogen

The photolysis of the spirodienone (XXVI) in ether[22] yields a series of *para*-substituted ethylphenols (XXVII)–(XXX), two of which [(XXIX) and (XXX)] contain the residue of an ether molecule $CH_3\dot{C}HOCH_2CH_3$ (X) in the α- and β-positions of the alkyl group:



(21)

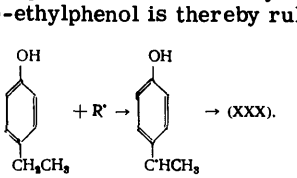
The overall yield of products (XXVII) and (XXVIII) is 15–25%. The phenols (XXIX) and (XXX) are formed in the proportion 37 : 63. The radical mechanism of the reaction is confirmed by the fact, when illumination is switched off, the reaction ceases and when the light is switched on again the reaction proceeds at the previous rate. This confirms the nature of the products, incorporating the ether residue, formed after the abstraction of hydrogen from the ether molecule. The mechanism of these reactions can be represented as follows:



(22)

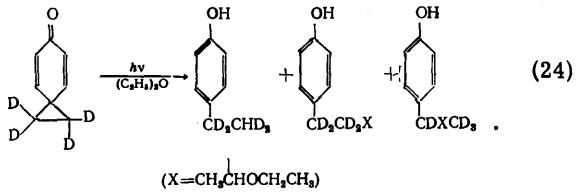
The authors believe that the intermediate quinonoid structure stabilises the transition state corresponding to the rearranged radical as a result of pairing all the electrons. The structure of the products isolated was demonstrated both by identification with compounds obtained by a specific synthesis and by ^1H NMR and mass spectrometry.

The same reaction was investigated in various solvents[23] (toluene, acetonitrile, t-butyl alcohol, and benzene). In all the solvents except toluene only polymers were obtained. It was shown that the products (XXIX) and (XXX) are not formed by the thermal process (100° and 200°C). The authors note that the proportions of these substances are independent of the initial concentration of compound (XXVI). This is evidence of a common intermediate species which leads to both substances; the formation of compound (XXX) as a result of a secondary reaction involving the abstraction of hydrogen from the α-position of *p*-ethylphenol is thereby ruled out:



(23)

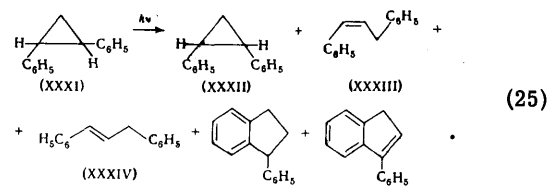
The study of the deuteriated analogue (XXVI) yielded convincing evidence for the rearrangement in the biradical[24]:



(24)

The distribution of deuterium in the reaction products was investigated by ^{1}H NMR and mass spectrometric methods. The authors showed that at least 95% of deuterium is retained in the products after the reaction. The distribution of deuterium in the products agrees almost exactly with predictions on the assumption of a biradical mechanism involving 1,2-migration of hydrogen (deuterium) rather than a series of intermolecular reactions with abstraction of hydrogen. The ratio (XXX)/(XXIX) not only does not increase but actually decreases on photolysis of (XXVI) in the presence of (XXVII), which confirms the intramolecular mechanism of the 1,2-migration of hydrogen.

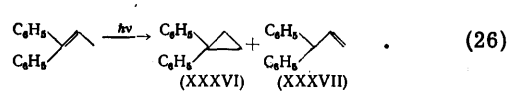
The hypothesis of the 1,2-migration of hydrogen in the biradicals has been put forward in a number of studies[25-27] to account for the mechanism of the formation of the individual products in reactions involving the opening or formation of the cyclopropane ring. Irradiation of *trans*-1,2-diphenylcyclopropane in benzene solution[25] yields a series of products with the following structures:



(25)

The authors believe that these substances are formed via the biradical C_6H_5 C_6H_5 (XXXV). The formation of compounds (XXXIII) and (XXXIV) from (XXXV) requires the hypothesis of 1,2-migration of hydrogen. The structure of compound (XXXIII) was demonstrated by its reduction to 1,3-diphenylpropane and by examining the mass and ^{1}H NMR spectra. In addition, an independent synthesis of compound (XXXIII) was achieved. Irradiation of (XXXIV) yields, apart from other products, compounds (XXXI) and (XXXII), which also requires the assumption of 1,2-migration of hydrogen in the biradical.

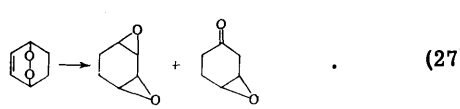
A similar example was quoted in another investigation[26]:



(26)

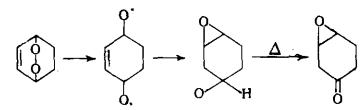
The formation of compound (XXXVI) can be explained by 1,2-migration of hydrogen and that of compound (XXXVII) by two 1,2-migrations or one 1,3-migration of hydrogen. However, in the above study a radical mechanism for the reaction was merely postulated without any evidence.

endo-Peroxides of the type of ascaridole yield diepoxides and ketoepoxides on photolysis (or thermolysis)[27]:



(27)

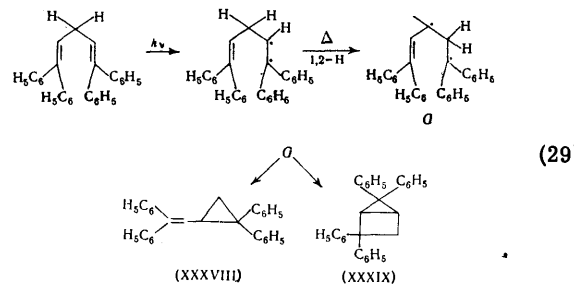
The formation of diepoxides is the normal reaction of compounds of this type. On the other hand, the authors explained the formation of ketoepoxides by a rearrangement in the intermediate biradical with 1,2-migration of hydrogen:



(28)

Since the diepoxides are stable under the chosen conditions, there is no reason to suppose that the formation of ketoepoxides is a result of secondary reactions of the diepoxides.

In one of their latest studies, Zimmerman and coworkers[28] considered the rearrangement of the biradicals formed as a result of the photolysis of 1,1,5,5-tetraphenylpenta-1,4-diene:



(29)

The conversion of the initial diene over a period of 24 h (in t-butyl alcohol solution) is 23%, the yields of compounds (XXXVIII) and (XXXIX) being 12 and 11% respectively.

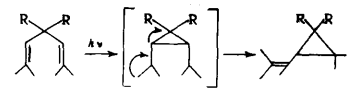
The structure of compound (XXXIX) was confirmed by hydrogenation to 1,1,3,3-tetraphenylcyclopentane. In addition the ^{1}H NMR spectra of (XXXVIII) and (XXXIX) were recorded and confirmed the above structure‡. The hypothesis of 1,2- or 1,5-migration of the hydrogen atom has been used to explain the formation of some of the products of the photolysis of various cyclo-octatrienes[39], but on the basis of the data put forward by the authors it is difficult to tell whether a rearrangement with migration of hydrogen or a stepwise isomerisation of the skeleton with the dissociation or migration of the double bond takes place.

A rearrangement of biradicals with 1,2-migration of hydrogen was noted in the photolysis of cycloalkanones (see Table 1).

b. 1,4- and 1,5-Migrations of Hydrogen

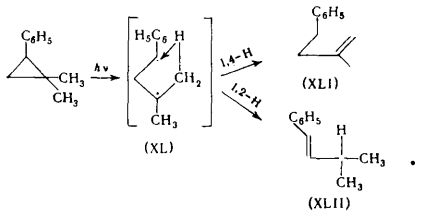
Rearrangements of biradicals with migration of hydrogen to centres in the molecule more remote than the adjacent atom are encountered much more frequently and have been investigated in a number of instances. The study of the opening and closure of the cyclopropane ring

‡ The photochemical rearrangements of cyclic and non-cyclic compounds containing the divinylmethane group, which leads to the formation of the cyclopropane ring in the molecule, for example via the mechanism



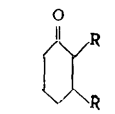
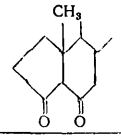
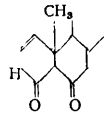
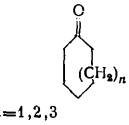
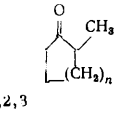
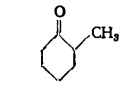
have been called the di-π-methane rearrangements[29-38].

also yielded examples of rearrangement with 1,4-migration of hydrogen in the biradical. 2,2-Dimethyl-1-phenylcyclopropane[40] was irradiated with ultraviolet light for 24 h in hexane solution. The authors postulated the formation of the biradical (XL), where 1,4- and 1,2-, migration of a hydrogen atom via the mechanism



(30)

Table 1.

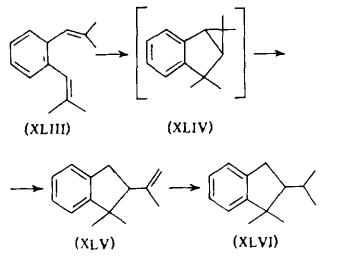
Initial ketone	Reaction conditions	Main products	References (type of migration)
 *cis*- and *trans*-isomers	u.v. (methanol + benzene)	RCH=CCH$_2$CH$_2$CH$_2$CHO R *cis*- and *trans*-isomers RCH$_2$CHCH$_2$CH$_2$CH$_2$COOCH$_3$ R RCH$_2$CHRCH$_2$CH$_2$CH=C=O	47, 48 (1,5-migration of hydrogen)
	u.v.		12 (1,4-migration of hydrogen)
 n=1,2,3	u.v. (λ=3130 Å)	 n=1,2,3	49 (1,2-migration of hydrogen)
	u.v. (λ=3130 Å)	CH$_3$CH=CHCH$_2$CH$_2$CH$_2$CHO *cis*- and *trans*-isomers CH$_2$=CHCH$_2$CH$_2$CHCHO CH$_3$	50 (1,5-migration of hydrogen)

is possible in principle. This results (in the given example) in the formation of 2-methyl-4-phenylbut-1-ene (XLI) with a yield exceeding 80%. On the other hand, the reaction involving 1,2-migration also plays an appreciable role in the case of 2,3-dimethyl-1-phenylcyclopropane. It is interesting to note that, when the isomerisation is carried out in benzene instead of hexane, the yield of the type (XLII) olefin is increased. This leads to the conclusion that benzene sensitises the 1,2-migration of hydrogen in the biradical.

These examples show that, other conditions being equal, the 1,4-migration of hydrogen in the biradical is preferred to 1,2-migration.

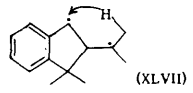
The same authors found[13] that 3,3-dimethyl-1-phenylbut-1-ene isomerises almost completely on photolysis in benzene with 1,4-migration of hydrogen in the intermediate biradical (see Scheme 14).

The authors suggested that the ultraviolet irradiation of *o*-di-isobutenylbenzene (XLIII) results in the formation of the cyclic compound (XLIV) with two ring closures, which is subsequently converted into compound (XLV) with opening of the cyclopropane ring[41]:



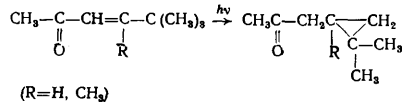
(31)

The structure of the product (XLV) was confirmed by ^{1}H NMR and also by its hydrogenation to (XLVI). The latter was also obtained by an independent procedure. It is suggested that the conversion of (XLIV) into (XLV) proceeds via the intermediate formation of the biradical (XLVII) and subsequent 1,4-migration of hydrogen.



It is noteworthy that in the studies mentioned above[13,40,41] the radical mechanism of the process was merely postulated and the problem of the intramolecular mechanism of hydrogen migration was not always specially considered.

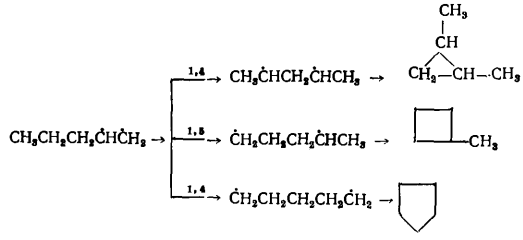
The photochemical conversion of 5,5-dimethyl-3-hex-2-enone into the isomeric ketone via the mechanism



(32)

has been described[42]. The structure of the products was confirmed by ^{1}H NMR and by independent synthesis. Although the authors in fact refrained from discussing the mechanism of the reactions (see Scheme 32), here too one can postulate 1,4-migration of hydrogen in the biradical with subsequent closure of a three-membered ring.

The formation of high yields of cyclic products (methylcyclobutene and dimethylcyclopropane) in the mercury-sensitised photolysis of pent-1-ene has been explained by a combination of 1,4- and 1,5-migration of hydrogen atoms[43]:

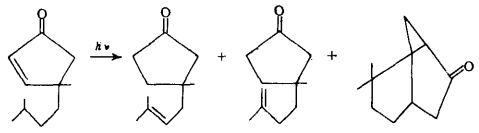


(33)

Cyclopentane is formed (Scheme 33) with greater difficulty (the radical centre moves from a secondary to a primary carbon atom) and therefore the yield of cyclopentane is low (1—2.5%). The yield of methylcyclobutane is 2.5 times greater than the yield of dimethylcyclopropane. Ethylcyclopropane was not found among the products identified, which the authors regard as evidence indicating that 1,2-migration of hydrogen does not occur.

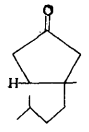
The isomerisation of the biradical with 1,2-, 1,4-, and 1,5-migration of hydrogen is possible in principle in this case, but the results show that 1,2-migration is relatively more difficult in the biradical, while migration to a more remote radical centre proceeds more readily.

Photolysis of 4-isopentyl-4-methylcyclopentenone (XLVIII) ($\lambda \simeq 3300$ Å) yields a mixture of three products (XLIX), (L), and (LI) (Scheme 34), which were isolated by gas–liquid chromatography and characterised by infrared spectroscopy and ^{1}H NMR.[44] In addition the structure was confirmed by a series of chemical reactions:



(XLVIII) (XLIX) (L) (LI) (34)

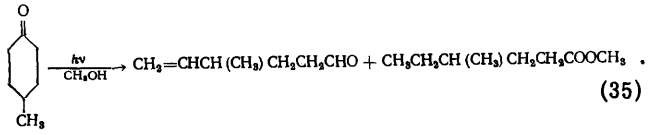
It is suggested that the formation of all the products can be explained by a sequence of rearrangements with migration of hydrogen via the intermediate biradical (LII) formed as a result of the 1,5-migration of hydrogen in the excited molecule of compound (XLVIII). However, the authors themselves refrained from a more concrete discussion of the mechanism of the formation of the reaction products:



(LII)

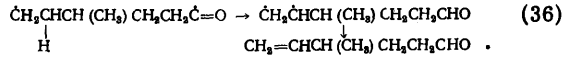
There are reviews[45,46] dealing with photochemical reactions of cycloalkanones. In particular, they deal also with reactions accompanied by rearrangements of biradicals with 1,4- or 1,5-migration of hydrogen atoms.

We shall consider in greater detail the last of a series of new studies[47-51] on the photolysis of cycloalkanones (Table 1), where the authors also devote some attention to the stereochemical aspect of the migration of hydrogen. When 4-methylcyclohexanone is irradiated in methanol solutions[51], products involving the dissociation of the 1,2-linkage are formed via the mechanism



(35)

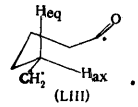
The formation of the aldehyde is explained by the 1,5-migration of hydrogen in the intermediate biradical:



(36)

By carrying out the reaction with deuterated analogues, it was possible to establish that 1,5-migration does in fact occur; moreover, having discovered by ^{1}H NMR the configuration of the initial deuteroketones and the distribution of deuterium in the final products, the authors established that there is a preferential (to the extent of 2/3) migration of the hydrogen in the axial position in the initial ketone but 1/3 of the hydrogen in the equatorial position also migrates, i.e. the stereospecificity of the reaction is low.

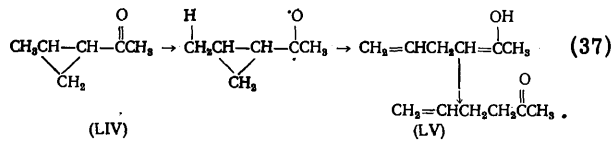
The authors regard this result also as confirmation of the intermediate formation of the biradical (LIII) with free rotation of the groups:



(LIII)

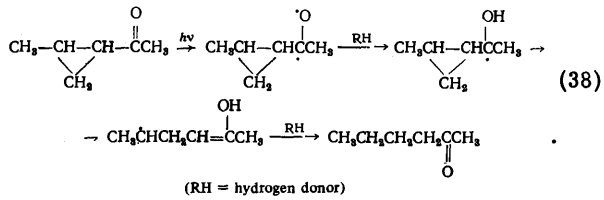
2. MIGRATION OF HYDROGEN FROM CARBON TO OXYGEN

The migration of hydrogen from carbon to oxygen was noted in the biradicals formed photochemically from conjugated cyclopropyl ketones with different structures[52,53]. For example, photolysis of the *cis*-isomer of compound (LIV) yields hex-1-en-5-one (LV) via the mechanism



(LIV) (LV) (37)

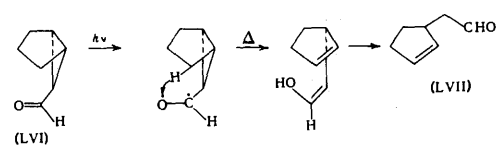
The structure of compound (LV) was established by comparing its[11]H NMR spectrum with that of an authentic specimen. The *trans*-isomer of compound (LIV) yields compound (LV) only after preliminary isomerisation to the *cis*-isomer (in pentane), whereas in isopropyl alcohol solution there is only abstraction of hydrogen from the solvent without isomerisation and with formation of aliphatic ketones via the mechanism



(RH = hydrogen donor) (38)

On the other hand, the *cis*-isomer gives rise to compound (LV) in yields up to 70% (determined by gas–liquid chromatography) even in isopropyl alcohol. According to the authors, this means that, when a rearrangement is possible, it proceeds faster than other parallel processes (for example, intermolecular abstraction of hydrogen from the solvent).

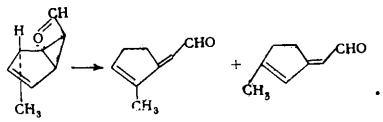
The isomerisation of the bicyclic *endo*-form of the aldehyde (LVI) also involves a rearrangement in the biradical to the extent of 30%:[54]



(LVI) (LVII) (39)

The fact that the *exo*-form of (LVI) does not give rise to (LVII) is evidence that the rearrangement proceeds without preliminary ring opening and confirms the necessity of forming a six-membered cyclic transition state which is most favourable for the rearrangement. A similar

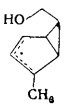
rearrangement was demonstrated also under thermal conditions (130° and 160°C in hexane) when the five-membered ring contains a double bond[55-57], for example:



(40)

(LVIII)

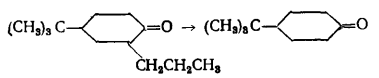
The aldehyde (LVIII) is formed preferentially. It is suggested that the rearrangement proceeds via the biradical (LIX).



(LIX)

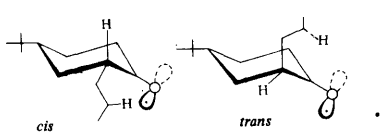
Judging from the previous investigation, this type of hydrogen migration is extremely probable, but Gilbert et al.[55] failed to quote any data which would make it possible to infer in greater detail the mechanism for the formation of the reaction products. In the photolysis of 2,3-epoxy-4,4-diphenylcyclohexanone it proved possible to compare the capacity of the hydrogen atoms and the diphenylmethyl group for migration in the biradical formed[11] (see Scheme 10).

Investigators who studied the photolytic cleavage of *cis*- and *trans*-4-t-butyl-2-propylcyclohexanones noted a significant role of stereochemical factors in the mechanism of the migration of hydrogen from the propyl group to oxygen[58,59]. The *cis*-isomer yields 4-t-butylcyclohexanone as the main product of the intramolecular hydrogen migration:



(41)

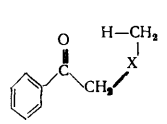
Under these conditions, the *trans*-isomer undergoes only epimerisation, yielding a ketone with the *cis*-configuration as the main product. The formula shows that conditions for the easy formation of a six-membered transition state for the intramolecular migration of hydrogen from carbon to oxygen are created only in the *cis*-conformation of cyclohexanones in the excited state:



cis *trans*

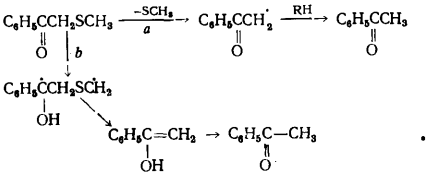
The addition of penta-1,3-diene does not affect the reaction of the *cis*-isomer. According to the authors, this shows that either the reaction proceeds via a singlet state or that cleavage of this type has a rate constant higher than 8×10^{10} s^{-1}.

A number of studies have been made on the photolysis of aliphatic-aromatic ketones with various heteroatoms X in the aliphatic chain:



The behaviour of such compounds depends significantly on the nature of X. Thus, when X = CH_2, O, S, or SO, a rearrangement with 1,5-migration of hydrogen in the triplet state proceeds to some extent, while for X = SO_2 only decomposition occurs.

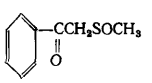
Acetophenone is formed in the photolysis of α-alkylthioacetophenone[60]. Two pathways leading to its formation can be postulated:



(42)

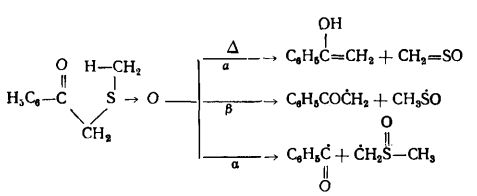
Pathway *a* involves β-elimination of the RS group with subsequent abstraction of hydrogen from a solvent molecule. Pathway *b* involves initial migration of hydrogen in the excited molecule with subsequent β-elimination in the biradical. When the photolysis was carried out in deuterated chloroform, the resulting acetophenone did not contain deuterium, which rules out pathway *a*. On the other hand, the photolysis of $C_6H_5COCH_2SCD_3$ yielded acetophenone with an appreciable deuterium content, which confirms pathway *b*. Separate experiments performed with a mixture of deuterated and non-deuterated starting materials showed that the formation of deuterated acetophenone in the corresponding yield cannot be accounted for by simple deuterium exchange or intermolecular deuterium transfer in the reaction.

Photolysis of the sulphoxide[61]



proceeds with formation of acetophenone, 1,2-dibenzoylethane (dimer), and $CH_3SO_2SCH_3$. The products were identified by gas–liquid chromatography using authentic specimens.

Various ways in which the reaction products can be formed are shown schematically in the original paper:



(43)

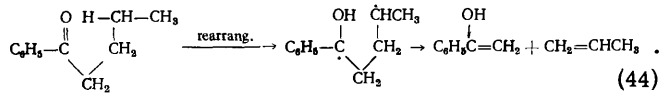
(α-cleavage, β-cleavage).

Judging from the reaction products, the α-decomposition pathway does not play a significant role. It was established that the relative yields of the final products depend significantly on the nature of the solvent. In methanol and acetonitrile the yield of acetophenone does not exceed 30%, while in isopropyl alcohol it reaches 80%, which is explained by the ease of abstraction of hydrogen from isopropyl alcohol. On the other hand, in benzene, which is a weak hydrogen donor, the yield of acetophenone is 67%. The authors believe[61] that in benzene solution acetophenone is most probably formed via pathway *a* (Scheme 43), which involves the initial 1,5-migration of hydrogen from carbon to oxygen and then β-cleavage of the biradical.

β-Decomposition (β pathway, Scheme 43) is preferred in polar solvents (alcohols, acetonitrile). Naturally, in this case the increased ease of hydrogen abstraction from the solvent (on passing from methyl to isopropyl alcohol) should imply an increase in the yield of acetophenone by facilitating the intermolecular hydrogen transfer. In the photolysis of valerophenone[62] the yield of acetophenone

increases significantly in the presence of polar solvents, but changes little when non-polar solvents are varied.

It is believed that more polar solvents accelerate β-decomposition after rearrangement with migration of hydrogen:



(44)

Table 2.

Solvent	C_6H_6	C_6H_{14}	$(CH_3)_3COH$	$(CH_3)_2CHOH$	C_6H_5OH	CH_3CN
Quantum yield of acetophenone	0.37	0.40	0.90	0.68	0.70	0.85

Table 2 shows that in this case the increase of the hydrogen-donating capacity of the solvent is hardly reflected in the yield of acetophenone, which makes it very likely that it is in fact formed as a result of the rearrangement.

It has been shown that the introduction of substituents into the ring of aliphatic aromatic ketones also affects the course of the reaction[63,64] (Table 3). The data in Table 3 show that it is so far difficult to note any consistent trend in the influence of substituents. Thus the introduction of the p-CH_3O group into the ketone (LX) increases the yield of acetophenone, while the introduction of the same substituent into the ketone (LXI) causes a sharp reduction of the yield.

Table 3.

Ketone (in benzene)	Quantum yield of aceto-phenone	Ketone (in benzene)	Quantum yield of aceto-phenone
$C_6H_5COCH_2OCH_3$ (LX)	0.57	$C_6H_5COCH_2OCH(CH_3)_2$	0.59
p-CH_3O—$C_6H_4COCH_2OCH_3$	0.72	$C_6H_5COCH_2CH_2CH_3$ (LXI)	0.34
p-CF_3—$C_6H_4COCH_2OCH_3$	0.43	p-CH_3O—$C_6H_4COCH_2CH_2CH_3$	0.09
$C_6H_5COCH_2OCH_2CH_3$	0.38		

The authors suggest that the formation of acetophenone reflects a rearrangement with migration of hydrogen. However, one also cannot rule out at least partial formation of acetophenone by the mechanism involving intermolecular abstraction of hydrogen.

When sulphones of the type $RSO_2CH_2C(O)R'$ [R = $C_6H_5CH_2$ or $(CH_3)_3C$; R' = CH_3 or C_6H_5] are irradiated, hydrogen migration does not occur[65].

The results presented here show that certain features of the rearrangements in biradicals differ from those in monoradicals. Thus, while the possibility of the 1,2-migration of hydrogen in monoradicals remains controversial, the above results indicate the occurrence of such rearrangements in biradicals. It is noteworthy that, in contrast to monoradicals, biradicals with a specific structure probably have a greater ability to stabilise the transition state or the final biradical, which facilitates for example, 1,2-migration of hydrogen in biradicals. Therefore one can hardly agree with certain investigators[22] who questioned the results obtained in the study of biradicals on the basis of the view expressed in a number of reviews that the probability of the 1,2-migration of hydrogen in the radical is low.

Thus the study of the reactions of biradicals reveals new types of possible rearrangements and their characteristic features.

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The Silyl Method of Synthesis of Nucleosides and Nucleotides

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Data on the silylation of pyrimidine and purine bases and on the application of trimethylsilyl derivatives of nitrogen-containing heterocycles in the synthesis of nucleosides, nucleotides, and their analogues have been reviewed systematically. The bibliography includes 205 references.

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I. INTRODUCTION

The silyl method discovered in 1963[1,2] rapidly gained a firm position among numerous methods for the synthesis of nucleosides. More than 500 syntheses of various nucleosides have already been carried out by the silyl method and their number continues to grow without interruption. This can be explained by the many advantages and distinctive features of the silyl method compared with others, particularly the Hilbert–Johnson method[3] of which it is a modification.

The principal stage in the synthesis of nucleosides by the silyl method is the interaction of silylated heterocyclic bases with acylated halogenoses. The silyl derivatives can be obtained in high yield directly from the heterocyclic bases (not only pyrimidines but also their aza-analogues, triazole, purine, and other nitrogen-containing condensed systems), while the trimethylsilyl groups remaining after the reaction can be readily removed by treating the product with water or alcohol. By varying the conditions of the reaction, it can be driven towards the preferential formation of the α- or β-anomer. The use of phosphorylated sugars in the reactions makes it possible to obtain nucleotides.

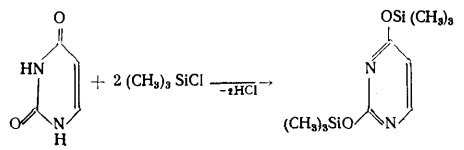
The first results obtained by the silyl method in the synthesis of nucleosides were described in a number of incomplete and now obsolete reviews[3-7] and examples of the silylation of heterocyclic bases published up to the middle of 1968 have been compiled in a table in a handbook on the silylation of organic compounds[8].

We have reviewed data on the silylation of pyrimidine and purine bases and on the application of trimethylsilyl derivatives of nitrogen-containing heterocycles in the synthesis of nucleosides† and nucleotides published up to May, 1973.

† Following Townsend and Revankar[9], in the present review the term "nucleosides" is applied to the *N*-glycosides of nitrogen-containing heterocycles.

II. SILYLATION OF PYRIMIDINES AND PURINES

When uracil is allowed to react with chlorotrimethylsilane in the presence of triethylamine, 2,4-bis(trimethylsilyl)uracil is obtained in 72% yield[1,10-21]:



The reaction is carried out in benzene[1] or dioxane[14,17], pyridine[22] or triethylamine being used as the hydrogen chloride acceptor.

When uracil is heated with hexamethyldisilazane, 2,4-bis(trimethylsilyl)uracil is formed in a high yield 90–96%).[23-27] To accelerate the silylation, chlorotrimethylsilane[28-33] or ammonium sulphate[29] is added to the reaction mixture.

For the purpose of chromatographic and mass-spectrometric analysis, uracil was silylated with *NO*-bis(trimethylsilyl)acetamide in the presence of a catalytic amount of chlorotrimethylsilane[31,34], ammonium chloride[31] (or without them[31,35,36]), and bis(trimethylsilyl)trifluoroacetamide[34,35].

In the silylation of thymine, a high yield (90–92%) of the 2,4-bis(trimethylsilyl) derivative is achieved both with chlorotrimethylsilane as the silylating agent[1,10,14,17,22,37] and on silylation with hexamethyldisilazane[11-13,16,20,21,23-25,28,30,32,38-43]. The latter reaction is carried out either in dimethylformamide (DMF) solution[38] or in an excess of hexamethyldisilazane[23]. The silylation of thymine with bis(trimethylsilyl)acetamide is carried out in acetonitrile solution[31] or at 100°C in the absence of solvent[34].

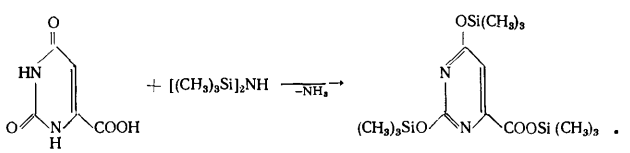
5-Alkyluracils[21,44], 5-alkoxymethyluracils[45], 5-substituted thiouracils[37,46], 6-chlorouracil[47], and 5- and 6-bromouracils[48] have also been silylated with chlorotrimethylsilane in the presence of triethylamine.

The reaction with hexamethyldisilazane yielded 2,4-bis(trimethylsilyl)derivatives of 5-trifluoromethyluracil[30,49,50], 5-alkoxyuracils[51], 5-alkoxymethyluracils[25,52],

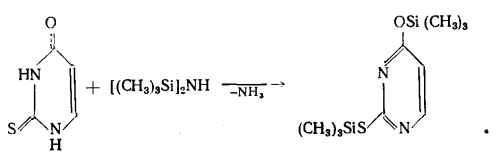
5-fluorouracil[25,30,50,53,54], 5-chlorouracil[25], 5-bromouracil[25], 5-iodouracil[25], 5-formyluracil[30,52,55], 5-alkyluracils[56], 5,6-dialkyluracils[57,58], 5-bromo-6-methyluracil[57], 5-iodo-6-methyluracil[57], 6-alkyluracils[57,58], 6-alkylthiouracils[59,60], and orotic acid esters[57]. 6-Vinyluracil has been silylated by bis(trimethylsilyl)acetamide in acetonitrile solution[61].

When 5-hydroxymethyluracil reacts with chlorotrimethylsilane in the presence of triethylamine[62] or with hexamethyldisilazane in the presence of chlorotrimethylsilane[30] or ammonium sulphate[52], all three hydroxy-groups are silylated with formation of a tris(trimethylsilyl) derivative. The reaction between barbituric acid and hexamethyldisilazane takes place quantitatively with formation of 2,4,6-tris(trimethylsiloxy)pyrimidine[53,63]. A similar tris(triethylsiloxy)-derivative is formed when barbituric acid reacts with aminotriethylsilane[64].

The carboxy-group of orotic acid is also silylated by hexamethyldisilazane, which leads to the formation of the trimethylsilyl ester of 2,4-bis(trimethylsilyl)orotic acid[57]:



When hexamethyldisilazane or its mixture with chlorotrimethylsilane reacts with 2-thiouracil[65,66], 5-alkyl-2-thiouracils[56,65-67], 5-ethoxycarbonylmethyl-2-thiouracil[66,68,69], 2,4-bis(trimethylsilyl) derivatives containing Si—O and Si—S bonds are formed. For example:

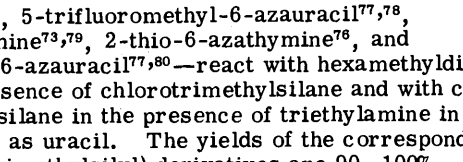


2-Selenouracil is silylated by hexamethyldisilazane similarly[70].

One trimethylsilyl group can be introduced with the aid of these reagents into the molecules of 4-*O*-ethyluracil[11,14,15,24,26], 4-*O*-ethylthymine[24,38,41,42], 4-methylthiopyrimidin-6-one[71], and 6-methyl-4-methylthiopyrimidin-2-one[58].

6-Azauracil[32,72-75] and its derivatives—2-thio-6-azauracil[65,76], 5-trifluoromethyl-6-azauracil[77,78], 6-azathymine[73,79], 2-thio-6-azathymine[76], and 5-bromo-6-azauracil[77,80]—react with hexamethyldisilazane in the presence of chlorotrimethylsilane and with chlorotrimethylsilane in the presence of triethylamine in the same way as uracil. The yields of the corresponding 3,5-bis(trimethylsilyl) derivatives are 90—100%.

When cytosine was allowed to react with chlorotrimethylsilane in the presence of triethylamine[1,10] or pyridine[22], the bis(trimethylsilyl) derivative containing Si—O and Si—N bonds was obtained in 70% yield:

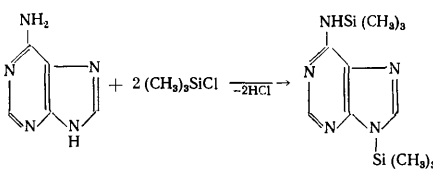


The use of hexamethyldisilazane as a silylating agent makes it possible to obtain *NO*-bis(trimethylsilyl)cytosine in 90% yield[24,29-31]. For the purpose of chromatography, cytosine has also been silylated with bis(trimethylsilyl)-acetamide[31,34,35] and bis(trimethylsilyl)trifluoroacetamide[31].

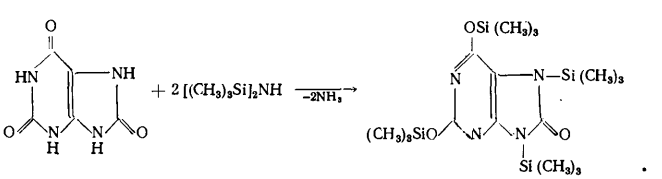
5-Methylcytosine[35], 6-methylcytosine[58], 4-acetylcytosine[1,10,16,20,24,28,32,81,82], 5-bromocytosine[83], 5-fluoro-4-*p*-toluoylcytosine[53], and 5-hydroxymethylcytosine[24] are silylated similarly.

High yields of trimethylsilyl derivatives are obtained also by the silylation with hexamethyldisilazane of other aminopyrimidines: 4-aminopyrimidin-6-one[71], 4-amino-6-hydroxypyrimidine-2-thione[59], 6-aminouracil[59], 5,6-diaminouracil[84,85], 6-alkoxy-2,4,5-triaminopyrimidines[86], and also 5-azacytosine[63,87,88], and 2-thio-5-azacytosine[87,89]. The hydrogen atom in all these hydroxy-, mercapto-, and amino-groups is substituted by the trimethylsilyl group.

When adenine[1,10,22,27], 6-benzoyladenine[1,10,11,15,28,32,90,91], hypoxanthine[1,10,14,15,91], xanthine[1,10,22], guanine[1,10,29], and theophylline[11,14,15] were allowed to react with chlorotrimethylsilane in the presence of triethylamine or pyridine, their mono-, bis-, and tris-(trimethylsilyl) derivatives were obtained respectively in 80—90% yield. In all cases one trimethylsilyl group is linked to a nitrogen atom of the imidazole ring. For example, the reaction with adenine proceeds as follows:



On heating with hexamethyldisilazane, hypoxanthine[22,23] is converted into 6,9-bis(trimethylsilyl)hypoxanthine; under analogous conditions, xanthine[29] gives rise to 2,6,9-tris(trimethylsilyl)xanthine; 6,9-bis(trimethylsilyl)-adenine is formed from adenine[29,31,92] and guanine[29] is converted into the 2,6,9-tris(trimethylsilyl) derivative. On heating with hexamethyldisilazane in an autoclave at 200°C (14 h), uric acid is converted into 2,6,7,9-tetrakis-(trimethylsilyl)uric acid in 70% yield[64,84]:



Tetrakis(triethylsilyl)uric acid was obtained in 90% yield by the reaction of uric acid with aminotriethylsilane[2,64,93,94].

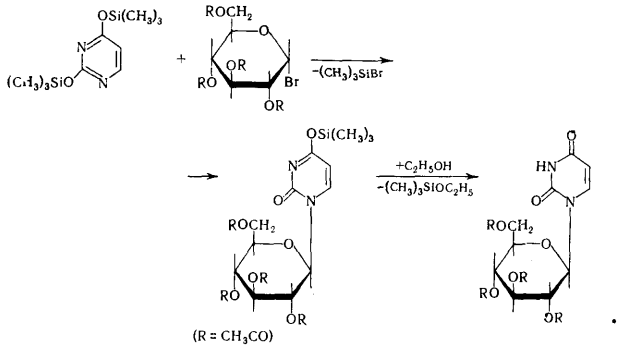
NO-Bis(trimethyl)acetamide has been used successfully in the silylation of hypoxanthine[34,35], xanthine[34,35], adenine[31,34,35], and guanine[31,34,35].

In contrast to the bases themselves, the *N*- and *O*-trimethylsilyl derivatives of hydroxy- and amino-pyrimidines are liquids or solids with comparatively low melting points and are readily soluble in non-polar solvents. They are purified by vacuum distillation or crystallisation. However, heterocyclic amines are frequently silylated by an excess of hexamethyldisilazane in the presence of a catalytic amount of chlorotrimethylsilane, the excess hexamethyldisilazane is removed after the reaction *in vacuo*, and the silyl derivative obtained is used subsequently in the synthesis of nucleosides without additional purification.

III. SYNTHESIS OF PYRIMIDINE NUCLEOSIDES

1. Uracil Nucleosides

Trimethylsilyl derivatives of hydroxypyrimidines react with acylhalogenoses, halogenotrimethylsilane being evolved and an acylated pyrimidine nucleoside being formed. Initially it was suggested that the reaction be carried out by fusing the reactants at 180—195°C at atmospheric pressure[1,12,23,28,95]. For example, when 2,4-bis(trimethylsilyl)uracil is fused with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide at 180—195°C, bromotrimethylsilane is evolved. The subsequent elimination of a second trimethylsilyl group by aqueous ethanol gives 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-uracil in 42% yield[95]:



The β-anomers were also obtained by the reaction of 2,4-bis(trimethylsilyl)uracil with 2,3,5-tri-*O*-benzoyl-D-xylofuranosyl chloride[18,19,96] (yield 73%) and 3,5-di-*O*-acetyl-2-deoxy-2-trifluoroacetamido-D-xylofuranosyl chloride[97] (yield 48%).

Mixtures of anomers with the β-anomer predominating (about 80%) were obtained by the reactions of 2,4-bis(trimethylsilyl)uracil with 2,3,5-tri-*O*-benzoyl-4-thio-β-D-arabinofuranosyl chloride[20] and 2,3,4,6-tetra-*O*-acetyl-D-galactopyranosyl bromide[98] at 130—140°C. On the other hand, when 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl bromide is employed as the glycosidic component, both anomers are obtained in equal amounts[12], while on fusion with 2,3,5-tri-*O*-acetyl-D-lyxofuranosyl chloride the product is 1-(2,3,5-tri-*O*-acetyl-D-lyxofuranosyl)uracil containing 78% of the α-anomer[12].

The reactants were heated at 140°C in the vacuum generated by a water pump in order to synthesise 1-(2,3,4,5,6-penta-*O*-acetyl-1-ethylthio-D-glucosyl)-uracil (yield 45%).[99] The reaction of 2,4-bis(trimethylsilyl)uracil with 3-*C*-acetoxymethyl-2,5-di-*O*-acetyl-3-deoxy-3-phthalimido-D-ribofuranosyl chloride was carried out by refluxing their solution in benzene for two days. This led to the formation of the corresponding β-nucleoside in 23% yield[100].

The silyl method has been used successfully also to synthesise nucleoside analogues in the molecules of which the pyrimidine base is linked to tetrahydrofuran or tetrahydropyran[101,102,103]. For example, 2,4-bis(trimethylsilyl)uracil reacts at a temperature as low as -20°C with 2-chlorotetrahydrofuran, the product being 1-(2-tetrahydrofuryl)uracil[102].

When 2,4-bis(trimethylsilyl)uracil is fused together with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride at 190°C for 40 min, a mixture of anomeric 1-(2,3,5-tri-*O*-benzoyl-D-ribofuranosyl)uracils is formed‡. The yields of the β- and α-anomers are 58 and 9% respectively[17,23,28]. When the reaction was carried out in benzene solution at room temperature in the presence of $AgClO_4$, the overall yield of the nucleoside (52%) did not increase[24,25]. The addition of $HgBr_2$ to the reaction mixture was much more effective—after a 3 h reaction with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide at room temperature, only the β-anomer was formed in 90% yield[32,105]. In an analogous reaction the yield of 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)uracil was 93%.[32]

The 1-β-anomer was formed in 59% yield in the reaction of 2,4-bis(trimethylsilyl)uracil with 2-*O*-acetyl-5-*O*-benzoyl-3-deoxy-3-diethoxyphosphinylmethyl-D-ribofuranosyl chloride in the presence of a mixture of $HgCl_2$ and HgO.[33] The mixture of mercury(II) bromide and oxide proved to be a better catalyst than $AgClO_4$ also in the reaction of 2,4-bis(trimethylsilyl)uracil with 3,4-di-*O*-*p*-toluoyl-2-deoxy-D-ribopyranosyl chloride. In the first case the yield of the mixture of anomers ($\alpha:\beta$ = 77 : 23) was 78%, while in the second it was only 36%, but the anomer ratio remained almost the same (72 : 28).[26] The replacement of the *p*-toluoyl derivative by the *p*-nitrobenzoyl derivative in the reaction in benzene at room temperature in the presence of $HgBr_2$—HgO did not affect the yield and ratio of the anomers[26].

The employment of 1-(3,4,6-tri-*O*-tosyl-1-deoxy-β-D-psicofuranosyl) bromide instead of the chloride did not influence the yield of the β-nucleoside in its synthesis from 2,4-bis(trimethylsilyl)uracil in the presence of mercury(II) acetate (17%).[106]

In many cases the corresponding nucleosides were obtained in high yields also in the presence of $AgClO_4$. For example, the yields of 1-(2,3,4-tri-*O*-acetyl-L-arabinopyranosyl)uracil and 1-(2,3,4,6-tetra-*O*-acetyl-D-galactopyranosyl)uracil synthesised from 2,4-bis(trimethylsilyl)uracil and the corresponding bromo-sugars in the presence of $AgClO_4$ were 90 and 86%.[24,25] However, the yields of the nucleosides obtained by this method from 2,4-bis(trimethylsilyl)uracil and 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl bromide, 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride, and 3,5-di-*O*-*p*-toluoyl-2-deoxyribofuranosyl chloride are much lower—44, 52, and 25% respectively[24,25].

When Lewis acids are used as catalysts in the synthesis of nucleosides by the silyl method, fully acylated sugars may be introduced into the reaction with 2,4-bis(trimethylsilyl)uracil. In the presence of antimony pentachloride a high yield of the nucleoside is achieved even at room temperature[107]. For example, when a solution of 2,4-bis(trimethylsilyl)uracil and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribose in 1,2-dimethoxyethane is stirred for 100 min at 20°C in the presence of $SbCl_5$, 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)uracil is obtained in 55% yield. Much less satisfactory results are achieved when boron trifluoride-ether is employed[107].

Depending on the nature of the catalyst employed and the reaction temperature, the interaction of 2,4-bis(trimethylsilyl)uracil with triacetylglycal gives rise to different products. When the reaction is carried out at -20°C

‡ 2,3,5-Tribenzoyl-L-uridine was synthesised similarly[104].

in the presence of BF_3-ether, the product is 3-(4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hexeno-2-pyranosyl)-uracil ($\alpha:\beta = 35:32$). When a solution of the reactants in ethyl acetate is refluxed for 1 h, 1,2,3-trideoxy--3-(3'-uracilyl)-D-*arabino*-hex-1-enopyranose is formed in 78% yield, while in the presence of $SbCl_5$ an 87% yield of 1-(4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-eno-pyranosyl)uracil ($\alpha:\beta = 23:26$) is obtained[108]. $AlCl_3$, $TiCl_4$, and $SnCl_4$ have an effect similar to that of BF_3, but the yields of the reaction products are lower. $FeCl_3$, $SbCl_3$, and $Cu(BF_4)_2$ act like $SbCl_5$, while $BiCl_3$ and PCl_5 do not catalyse the reaction[108].

Condensation of 2,4-bis-(trimethylsilyl)uracil with triacetylgalactal in ethyl acetate solution in the presence of $SbCl_5$ at 23°C for 5 min leads to a mixture of anomers of 1-(4,6-di-*O*-acetyl-2,3-dideoxy-D-*threo*-hexeno-2-pyranosyl)uracil from which the crystalline α-anomer and the amorphous β-anomer were isolated in yields of 40 and 24% respectively[109].

2. Thymine Nucleosides

The reaction of 2,3,4-6-tetra-*O*-acetyl-α-D-gluco-pyranosyl bromide with 2,4-bis(trimethylsilyl)thymine results in the formation of 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)thymine. Its yield depends to a considerable degree on the reaction conditions and the nature of the catalyst employed (Table 1).

Table 1. Dependence of the yield of 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)thymine on the conditions of the reaction of 2,4-bis(trimethylsilyl)thymine with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide[41,95].

Catalyst	Solvent	Reaction temp., °C	Duration, h	Yield, %
—	Benzene	100	20	27
—	—	100 (vacuum)	3	41
—	—	170—190	0.5	52
$AgClO_4$	ditto	20	0.25	61
$AgClO_4$	»	20	12	66
HgO	»	50	4	65
$HgCl_2$/HgO	»	50	4	72
$HgBr_2$/HgO	»	50	4	84
$HgBr_2$/HgO	»	110	5	86

Thus, while the yield of the 1-β-nucleoside in the reaction in boiling benzene is only 27% after 20 h, [41] at 170—190°C in a stream of nitrogen the yield is 52% after 30 min[95]. In the presence of $AgClO_4$ in benzene solution the yield reaches 61% after only 15 min at 20°C. The increase of the reaction time to 12 h has little influence on the yield. The maximum yield (86%) was achieved on refluxing a benzene solution of the reactants for 5 h in the presence of a mixture of $HgBr_2$ and HgO.[41] A mixture of $HgCl_2$ and HgO proved to be less active. The replacement of α-acetylbromoglucose by β-acetylchloroglucose reduced the yield of the nucleoside from 72 to 56%.[41]

In many cases the yields of the nucleosides obtained from 2,4-bis(trimethylsilyl)thymine in the presence of $HgBr_2$—HgO and $AgCl_4$ are similar. For example, the yields of 1-(2,3,4-tri-*O*-acetyl-α-L-arabinopyranosyl)-thymine were 88 and 78%,[41] which is much more than in the synthesis of the same compound by the mercury method (22%) [110] or by the Hilbert—Johnson method (13%);[111] the yields of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)thymine were 80 and 75%,[41] which is also higher than the yields achieved by the mercury method (50%) [110] and the Hilbert—Johnson method (8% each of the α- and β-anomer)[112]; the yields of 1-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)thymine were 45 and 50%,[41] those of 1-(3,5-di-*O*-*p*-toluoyl-2-deoxy-D-ribofuranosyl)thymine were 55 and 45% (with the same ratio of the α- and β-anomers equal to 31:69)[41], and those of 1-(3,4-di-*O*-acetyl-2-deoxy-D-xylopyranosyl)thymine were 88 and 80%.[40] However, in the last case the ratios of the anomers in the mixtures were not the same: in the presence of $AgClO_4$ the α- and β-anomers are formed in almost equal amounts (48:52), while in the presence of $HgBr_2$—HgO the α-anomer predominates (60:40).[40]

When 2,4-bis(trimethylsilyl)thymine reacts with 2-deoxy-3,5-di-*O*-*p*-nitrobenzoyl-D-ribofuranosyl chloride in the presence of $HgBr_2$—HgO, a mixture of anomers is obtained in 80% yield, in which the α-anomer also predominates (79:21).[42] The use of the *p*-toluoyl derivative in this reaction alters the ratio in favour of the β-anomer[41]. On the other hand, mercury acetate gives a greater amount of the α-anomer ($\alpha:\beta = 56:24$) also in the reaction of 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride in DMF at 20°C.[41]

The β-anomers are obtained by the reaction of 2,4-bis-(trimethylsilyl)thymine with 1-deoxy-3,4,6-tri-*O*-tosyl-D-psicofuranosyl bromide in the presence of mercury(II) acetate[106], with 2,4,6-tri-*O*-acetyl-3-deoxy-D-galacto-pyranosyl chloride and 2,5,6-tri-*O*-acetyl-3-deoxy-D-galactofuranosyl chloride in the presence of $AgClO_4$,[39] and with 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride[43], 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl chloride[113], 3,5,6-tri-*O*-acetyl-2-deoxy-2-(2',4'-dinitroanilino)-α-D-glucopyranosyl bromide[114], 3,5,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl chloride[115], 3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoro-acetamido-α-D-glucopyranosyl bromide[116], 3,5-di-*O*-acetyl-2-deoxy-2-trifluoroacetamido-D-xylo-furanosyl chloride[13], and many other 2-trifluoroacetamido-halogenoses[113,115-117] at 120—140°C at water pump vacuum.

The interaction of 2,4-bis(trimethylsilyl)thymine with 2-deoxy-*C*-methyl-2-(R)-3,5-di-*O*-*p*-toluoyl-*erythro*-D-pentofuranosyl chloride in acetonitrile at room temperature for 24 h leads to a mixture of anomers from which 1-[2-deoxy-*C*-methyl-2(R)-3,5-di-*O*-*p*-toluoyl-*erythro*-D-pentofuranosyl]thymine was isolated in 42% yield[118].

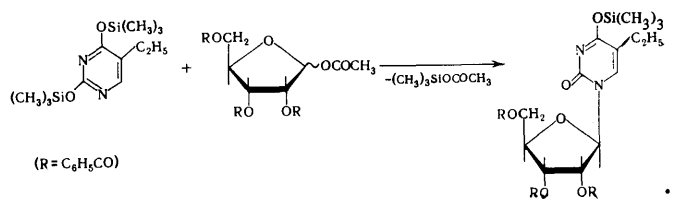
By using tin and antimony halides as catalysts, it is also possible to obtain thymine nucleosides from acylated sugars. Thus the reaction of 2,4-bis(trimethylsilyl)-thymine with 1,2,3-tri-*O*-acetyl-5-deoxy-5-fluoro-β-D-ribofuranose in 1,2-dichloroethane solution in the presence of $SnCl_4$ at 20°C for 4.5 h gave a 70% yield of 1-(2,3-di-*O*-acetyl-5-deoxy-5-fluoro-β-D-ribofuranosyl)-thymine[119]. In the analogous reaction with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose in the presence of $SbCl_5$ in 1,2-dimethoxyethane solution the yield of the β-nucleoside was 35%.[107]

The same behaviour was observed in the reaction of 4-ethyl-2-trimethylsilylthymine[24,41,42] with halogenoses as for 2,4-bis(trimethylsilyl)thymine. For example, in the presence of $HgBr_2$—HgO the yield of 1-(2,3,4-triacetyl-α-L-arabinopyranosyl)-4-ethylthymine was higher than in

the presence of $AgClO_4$ (80 and 55% respectively)[41] and the ratio of the α- and β-anomers in the reaction with 2-deoxy-3,5-di-*O*-*p*-nitrobenzoyl-D-ribofuranosyl chloride was 64 : 36,[42] while in the reaction with the *p*-toluoyl derivative the β-anomer predominates (39 : 61).[41]

3. Nucleosides of Other 5-Substituted Uracils

The use of $SnCl_4$, $ZnCl_2$, $TiCl_4$, $AlCl_3$, or $BF_3.(C_2H_5)_2O$ as catalysts in the silyl synthesis of nucleosides in solution in 1,2-dichloroethane, acetonitrile, carbon disulphide, or DMF made it possible to employ instead of 1-halogeno-sugars the more stable and more readily available 1-alkoxy- or 1-acyloxy-derivatives[75,120]. For example, the reaction of 5-ethyl-2,4-bis(trimethylsilyl)-uracil with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose in 1,2-dichloroethane at 22°C in the presence of $SnCl_4$ (0.72 mole per mole of sugar) for 4 h gave a 68% yield of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-5-ethyluracil[75]:



Under the same conditions 5-nitro-2,4-bis(trimethylsilyl)uracil was converted after 2 h into the β-nucleoside in 62% yield[75].

However, the synthesis of 2′,3′,5′-tri-*O*-benzoyl-5-butyluridine in the presence of the $HgCl_2$—HgO mixture gave much better results than when $SnCl_4$ was employed[56].

5-Allyl-1-(3,5-di-*O*-*p*-chlorobenzoyl-2-deoxy-β-D-ribofuranosyl)uracil was obtained in a low yield (23%) by the fusion method at 125—130°C *in vacuo* (25 mmHg).[44] The fusion method (at 185—195°C for 0.5 h) gave more satisfactory results (yield 70—88%) for 5-alkoxymethyluracils[45]. A mixture of anomers containing about 80% of the β-anomers was obtained.

When 5-benzyloxymethyl-2,4-bis(trimethylsilyl)-uracil was fused together with 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride, 5-benzyloxymethyl-1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl)uracil was obtained in 60.5% yield with an α- and β-anomer ratio of 1 : 4.[45] At room temperature in benzene solution the same reactants gave 66% of the nucleoside with an anomer ratio of 38 : 62. When the reaction was carried out in acetonitrile, the content of the α-anomer rose (66 : 34 for an overall yield of 71%)[52] and in the presence of $AgClO_4$ or $HgBr_2$ in benzene the main reaction product was the β-anomer[25,121]. In contrast, the reaction of 5-methoxy-2,4-bis(trimethylsilyl)uracil with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile solution for 45 h have a high yield (75%) of the β-nucleoside[51]. In the case of the analogous derivatives of 5-hydroxymethyluracil[52,62,121] the highest yield of the β-anomer (80—85%) was also observed when the reaction was performed in acetonitrile (30 h at 20°C)[62], while in benzene in the presence of $HgCl_2$ the yield of the α-anomer increased to 34% (for an overall yield of the anomers of 87%)[62]. The yield of the 5-formyluracil derivative was much lower (31%).[52,55]

A study of the reaction of 5-alkylthio-2,4-bis(trimethylsilyl)uracil and of 5-acetylthio-2,4-bis(trimethylsilyl)uracil with 3,5-di-*O*-*p*-chlorobenzoyl-2-deoxy-α-D-ribofuranosyl chloride showed that, under the conditions promoting the rapid removal of the chlorotrimethylsilane formed, the main reaction product is the β-nucleoside, while the addition of more chloromethylsilane to the reaction mixture results in the preferential formation of the α-anomer[37,46,122] (Table 2). In agreement with this finding, when the reaction of 5-acetylthio-2,4-bis(trimethylsilyl)uracil with 2,3,5-tri-*O*-*p*-chlorobenzoyl-α-D-ribofuranosyl chloride was carried out at 110°C *in vacuo*, the β-anomer was also formed[122].

Table 2. Dependence of the yield of the anomers of 1-(3,5-di-*O*-*p*-chlorobenzoyl-2-deoxy-D-ribofuranosyl)-5-methylthiouracil (I) and 5-acetylthio-1-(3,5-di-*O*-*p*-chlorobenzoyl-2-deoxy-D-ribofuranosyl)uracil (II) on the reaction conditions[37,46,122].

Solvent	Reaction temp., °C	Reaction time, h	Yield of (I), %	Anomer ratio $\alpha:\beta$	Yield of (II), %	anomer ratio $\alpha:\beta$
Benzene	80	1.5	51	18:82	45	More of α
Ditto	25	150	49	20:80	—	—
»	37	110	—	—	11	more of α
»	Azeotropic distillation with addition of benzene	—	36	β only	43	20:80
»	Azeotropic distillation with addition of benzene and $(CH_3)_3SiCl$	—	47	77:23	—	—
—	100–115 [without distillation of $(CH_3)_3SiCl$]	0.25	—	—	39	α only
—	100–110 (10–20 mmHg)	0.25	58	β only	50	β only

Depending on the structure of the pyrimidine derivative employed, the synthesis of 5-trifluoromethyl-1-(2-deoxy-3,5-di-*O*-*p*-nitrobenzoyl-D-ribofuranosyl)uracil from 5-trifluoromethyl-2,4-dimethoxypyrimidine and 5-trifluoromethyl-2,4-bis(trimethylsilyl)uracil can be driven towards the preferential formation of a particular anomer. In the reaction involving 5-trifluoromethyl-2,4-dimethoxypyrimidine the main reaction product was the α-anomer (83%), while the β-anomer predominated (67%) in the mixture of products in the reaction of the 2,4-bis(trimethylsilyl) derivative in the presence of mercury(II) acetate[49].

The β-anomer is also formed in 55% yield in the reaction of 5-trifluoromethyl-2,4-bis(trimethylsilyl)uracil with 3-deoxy-2,5-di-*O*-*p*-nitrobenzoyl-β-D-*erythro*-pentofuranosyl bromide in acetonitrile solution at room temperature[50].

The condensation of 5-halogeno-2,4-bis(trimethylsilyl)-uracils with various halogenoses (acetylbromoglucose, acetylbromogalactose, L-acetyl-bromoarabinose, 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride, and 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride) takes place at room temperature in benzene solution in the presence of $AgClO_4$ and the yields of products are high[25].

When 5-fluoro-2,4-bis(trimethylsilyl)uracil was heated with 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride in boiling toluene, a mixture consisting of 25% of the α-anomer and 75% of the β-anomer was obtained[53].

β-Anomers are formed preferentially also in the reaction of 5-fluoro-2,4-bis(trimethylsilyl)uracil with 3-deoxy-2,5-di-*O*-*p*-toluoyl-α-D-*erythro*-pentofuranosyl

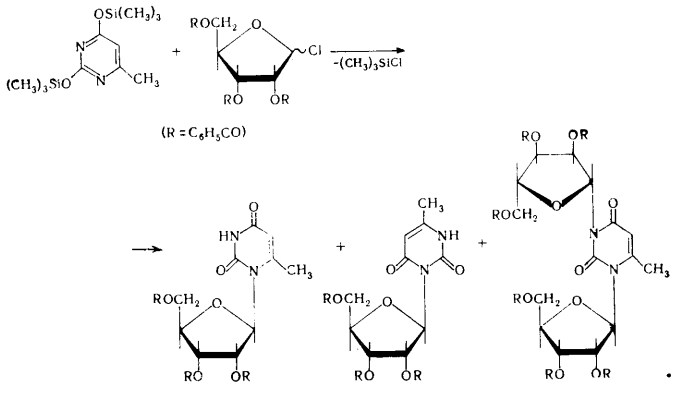
bromide[50] in acetonitrile at 20°C and with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide at 150°C at a reduced pressure[54].

The reaction of 5-fluoro-2,4-bis(trimethylsilyl)uracil with 2-chlorotetrahydrofuran yielded 5-fluoro-1-(2-tetrahydrofuryl)uracil[101,103] (fluorafur), which proved to be effective in the treatment of cancer of the gastrointestinal canal[123].

The reaction of trimethylsilyl derivatives of 5-bromo- and 5-iodo-uracils with 2,3,5-tri-*O*-benzoyl-β-D-xylofuranosyl chloride in the presence of $HgBr_2$—HgO in benzene solution resulted in the formation of β-nucleosides in 36 and 43% yields respectively[96].

Nucleosides of 6-Substituted Uracils

Glycosylation of 6-methyluracil usually results in the formation of N_3-glycosides and $N_{1,3}$-diglycosides or a mixture of isomers[124]. This was also observed when an attempt was made to synthesise 6-methyluridine by the silyl method. The reaction of 6-methyl-2,4-bis(trimethylsilyl)uracil with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride in acetonitrile solution at room temperature gave a low yield of the N_3-isomer[58]. An increase of the temperature of the reaction mixture to boiling and the addition of mercury(II) acetate resulted in a mixture of the N_1-, N_3-, and $N_{1,3}$-diribosyl derivatives in proportions of 4 : 11 : 33.[125] When the reaction was carried out in benzene in the presence of $HgBr_2$—HgO, a mixture of the same products was formed in proportions of 2 : 5 : 4.[57] The N_3-isomer also predominated (4 : 5 : 1) in the products of the reaction with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide:



In contrast, the reaction of 5,6-dimethyl-2,4-bis(trimethylsilyl)uracil with the same halogenoses in the presence of $HgBr_2$—HgO resulted in the formation of a high yield (about 90%) of the β-N_1-nucleosides (the yield of the $N_{1,3}$-derivatives was not more than 2—4%).[57]

In all other reactions of trimethylsilyl derivatives of 6-methylthiouracil[59,60], 6-aminouracil[59], 6-hydroxyuracil[59], and 6-chlorouracil[47] with various acylated halogenoses, N_3-derivatives were formed.

5. Nucleosides of Cytosine and Its 5- or 6-Substituted Derivatives

The reactions of 4-acetyl-2,4-bis(trimethylsilyl)-cytosine with 2,3,4-tri-*O*-acetyl-L-arabinopyranosyl chloride, 2,3,4,6-tetra-*O*-acetyl-D-galactopyranosil chloride, 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl bromide, 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride, and 2-deoxy-3,5-di-*O*-*p*-toluoylribofuranosyl chloride in the presence of $AgClO_4$ give rise smoothly to the corresponding nucleosides[24]. The maximum yield (70%) was observed for the galactose derivative[24]. The yield of 4-acetyl-1-(2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl)-cytosine in this reaction was only 38%,[24] which is nevertheless higher than in its synthesis by the fusion of the initial reactants at 180—195°C (15%).[23,95] When the reactants are fused at 100—120°C *in vacuo* (80—90 mmHg) with simultaneous distillation of the halogenotrimethylsilane formed, the yield of the nucleoside is sometimes greatly increased. For example, the condensation of 4-acetyl-2,4-bis(trimethylsilyl)cytosine with 2-*O*-acetyl-5-*O*-ethoxycarbonyl-3-*O*-tosyl-D-xylofuranosyl chloride at 120°C (80—90 mmHg) for 3 h gave 4-acetyl-1-(2-*O*-acetyl-5-ethoxycarbonyl-3-*O*-tosyl-β-D-xylofuranosyl)cytosine in 80% yield[81]. The yield increases to 92% when the reaction is carried out in benzene solution at room temperature in the presence of $HgBr_2$ for 12 h.[81]

Condensation at reduced pressure was also used to synthesise 1-(3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-β-D-galactopyranosyl)cytosine[113] and 1-(3,5,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-β-D-glucofuranosyl)cytosine[115].

The reaction of 2,4-bis(trimethylsilyl)cytosine with 2,5-*O*-benzoyl-3-deoxy-3-fluoro-D-xylofuranosyl bromide in acetonitrile at room temperature resulted in the formation in 4 days of the corresponding 1-β-nucleoside in 65% yield[126].

When $SnCl_4$ is employed as the catalyst, the 1-acetyl derivative of the sugar can be used also in the synthesis of nucleosides from cytosine and its derivatives[82,127].

On heating 4-acetyl-5-fluoro-2,4-bis(trimethylsilyl)-cytosine with 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl bromide in toluene solution, a mixture is formed with a 40 : 60 ratio of the α- and β-anomers[53].

β-N_1-ribosyl derivatives are formed in the reaction of 6-methyl-2,4-bis(trimethylsilyl)cytosine and 4-acetyl-6-methyl-2,4-bis(trimethylsilyl)cytosine with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride in acetonitrile solution[125]. When ribosyl bromide is employed, their yield reaches 40% after 3 days[58]. The reaction with 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride also yields the N_1-nucleoside in the form of an anomer mixture with the β-anomer predominating[58]. However, the reaction of 2,3,5-tri-*O*-benzoylribofuranosyl chloride with 5,6-dimethyl-2,4-bis(trimethylsilyl)cytosine yields the O_2-riboside as the main product. The ratio of the O_2- and N_1-derivatives is 76 : 24.[125] Similarly the reaction of the trimethylsilyl derivative of 6-amino-2-thiouracil with 2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl bromide results in the formation of the β-S_2-derivative in 40% yield[59].

6. Derivatives of Various Hydroxy-, Thio-, Seleno-, and Amino-pyrimidines

When 2,4-bis(trimethylsilyl)-2-thiouracil[65], 5-benzyloxy-2,4-bis(trimethylsilyl)-2-thiouracil[68], 5-methoxy-2,4-bis(trimethylsilyl)-2-thiouracil[69], and 5-ethoxycarbonyl-2,4-bis(trimethylsilyl)-2-thiouracil[69] react with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride in benzene solution at room temperature in the presence of $AgClO_4$, the β-anomers of N_1-ribofuranosides are formed in yields of 71—78%. Under the same conditions, 5-ethyl-2,4-bis(trimethylsilyl)-2-thiouracil reacts with

2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride to give a mixture of anomers with an overall yield of 82% and a 76 : 24 ratio of the α- and β-anomers[65,69].

A high yield (95%) of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-thiocytosine was achieved by the reaction of 2,4-bis(trimethylsilyl)-2-thiocytosine with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose in 1,2-dichloroethane solution in the presence of $SnCl_4$.[81] 2',3',5'-Tri-*O*-benzoyl-5-cyano-2-thiocytidine[128], 2',3',5'-tri-*O*-benzoyl-2-thiouridine[128], 2',3',5'-tri-*O*-benzoyl-5-butyl-2-thiouridine[56], and 2',3',5'-tri-*O*-benzoyl-2-selenouridine[70] were obtained by this procedure.

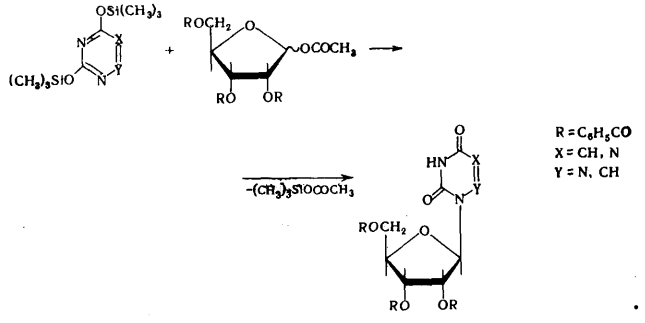
A number of nucleosides were obtained from 4,6-dihydroxy-[129], 4-amino-, and 4-alkylthio-6-hydroxypyrimidines[71]. For example, the reaction of 6-trimethylsiloxy-4-trimethylsilylaminopyrimidine with 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride in acetonitrile at 20°C gave a 75% yield of 4-amino-1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl)pyrimidin-6-one containing more than 90% of the α-anomer. Under the same conditions, 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide gives rise to the β-anomer in 61% yield[71].

7. 6-Aza-analogues of Pyrimidine Nucleosides

The synthesis of the nucleosides of 6-azauracil and 6-azathymine by the mercury method is complicated by the formation of a mixture of N_1- and N_3-isomers[130], while the Hilbert–Johnson method is inapplicable owing to the unavailability of the initial 3,5-dialkoxy-derivatives[131].

When 2,4-bis(trimethylsilyl)-6-azauracil is fused together with various halogenoses *in vacuo*[72,73] and also when the reaction is carried out in benzene or in toluene at room temperature in the presence of mercury(II) acetate[72,74], the corresponding β-N_1-nucleosides are formed in low yields. The use of $HgBr_2$ instead of $Hg(OCOCH_3)_2$ greatly increases the yield of nucleosides (to 90%).[32]

High yields of β-nucleosides are achieved when 1-*O*-acetyl derivatives[75,120,128,134,135] are employed instead of the halogenoses[132,133]. Thus the reaction of 2,4-bis-(trimethylsilyl)-6-azauracil with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose in 1,2-dichloroethane solution at 22°C in the presence of $SnCl_4$ for 4 h resulted in the formation of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-azauracil in 92% yield[75]. When $SnCl_4$ is replaced by $ZnCl_2$ in this reaction and also when the latter is carried out in nitromethane, the yield of the product falls somewhat (83%). Other solvents proved to be less effective (Table 3)[128].



When 2,3,5-tri-*O*-benzoyl-D-arabinofuranosyl chloride is employed in this reaction, a mixture of 1-(2,3,5-tri-*O*-benzoyl-$\alpha\beta$-D-arabinofuranosyl)-6-azauracil containing 56% of the β-anomer is formed[75].

2,4-Bis(trimethylsilyl)-6-azathymine reacts in benzene with 2-deoxy-3,5-di-*O*-*p*-toluoyl-α-D-ribofuranosyl chloride even at room temperature. However, the yield of the β-N_1-nucleoside after interaction for 48 h was only 38%.[79] The increase of reaction temperature to 90°C in the absence of solvent has little effect on the yield of product[73]. When the reaction was carried out with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride in boiling acetonitrile in the presence of $Hg(OCOCH_3)_2$, the yield of nucleoside rose to 68%,[79] while the use of the 1-*O*-acetyl derivative in the presence of $SnCl_4$ gave 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-azathymine in 77% yield[75].

Table 3. Dependence of the yield of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-azauracil on the nature of the solvent[75,128]*.

Solvent	Reaction temp., °C	Reaction time, h	Yield of nucleoside, %	
			unpurified	recrystallised
1,2-Dichloroethane	20	4	97	92
Acetonitrile	20	4	97	82.5
Tetrahydrofuran	65	3	98	75
Carbon tetrachloride	77	4	93	73
Dimethylformamide	153	4	77.5	68.5
Carbon disulphide	46	4	87	67
Benzene	80	6	80.5	66
Toluene	111	6	86	66
1,4-Dioxane	100	4	77	57

*5 mmoles of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose, 6.25 mmoles of 2,4-bis(trimethylsilyl)6-azauracil, 3.6 mmoles of $SnCl_4$, and 100 ml of the solvent were taken.

The corresponding 1-ribofuranosyl derivatives were obtained in 50% yield from 5-trimethylsiloxy-2,4-bis-(trimethylsilyl)methyl-6-azauracil[121,136,137] and 5-trifluoromethyl-2,4-bis(trimethylsilyl)-6-azauracil[78,138] in the presence of $Hg(OCOCH_3)_2$ in benzene at room temperature. In the second case the same yield of the nucleoside was achieved also by the fusion method[77]. The fusion method was likewise employed to synthesise derivatives of 5-bromo-6-azauracil[77,80].

The reaction of *OS*-bis(trimethylsilyl)-2-thio-6-azauracil with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride in benzene solution in the presence of $AgClO_4$ resulted in the formation of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-thio-6-azauracil in 78% yield[65,139]. Similar yields of the β-anomers were achieved when 2,3,5-tri-*O*-acetyl-1-*O*-methyl-D-ribofuranose or 1,2,3,4,6-penta-*O*-acetyl-D-glucopyranose were employed as the glycosidic components and the reaction was carried out in the presence of $SnCl_4$.[75]

8. 5-Aza-analogues of Pyrimidine Nucleosides

The application of the silyl method gave rise for the first time to the possibility of synthesising the antibiotic

5-azacytidine by the direct glycosylation of the 1,3,5-triazine ring. For this purpose, 2,4-bis(trimethylsilyl)-5-azacytosine was condensed with 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide in acetonitrile solution at room temperature for 3 days and 5-azacytidine was obtained in 34% yield after the removal of protecting groups with ammonia[63]. 1-(2-Deoxy-$\alpha\beta$-D-ribofuranosyl)-5-azacytosine, 1-(β-D-ribofuranosyl)cyanuric acid, and 3-methyl-1-(β-D-ribofuranosyl)cyanuric acid were obtained similarly[63]. The addition of $HgBr_2$—HgO to the reaction mixture increases somewhat the yield of nucleosides[88]. When 2,4-bis(trimethylsilyl)-5-azacytosine is fused together with 2,3,5-tri-*O*-benzyl-D-arabinofuranosyl chloride at 195°C, the α-anomer is formed in 8% yield, while on carrying out the reaction at 20°C in methylene chloride for 11 days, the product is the β-anomer in 47% yield[63].

2,4-Bis(trimethylsilyl)-5-azacytosine reacts readily with 1-*O*-acetyl derivatives of sugars in 1,2-dichloroethane solution in the presence of $SnCl_4$. 1-(2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl)-5-azacytosine and 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-5-azacytosine (in yields of 52 and 70%)[87,140] as well as 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-5-azacytosine (yield 55%)[87] were obtained in this way. A number of nucleosides of 2-thio-5-azacytosine were synthesised by similar procedures[87,89].

IV. SYNTHESIS OF NUCLEOSIDES CONTAINING CONDENSED PYRIMIDINE SYSTEMS

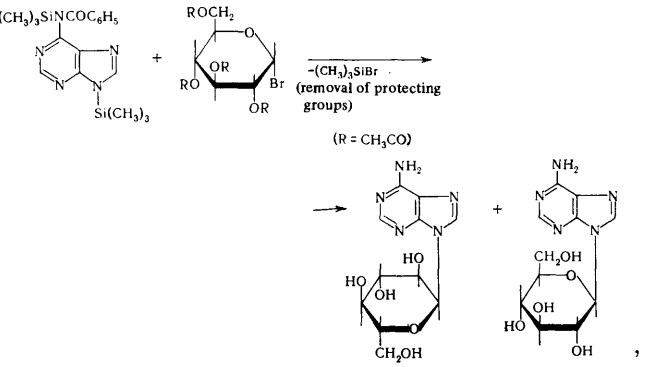
1. Purine Nucleosides

When 6,9-bis(trimethylsilyl)adenine was allowed to react with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile solution at 20°C the product contained 27% of the 3-β-nucleoside and 10% of the 9-β-nucleoside[92]. Under the same conditions, 8-bromo-6,9-bis(trimethylsilyl)adenine gave an 80% yield of the 3-β-nucleoside and a 7% yield of the 9-β-nucleoside. On replacing 1-bromoribose by the corresponding 1-*O*-acetyl derivative and on carrying out the reaction in the presence of $SnCl_4$, the yield of the 9-β-isomer was raised to 20%, which is still lower than the yield of the 3-β-nucleoside (39%).[92]

Condensation of 8-bromo-6,9-bis(trimethylsilyl)-adenine with 2,3,5-tri-*O*-benzoyl-D-arabinofuranosyl bromide in acetonitrile at 20°C for 24 h led to the formation of the 3-α-nucleoside in 73% yield, while condensation with 2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl chloride gave the 3-β-isomer (37%).[92]

On heating 6,9-bis(trimethylsilyl)-6-benzoyladenine with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride at 150—160°C for 3.5 h and subsequent debenzoylation by sodium methoxide, adenosine was obtained[28]. A mixture of nucleosides containing the 9-β- and 7-β-isomers in proportions of 57 : 43 was obtained in benzene at room temperature in the presence of $HgBr_2$.[32,141] Under the same conditions, 3,5-di-*O*-benzoyl-2-*S*-benzyl-2-thio-D-ribofuranosyl chloride gives 22% of the 9-β-nucleoside, 5% of the 9-α-nucleoside, and 9% of a mixture of the 7-α- and 7-β-nucleosides, while 3,5-di-*O*-benzoyl-2-*S*-methyl-2-thio-D-ribofuranosyl chloride yields 34% of the 9-β-nucleoside, 10% of the 9-α-nucleoside, and 12% of a mixture of the 7-α- and 7-β-nucleosides[141].

9-β-D-Glucopyranosyladenine was obtained by the reaction of 6,9-bis(trimethylsilyl)-6-benzoyladenine with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl chloride, while the reaction with α-acetylbromoglucose gave a mixture of 9-α- and 9-β-D-glucopyranosyladenines containing equal amounts of the anomers[23,90,91]:



6,9-Bis(trimethylsilyl)hypoxanthine reacts similarly[23,28,90,91].

In the synthesis of 2-acetamido-6-chloro-9-(2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentofuranosyl)-9*H*-purine the yield of the nucleoside increases somewhat following the addition of an excess of chlorotrimethylsilane, while an excess of the halogenose reduces it and an excess of the base has no effect whatever. The use of an excess of chlorotrimethylsilane together with mercury(II) cyanide promotes the decomposition of the sugar, best (almost quantitative) yields of the nucleoside being achieved in the presence of $Hg(CN)_2$ without the introduction of additional chlorotrimethylsilane. A mixture of the α- and β-anomers with the α-anomer predominating is then formed. The addition of chlorotrimethylsilane has little influence on the anomer ratio[142].

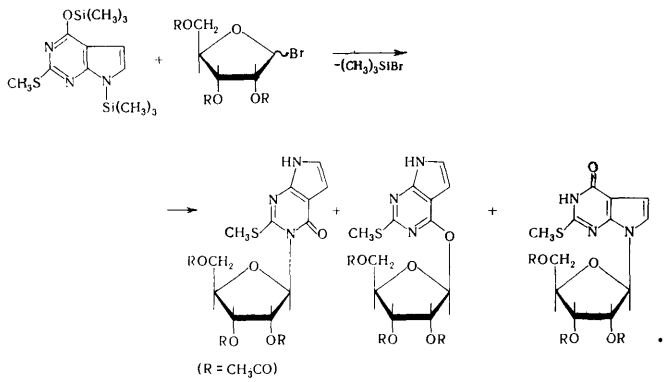
The first nucleoside obtained from xanthine by direct glycosylation was 3-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)xanthine formed by the reaction of 2,6,9-tris-(triethylsilyl)xanthine with 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl bromide in nitromethane in the presence of $AgClO_4$.[86,94] When the reaction is carried out with 2,6,9-tris(trimethylsilyl)xanthine in acetonitrile, the 3,7-β-diglucoside is obtained[143]. The 3,7-disubstituted product is formed also in the reaction with 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride in acetonitrile at 35° or 65°C. Under milder conditions (polar solvent, room temperature), the products of this reaction are 7-(2-deoxyribosyl)- and 7,9-di-(2-deoxyribosyl)-xanthines[143]. The reaction of 2,6,9-tris(trimethylsilyl)-xanthine with 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2′,4′-dinitroanilino)glucopyranosyl bromide yields a mixture of products, among which the 1- and 7-glucosides were identified[143]. The condensation of 2,6,7,9-tetrakis(triethylsilyl)uric acid with 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl bromide, 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide, and 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in toluene in the presence of $AgClO_4$ resulted in the formation of the 3-β-nucleosides in yields of 70, 56, and 90% respectively[2,86,94].

After the successful application of the silyl method in the synthesis of purine nucleosides, the range of condensed heterocycles employed in this reaction was greatly extended by the inclusion of systems in which the pyrimidine ring is linked not only to the imidazole ring but also to the pyrrole, pyrazole, triazole, benzene, pyridine, or pyrazine ring.

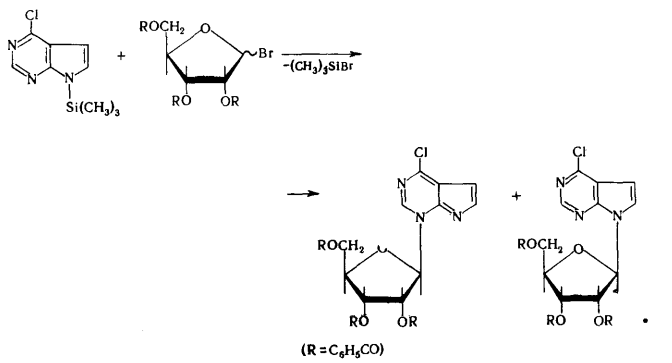
2. Derivatives of Pyrrolo[2,3-*d*]- and Pyrazolo[3,4-*d*]-pyrimidines

When 4-chloro-7-trimethylsilylpyrrolo[2,3-*d*]pyrimidine was allowed to act with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in boiling benzene in the presence of HgO for 18 h, a mixture of the 1-β- and 7-β-nucleosides was obtained, the yields of the isomers being 11 and 18% respectively[144]. Under the same conditions, the main products of the reaction with 4-chloro-5-cyano-6-methyl-7-trimethylsilylpyrrolo[2,3-*d*]pyrimidine are the 1-β- and 3-β-ribosides (yields 46 and 31%), while the 7-β-isomer is formed in a smaller amount (17%). The reaction of 4-chloro-2-methylthio-7-trimethylsilylpyrrolo[2,3-*d*]pyrimidine and 5-bromo-4-chloro-2-methylthio-7-trimethylsilylpyrrolo[2,3-*d*]pyrimidine with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile at 25°C in the presence of Ag_2O for 3 days gives exclusively the 7-isomers in yields of 82 and 48% respectively[144].

A mixture of the 3-, and 4-, and 7-ribosides is formed in overall yields of 79 and 94% on ribosylation of 2-methylthio-4,7-bis(trimethylsilyl)pyrrolo[2,3-*d*]pyrimidin-4-one with 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide in boiling benzene in the presence of $HgBr_2$—HgO for 18 h or in acetonitrile at room temperature for 48 h:



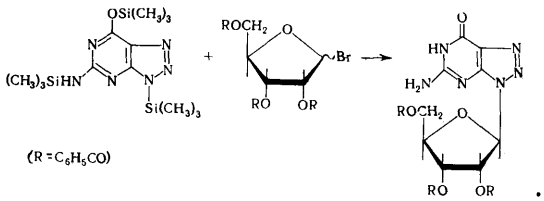
The 7-isomer predominates in the first case (64%) and the 4-isomer in the second (76%):[144]



The analogous reaction of 4-chloro-*N*-trimethylsilylpyrazolo[3,4-*d*]pyrimidine at 105—110°C *in vacuo* gave the 7-β-nucleoside in 30% yield[145].

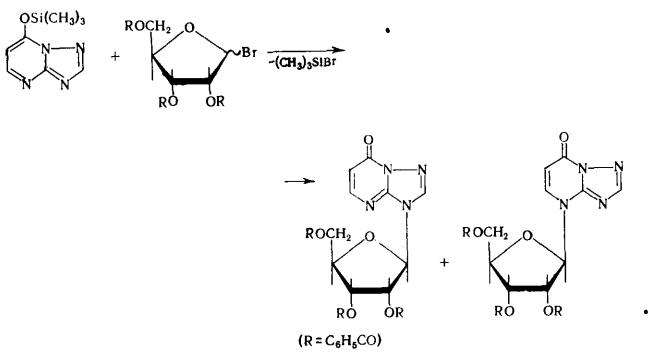
3. Derivatives of Triazolopyrimidines

When 3-tri-methylsilyl-5-7-trimethylsiloxy-trimethylsilylamino-v-triazolo[4,5-*d*]pyrimidine reacted with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile solution at 20°C for 6 days, 5-amino-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-v-triazolo[4,5-*d*]pyrimidin-7-one was formed in 43.5% yield[146].



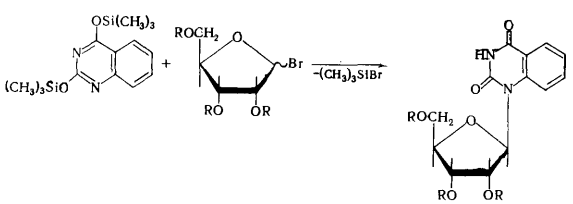
In contrast to this, the trimethylsilyl derivatives of thiazolo]5,4-*d*]pyrimidine-5,7-dione yielded a mixture of the 4-α- and 4-β-nucleosides[147]. A mixture of the 2- and 3-nucleosides (α- and β-anomers) was formed in the reaction of 7-methylthio-3-trimethylsilyl-v-triazolo-[4,5-*d*]pyrimidine with 2,3,5-tri-*O*-benzyl-D-arabinofuranosyl chloride at 120°C *in vacuo*[148].

When 7-trimethylsiloxy-*sym*-triazolo[2,3-*a*]pyrimidine reacts with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile at room temperature, a mixture of 3- and 4-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-*sym*-triazolo-[2,3-*a*]pyrimidin-7-ones is obtained in which the amount of the 3-isomer exceeds by a factor of 1.7 that of the 4-isomer[149]:



4. Quinazoline Nucleosides

The reaction of 2,4-bis(trimethylsiloxy)quinazoline with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile at room temperature for 2 days resulted in the formation of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)quinazoline-2,4-dione in 80% yield[144]. A similar result was obtained when the reaction was carried out in boiling benzene in the presence of $HgBr_2$—HgO.[57]

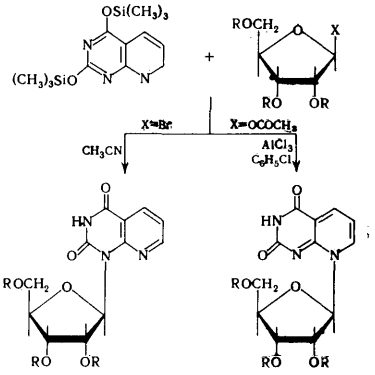


When 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride was employed in this reaction, the product was a mixture of anomers in 60% yield, from which it was possible to isolate 25.4% of the β-anomer and about 1% of the α-anomer[150].

β-Anomers were obtained on ribosylation of 2- and 4-trimethylsiloxyquinazolines in acetonitrile in the presence of $SnCl_4$.[151]

5. Pyrido[2,3-*d*]pyrimidine Nucleosides

The reaction of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide with 4-trimethylsiloxy- and 2,4-bis(trimethylsiloxy)-pyrido[2,3-*d*]pyrimidine in acetonitrile results in the formation of the corresponding 1-β-nucleosides[152]. On the other hand, if the second compound is introduced into the reaction with tetra-*O*-acetyl-β-D-ribofuranose in chlorobenzene in the presence of $AlCl_3$ at 20°C, the product is 8-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-pyrido[2,3-*d*]pyrimidine-2,4-dione[152]:

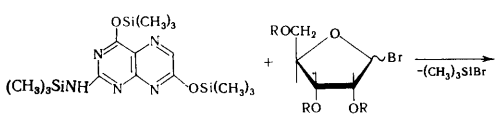


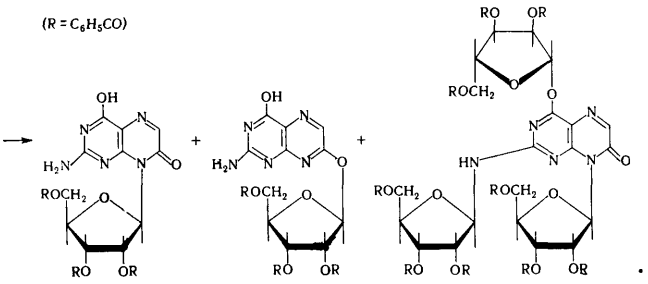
When tetra-*O*-acetyl-β-D-ribofuranose is heated with the bis(trimethylsilyl) derivative of 6-ethoxycarbonyl-2-methylthiopyrido[2,3-*d*]pyrimidine-4,5-dione at 155–160°C *in vacuo*, the 8-β-nucleoside is also formed[153].

6. Pteridine Nucleosides

The study of the reaction of trimethylsilyl derivatives of hydroxy- and amino-pteridines with halogenoses and fully acylated sugars established that, when the hydroxy-group is in the 7-position of pteridine (i.e. in the pyrazine ring), β-N_8-nucleosides are formed in most cases in the reaction with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in boiling benzene in the presence of $HgBr_2$–HgO,[154] and also with 1-*O*-acetyl-2,3,5-tribenzoyl-β-D-ribofuranose in the presence of $SnCl_4$ [155] or $ZnCl_2$.[156]

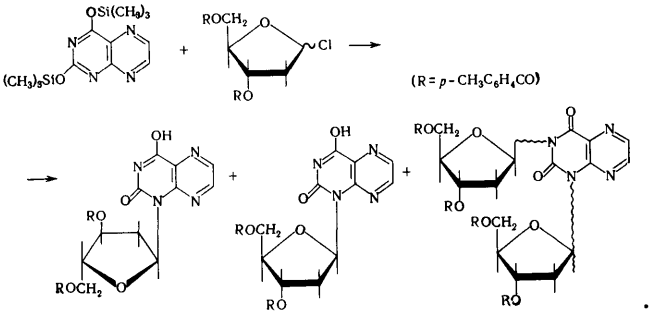
However, the 6-methyl-2-dimethylamino-[154,155] and 4-alkoxy-2-amino-derivatives[155] give rise to the formation of a mixture of the β-N_8- and β-O_7-isomers. The reaction with the 2-amino-7-hydroxy-derivative gives rise to the β-N_8-riboside (21%) and the 2,8-diriboside (4.5%).[156] But 2-amino-4,7-dihydroxypteridine yields, apart from the β-N_8- and β-O_7-isomers, also the 2,4,8-tririboside (4%):[155]





On the other hand, when the hydroxy-group is in the 2-position of pteridine (i.e. in the pyrimidine ring), then the reaction with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in the presence of $HgBr_2$–HgO yields the β-N_1-nucleoside[157] with a small admixture of the 1,3-diriboside in the case of the 2,4-dihydroxy-derivatives.

The reaction of 2,4-bis(trimethylsiloxy)pteridine and 2-trimethylsiloxy-4-trimethylsilylaminopteridine with 2-deoxy-3,5-di-*O*-*p*-toluoylfuranosyl chloride in the presence of $HgBr_2$–HgO gives rise to the formation of a mixture of 1-α-, 1-β-, and 1,3-dideoxyribosides in which the 1-β-anomer predominates[157]:

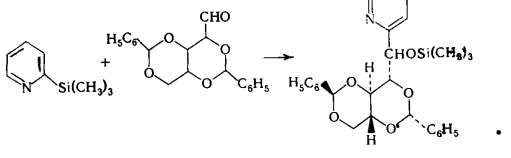


V. SYNTHESIS OF NUCLEOSIDES CONTAINING OTHER HETEROCYCLIC BASES

1. Pyridine Derivatives

The reaction of 2-trimethylsiloxypyridine with 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl bromide in nitromethane at 20°C in the presence of $AgClO_4$ gave 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-pyridone in 70% yield[86,94]. 1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-4-hydroxy-2-pyridone was obtained in 68% yield from 2,4-bis-(trimethylsiloxy)pyridine and 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide in acetonitrile[158–160], while heating of the same silyl derivative with 2-deoxy-3,5-di-*O*-*p*-toluoylribofuranosyl chloride *in vacuo* at 110°C gave 4-hydroxy-1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-αβ-D-ribofuranosyl)-2-pyridone[159,160]. The N_1-nucleosides of 4-hydroxy-5-methoxycarbonyl-2-pyridone were obtained in acetonitrile at room temperature[159,161].

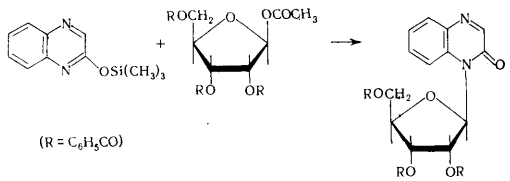
The enhanced reactivity of the Si–C bond in trimethyl-(2-pyridyl)silane permits its employment for the synthesis of *C*-nucleosides (for example, by the reaction with 2,4:3,5-di-*O*-benzylidene-D-ribose)[162]:



2. Pyridazine, Pyrazine, and Quinoxaline Nucleosides

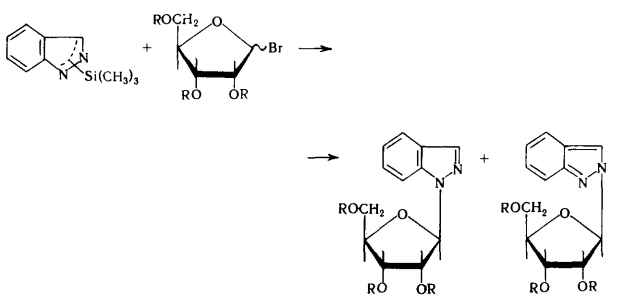
The reaction of 3,6-bis(trimethylsiloxy)pyridazine with 2-chlorotetrahydrofuran at temperatures between −20° and 10°C for 6 h or with 2-chlorotetrahydropyran at 15—50°C for 7 h in benzene solution resulted in the formation of analogues of pyridazine nucleosides—1-(2-tetrahydrofuryl(-3-hydroxypyridazin-6-one (yield 50%) and 3-hydroxy-1-(2-tetrahydropyranyl)pyradazin-6-one (yield 44.5%)—which inhibit DNA polymerase[163].

1-(2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl)-1,2-dihydropyrazin-2-one was obtained by the reaction of 2-trimethylsiloxypyrazine with 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose in boiling 1,2-dichloroethane in the presence of $TiCl_4$.[164] 2-(Trimethylsiloxy)quinoxaline reacts similarly[165]. The yield of 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)quinoxaline when the reaction was carried out in the presence of $SnCl_4$ did not exceed 10%, as in the presence of $HgBr_2$—HgO:[165]



3. Indazole Nucleosides

The 1- and 2-(β-D-ribofuranosyl)indazoles were obtained in proportions of 1:5 by heating *N*-trimethylsilylindazole with 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide at 75—80°C *in vacuo* (1.5 mmHg) in the presence of sodium iodide[166]:



The 2-β-D-ribofuranosyl derivatives of 4-, 5-, and 6-nitroindazoles[166] and 3-cyanoindazole[167] were synthesised similarly. In the last case the yield of the nucleoside was 23%. The yield in boiling benzene in the presence of $HgBr_2$—HgO reached 85%.[167]

4. Pyrazole, Imidazole, Benzimidazole, and Imidazo-[4,5-*c*]pyridine Nucleosides

When 1-trimethylsilylbenzimidazole is fused *in vacuo* with various *O*-acylhalogenoses, a mixture of the α- and β-anomers of the corresponding N_1-nucleosides is formed[168-173]. The ratio of the anomers in the mixture obtained from 1-trimethylsilylbenzimidazole and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide is 43:57,[168] while in the case of the glucopyranosyl derivative the ratio is 56.5:43.5.[168]

Condensation of 2-chloro-1-trimethylsilylbenzimidazole with 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide at 110°C in the presence of NaI resulted in the formation of 2-chloro-1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-benzimidazole in 69% yield[174]. 2-Chloro-5,6-dimethyl-1-trimethylsilylbenzimidazole[175], 1-trimethylsilyl-2-trimethylsilylthiobenzimidazole[174], and 4,6-dichloro-1-trimethylsilylimidazo[4,5-*c*]pyridine[176] react similarly. The ratio of the α- and β-anomers in the synthesis of 1-(2,3,5-tri-*O*-acetyl-αβ-D-ribofuranosyl)-5-carbamoyl-4-(3,3-dimethyl-1-triazino)imidazole is 65:35.[177] Only the 1-β-riboside was isolated after the reaction of the analogous pyrazole derivative[178].

1-Methyl-2-trimethylsilylimidazole reacts with 1,6-diformyl-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-1,5-pyranoside like trimethyl-(2-pyridyl)silane with formation of the corresponding *C*-nucleoside[162,179].

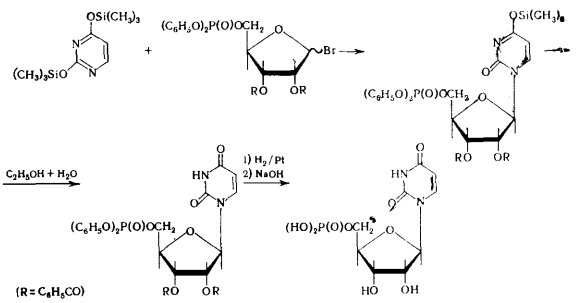
5. Triazole and Benzotriazole Nucleosides

The silyl method has been used successfully also in the synthesis of 1-(β-D-ribofuranosyl)urazole[180] and its 2- and 4-methylderivatives[180], 1-(β-D-2-deoxyribofuranosyl)-urazole[180], the methyl esters of 1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-1,2,4-triazole-3- and 5-carboxylic acids[181,182], and N_1-nucleosides of benzotriazole[170,171,183,184].

VI. SYNTHESIS OF NUCLEOTIDES

The commonest method of synthesising nucleotides involves the phosphorylation of the protected nucleoside. The possibility of the direct condensation of phosphorylated sugars with derivatives of pyrimidine or purine bases has been much less thoroughly investigated[185,186]. The silyl method proved to be very convenient for this purpose.

When 2,4-bis(trimethylsilyl)uracil was heated with 2,3-di-*O*-benzoyl-5-diphenylphosphoryl-D-ribofuranosyl bromide at 100—110°C for 30 min, 1-(2,3-di-*O*-benzoyl-5-diphenylphosphoryl-α-D-ribofuranosyl)uracil was formed in 38% yield together with its β-anomer in 11% yield[11,13,15]; after treatment with aqueous ethanol and catalytic dephenylation followed by deacylation, the latter was converted into uridine 5′-phosphate[11]:



Under analogous conditions, 2,3-di-*O*-benzoyl-5-diphenylphosphoryl-L-ribofuranosyl bromide gives the α- and β-anomers in yields of 34.5 and 18% respectively[16]. The yields of 1-[2,3,4-tri-*O*-acetyl-6-bis-(*p*-nitrophenyl)-phosphoryl-β-D-glucopyranosyl]uracil[11], 1-[2,3-di-*O*-benzoyl-5-diphenylphosphoryl-β-D-ribofuranosyl]-4-ethyluracil[11], and the α- and β-anomers of L-ribofuranosylthymine 5′-phosphate[16] are 18.5%, 35%, 34.3, and 17% respectively.

The α-anomer was obtained in 26% yield on heating 2,4-bis(trimethylsilyl)thymine with 2,3-di-*O*-benzoyl-5-diphenylphosphoryl-D-ribofuranosyl bromide at 100–110°C.[13] When the same reaction was carried out *in vacuo* (80–100 mmHg), the β-anomer was formed in 48% yield[15]. In the presence of $HgBr_2$ the reaction can be carried out in benzene at room temperature. The yield of the β-anomer then reaches 92% after 3 h.[32] In the presence of $HgBr_2$, 4-acetyl-1-(2,3-di-*O*-benzoyl-5-diphenylphosphoryl-β-D-ribofuranosyl)cytosine was also obtained in a high yield[32], while fusion of the reactants leads to a mixture of the α- and β-anomers in proportions of 68 : 32.[16,187]

6-Benzoyl-9-(2,3-di-*O*-benzoyl-5-diphenylphosphoryl-D-ribofuranosyl)adenine was obtained in 37.6% yield[14,15,187,188] and with a 43 : 57 ratio of the α- and β-anomers[188] by fusing 6-benzoyl-6,9-bis(trimethylsilyl)-adenine with 2,3-di-*O*-benzoyl-5-diphenylphosphoryl-D-ribofuranosyl bromide. When the reaction is carried out in benzene at room temperature in the presence of $HgCl_2$, the yield of the β-nucleotide is increased to 67% but a mixture of the 9- and 7-isomers is then formed in proportions of 58 : 42.[32]

Condensation of 6,9-bis(trimethylsilyl)hypoxanthine and trimethylsilyltheophylline with 2,3-di-*O*-benzoyl-5-diphenylphosphoryl-D-ribofuranosyl bromide at 100–110°C leads to the formation of 9-(2,3-di-*O*-benzoyl-5-diphenylphosphoryl-β-D-ribofuranosyl)hypoxanthine in 59.2% yield and of the 7-β-nucleotide of theophylline in 73% yield[11,15].

ADDENDUM

A series of studies on the synthesis of nucleosides and their analogues using trimethylsilyl derivatives of heterocyclic bases were published recently (from May to October, 1973), which is evidence of a growing popularity of the trimethylsilyl method of synthesis. For example, 2,3,5-tri-*O*-benzoyl-5-isopropyl- and 2,3,5-tri-*O*-benzoyl-5-t-butyl-uridines (*anti*-conformations)[189] as well as 1,2-dihydro-1-(3,5-di-*O*-*p*-chlorobenzoyl-2-deoxy-$\alpha\beta$-D-*erythro*-pentofuranosyl-2-oxopyrazine 4-oxide[190], which is an analogue of deoxyuridine, were resynthesised by this method. Condensation of 2,4-bis(trimethylsilyl)-uracil[191] and 5-trimethylsiloxy-2,4-bis(trimethylsilyl)-uracil[192] with 2-chlorotetrahydrofuran and with 2-chlorotetrahydropyran led to the formation of the corresponding N_1-tetrahydrofuryl and N_1-tetrahydropyranyl derivatives.

5-Hydroxy-1-(β-D-ribofuranosyl)pyrimidin-2-one[193] and 3-methoxycarbonyl-, 3-cyano-, and a number of other 3-substituted 1-(β-D-ribofuranosyl)-1,2,4-triazoles[194] were also successfully synthesised via the silyl derivatives of the bases. Studies have been made on the condensation of trimethylsilyl derivatives of thymine with acyclic sugars[195] and of a number of trimethylsilyl derivatives of uracil, 6-azauracil, and their 2-thio-derivatives with oligosaccharides[196].

Nucleoside analogues containing various condensed systems as the aglycones were obtained by the silyl method: 3-($\alpha\beta$-D-galactopyranosyl)-2-methyl-7-nitroimidazo[4,5-*c*]pyridine[197], 6-bromo-1-(β-D-glucopyranosyl)-2-methyl-1*H*-imidazo[4,5-*b*]pyridine[198], 6-bromo-1-(β-D-galactopyranosyl)-1*H*-imidazo[4,5-*b*]-pyridine[198], 5,6-dimethyl-1-(β-D-ribofuranosyl)imidazo-[4,5,*b*]-pyrazine[199], 2-β-D-(2,3,5-tri-*O*-benzoylribofuranosyl)- and 2-β-D-(2,3,4,6-tetra-*O*-acetylglucopyranosyl)-5,6-dihydro-4-hydroxymercapto-7*H*-pyrrolo[2,3-*d*]-pyrimidines[200], and 2-ethyl-6-(β-D-ribofuranosyl)oxazolo-[5,4-*d*]pyrimidin-7-one[201].

The synthesis of pteridine nucleosides from the trimethylsilyl derivatives of various hydroxy- and amino-pteridines was investigated in greater detail[202–204].

The employment of the trimethylsilyl method for the synthesis of pyrimidine nucleosides was also briefly considered in a recently published review devoted to the methods of synthesising pyrimidine nucleosides[205].

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Photochemistry of Aromatic Sulphonyl Compounds

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The spectra of aromatic sulphonyl compounds $ArSO_2X$—sulphonic acids, their derivatives, and sulphones X = OH, OAlk, OAr, Hal, NH_2, N_3, Alk, Ar)—are examined, information is reported on the photoreactions, and modern views are given on the mechanism of these processes. A list of 143 references is included.

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I. INTRODUCTION

Aromatic sulphonic acids, their derivatives (esters, amides, halides, and azides), and sulphones are extremely numerous and important compounds in organic chemistry, of both purely theoretical and practical interest. In contrast to dark chemistry and the photochemistry of other sulphur-containing compounds, until fairly recently hardly any investigation had been made of the photochemical properties of the present group of compounds. The chemistry of their excited states has begun to be developed only during the past 10–15 years in connection with the appearance of new physicochemical methods and the improvement of photochemical experimental techniques. A considerable number of publications have appeared in this field, but they have not been summarised in the Soviet literature†, and an attempt is made in the present paper. The literature has been covered up to 1973 inclusive.

† A review of the photochemistry of aromatic sulphonic acids will be found in Ref. 1.

II. SPECTRA OF COMPOUNDS $ArSO_2X$

The sulphonyl group SO_2, present in all the compounds under review, contains positively charged sulphur without a lone pair of electrons and on the whole has a planar structure[2]. Most investigators consider that, as a consequence, conjugation of the π-electron system of the aromatic residue with the sulphonyl group and through the latter with the X moiety is absent. In sulphonic acids and esters, sulphonamides, and sulphonyl halides, therefore, the effect of the SO_2X substituent is regarded as purely inductive or one in which the inductive effect predominates considerably over the conjugation effect[3,4]. The electronic absorption spectrum of the aromatic ring system is little affected in these compounds, being determined by the chromophores of the unsubstituted compound weakly perturbed by the sulphonyl group. Furthermore, even this slight effect of the SO_2X group is smaller the larger the number of aromatic rings in the fused structure. Introduction of an SO_2X substituent has little effect also on the

energy characteristics of photoexcited states of the aromatic system.

Nevertheless, attempts were sometimes made to reveal conjugation of the aromatic ring with the SO_2X substituent, e.g. in compounds $C_6H_5SO_2X$ (X = OH, OCH_3, Hal), from a study of the ultraviolet spectra [5,6]. The results reported below, however, largely contradict the authors' arguments.

The main spectral features of aromatic sulphonic acids attributable to the sulphonyl group are apparent also in such derivatives as esters, amides, and halides, which is confirmed not only by their electronic spectra [5]. Thus the same conclusion is reached from an investigation of these compounds by Raman and infrared spectroscopy (in particular the effect of nuclear substituents on the spectra) [7]. This permits us to use the sulphonic acids of benzene, naphthalene, anthracene, and anthraquinone, which are most often subjected to photochemical reactions, to examine the above features of the effect of the SO_2X group on the spectral characteristics of aromatic compounds.

Three absorption bands—at 210 nm (ϵ = 5000), 255–272 nm (ϵ = 200–400, split into four narrow peaks), and 293 nm (weak)—are present in the ultraviolet spectrum of aqueous benzensulphonic acid (I) [8,9]. The appearance of a band in the region of 270 nm is attributed [9] to the electron-accepting properties of the sulpho-group, evident in a displacement of electron density from the benzene ring to the positively charged sulphur atom.

Among the anilinesulphonic acids (IIa–c) sulphanilic acid (IIc) has been most thoroughly studied. Spectral investigations, as well as conductivity measurements on its aqueous solutions [10], have shown that it is not an internal salt [11] or a zwitterion [12]. In contrast to metanilic (IIb) and orthanilic (IIa) acids, which have absorption maxima at 293 and 294 nm respectively with lgϵ = 3.21 and 3.43, the spectrum of (IIc) has a shoulder (278–302 nm) in this region, and at shorter wavelengths a band develops from the second absorption band of benzenesulphonic acid, which is sometimes explained by partial conjugation of amino- and sulpho-groups through the benzene ring [10]. On protonation of the amino-group in an acid medium the spectra of all of the anilinesulphonic acids (IIa–c) approach the spectrum of benzenesulphonic acid [10,13], but in alkaline solutions that of aniline (III) [14].

Neither benzenesulphonic acid (I) nor its salts luminesce, owing to deactivation of the benzene ring and localisation of the π-electrons under the influence of the sulpho-group [15]. Delocalisation of π-electrons, due to the strong effect of the amino-group, is dominant with the anilinesulphonic acids (IIa–c). Sodium sulphanilinate luminesce in water at 293°K (Φ = 0.07) [16]. The phosphorescence spectrum of crystals of this acid contain [17] two bands at 405–460 and 460–540 nm, which decay at different rates and are assigned [17,18] to two triplet levels (51.2 and 69.2 kcal mole^{-1}).

The spectra of naphthalene-1- and -2-sulphonic acids (IVa) and (IVb), as well as that of naphthalene itself (V), contain three electronic bands—^1L_b, ^1L_a, and ^1B_b at 290–320, 250–290, and 210–240 nm respectively—corresponding to $\pi\pi^*$-transitions [19–21] (Platt's classification [22]). The considerable difference between the molecular orbitals of the 1- and 2-isomers (IVa) and (IVb) is responsible for the difference (though slight) between their absorption spectra [23]. The presence of a 1-sulpho-group leads to a bathochromic shift of the ^1L_a and ^1B_b bands, but the 2-isomer shows a bathochromic shift of the ^1L_b band; intensification of the longer-wavelength band is observed with both isomers. No change in direction of the moments of the electron transitions was observed on migration of the substituent from the 1- to the 2-position in the above isomers (IVa) and (IVb) [24]. The direction of the transition moments is obviously unaffected not only by change in the position of the sulpho-group in the naphthalene ring system but also by its introduction into the ring. Substituents which undergo conjugation behave differently; they usually change the direction of the moments of certain transitions of fused aromatic systems [19,24]. As with naphthalene [25,26], the ^1L_b and ^1B_b transitions of its 1- and 2-sulphonic acids (IVa) and (IVb) are evidently parallel to the long symmetry axis x, while the ^1L_a transition is perpendicular to it.

Introduction of a 4-amino-group into naphthalene-1-sulphonic acid displaces the ^1B_b band to longer wavelengths and halves its intensity; the ^1L_a band undergoes a bathochromic shift, and its intensity is doubled [20,27]. This effect, as with the anilinesulphonic acids, is due to interaction of the amino-group with the naphthalene ring, which overlaps the effect of the sulpho-group. The absorption curve of naphthionic acid (VI) coincides in neutral and alkaline solutions with the spectrum of 1-naphthylamine (VII), but in acid solutions approximates to the spectrum of naphthalene-1-sulphonic acid (IVa) [20,27].

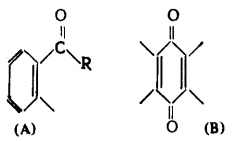
Both isomeric naphthalenesulphonic acids (IVa) and (IVb) fluoresce [28] in methanol–water matrices at 77°K. Naphthionic acid (VI) fluoresces intensely in aqueous solution (λ_{max} = 425 nm); the intensity increases over the pH range 0–6, and then remains constant with further increase in pH [29], owing to deprotonation of the amino-group. The quantum yield of the fluorescence of sodium 4-aminonaphthalene-1-sulphonate (VI) in water at 20°C is ~0.80. [30]

According to Smaller et al. [28] the fluorescence levels of naphthalene and of its 1- and 2-sulphonic acids differ by −1.2 and −1,3 kcal mole^{-1} respectively, the corresponding differences for the phosphorescence levels being −0.35 and −0.09 kcal mole^{-1}. Thus E_{S^1} and E_{T^1} for the naphthalenesulphonic acids (IVa) and (IVb) are ~89 and ~60 kcal mole^{-1}. [28] If the effect of the sulpho-group in the aminosulphonic acid (VI) is also neglected, the energies of the excited states can be assumed to be close to those for 1-naphthylamine (VII) (E_{T^1} ~ 54 kcal mole^{-1}). [31]

Both groups of absorption bands of anthracene(VIII)—shorter-wavelength ^1B_b at 230–260 nm and longer-wavelength ^1L_a at 290–390 nm—exhibit a slight bathochromic shift on introduction of a sulpho-group. With anthracene-1-sulphonic acid (IXa) the shift of the ^1L_a band is ~5–6 nm, several times larger than that of the ^1B_b band. With anthracene-2-sulphonic acid (IXb), on the other hand, the relative shift of ^1B_b exceeds that of ^1L_a. [32] These results are consistent with indications [33,34] that the introduction of an electron-accepting substituent at position 1 or 9 in anthracene displaces the longer-wavelength band more strongly than the shorter-wavelength band. Popov's study [24] of the polarisation spectra of the anthracenesulphonic acids (IXa) and (IXb) suggests that, as with anthracene (VIII) [35], the moment of the transition $^1L_a \leftarrow {}^1A_1$ is parallel to the long x-axis of the molecule, while the moment of the transition $^1B_b \leftarrow {}^1A_1$ is parallel to the short y-axis. These sulphonic acids luminesce in solution, in contrast to other anthracene derivatives containing electron-accepting substituents (nitro, carboxy) that conjugate with the anthracene ring system [36–38]. On the assumption that the energy levels of excited states of these sulphonic acids differ little from the levels of anthracene, we can estimate them as E_{S^1} = 76 and 72.5 kcal mole^{-1} for anthracene in solution and in the crystalline state, and E_{T^1} = 42.5 kcal mole^{-1}. [39]

Introduction of a sulpho-group at position 1 or 2 in

anthraquinone (X) produces a slight bathochromic shift (>5 nm) of the absorption bands with a slight increase in their intensity. The spectrum of anthraquinone itself (X) comprises six bands—at 243.5, 252.5, 262.8, 272, 325.5, and 405 nm—and is often regarded as resulting from the superposition of the spectra of two chromophores (A) and (B)[40]



(A) (B)

All these bands other than the last have been assigned to $\pi\pi^*$-electron transitions[41-44]. The moments of the transitions of bands at 252.5, 262,8, and 325.5 nm are polarised along the short y-axis of the molecule[42,44,45], and that of the 272-nm band is polarised along the long x-axis[45]. The chromophore of anthraquinone is sometimes regarded[46] as two weakly interacting *ortho*-disubstituted benzenes, the three $\pi\pi^*$-states of anthraquinone being associated with the ^1L_b, ^1L_a, and ^1B_b bands of benzene[22]. Hence the bands at 252.5, 325.5, and 272 nm are assigned to $^1B_b \leftarrow {}^1A_1$, $^1L_b \leftarrow {}^1A_1$, and $^1L_a \leftarrow {}^1A_1$ transitions in the benzene ring[44,47]. The absorption at 405 nm, which is so weak that it is not always evident, has given rise to the most contradictory conclusions[40,48]; its transition moment lies in the plane of the molecule, and is polarised along the x-axis[44]. The lifetime of the phosphorescent state on excitation in this band[49,50] and the shifts it undergoes in various solvents[51] have enabled it to be assigned quite confidently to an $n\pi^*$-level of anthraquinone. The assignment of the 405-nm absorption to a $\pi\pi^*$-transition, which was based on theoretical calculations[52], seems very questionable.

The bands in the electronic spectra of anthraquinone-1- and -2-sulphonic acids are assigned in the same way as with anthraquinone[53]. Differences between the isomers resulting from the position of the sulpho-group are more clearly evident in the infrared spectra[2]. The spectrum of the ion of the sulphonic acid (XII) in the solid state contains an absorption band corresponding to carbonyl-stretching vibrations at 1678 cm^{-1}; in the ionised form of the 1-isomer (XIa) this is split into two, at 1678 and 1692 cm^{-1}. The latter corresponds to the 9-carbonyl group, and results from donor–acceptor interaction of the SO_2O^- group with the quinoid system of the molecule. Band splitting is observed also with the covalent anthraquinone-1-sulphonic acid: the carbonyl frequency has fallen to 1684 and 1664 cm^{-1} (carbonyls at positions 10 and 9), and absorption appears at 3200 cm^{-1}, due to hydroxyl involved in an intramolecular hydrogen bond.

Photoexcitation of anthraquinone (X) and its sulphonic acids may transfer their molecules to $S_{\pi\pi^*}$, $S_{n\pi^*}$, $T_{\pi\pi^*}$, and $T_{n\pi^*}$ states. According to most authors[44,50,54,55] the lowest excited state is $T_{n\pi^*}$, above this is located the $S_{n\pi^*}$ level ($\Delta\nu \simeq 1000$ cm^{-1}), after which follow the $T_{\pi\pi^*}$ and $S_{\pi\pi^*}$ levels. This is counterbalanced by Nurmukhametov's view[50] that the $T_{\pi\pi^*}$ level is located between the $S_{n\pi^*}$ and $T_{n\pi^*}$ levels. Evidence is provided by the absence of fluorescence from the S_{n^*} level in solutions of anthraquinone and its derivatives, owing to the high efficiency of the $S_{n\pi^*} \rightarrow T_{\pi\pi^*}$ interconversion due to the increase of spin–orbital coupling between states of different electron configurations[56].

Luminescence has not been observed in solutions of anthraquinonesulphonic acids; formation is available only on the phosphorescence of (XII) in a matrix at low temperatures[57]. The presence of a sulpho-group in the anthraquinone molecule, whether at position 1 or 2, has hardly any effect on the arrangement of energy levels. The energy of the lowest triplet level of anthraquinone $T_{n\pi^*}$ is ~62.5 kcal $mole^{-1}$,[57,58] and ~62 kcal $mole^{-1}$ in the 2-sulphonic acid (determined from the phosphorescence spectrum)[57]. Because of the impossibility of determining experimentally the energy of the lowest singlet state $E_{S_{n\pi^*}}$ of anthraquinone and its sulphonated derivatives, values were calculated from the electronic absorption spectra[59]: the results were respectively 66.5, 64.3, and 64.6 kcal $mole^{-1}$ for anthraquinone and its 1- and 2-sulphonic acids.

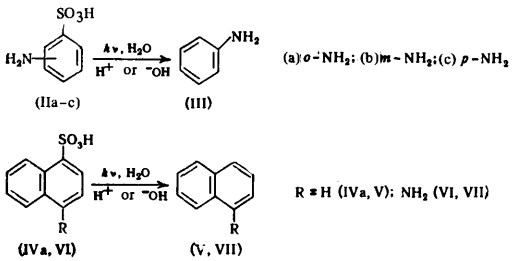
A rather different situation is found when the substituent X attached to the arylsulphonyl group possesses a sufficiently mobile π-electron system, as e.g. in diaryl sulphones and arenesulphonyl azides. Although published data on them are few and somewhat contradictory, the sulphonyl group in these compounds may be supposed to be better able to transmit the effect of conjugation. This is indicated in particular by a bathochromic shift (absorption in the range 230–245 nm) and a more than double hyperchromic effect on passing from methyl phenyl to diphenyl sulphone[60]. The measured dipole moments of a series of diaryl sulphones indicate a considerable displacement of electron density from the benzene rings to the sulphonyl group[61]. Since the sulphonyl sulphur atom does not possess a lone pair of electrons, which might have been involved in conjugation, it has been suggested[62] that 3*d*-orbitals of sulphur take part in this process.

There are indications that a similar effect occurs in aromatic sulphonyl azides[63]. The electronic spectra of the benzenesulphonyl azides that have been studied contain no bands in the region of 285 nm, where absorption by the benzene ring is absent, that might have been attributable to the azide group. The two bands observed—with a sharp maximum in the range 220–256 nm ($\lg\epsilon = 3.9$–4.5) and with a characteristic vibrational structure in the range 257–295 nm (2.5–3.4)—correspond to electron transitions between energy levels of the whole molecule. The red shifts of absorption bands I and II of benzene (by 19 and 10 nm respectively) on introduction of an azidosulphonyl group into the ring are substantially smaller than on introduction of an azido-group ($\Delta\lambda = 30$–45 nm). This is attributed[63] to a change in the character of the interaction between the substituent and the benzene ring: whereas the azido-group acts as an electron donor, the azidosulphonyl group possesses electron-accepting properties. The higher frequency of the azide-stretching vibrations in the infrared spectra of aromatic sulphonyl azides than in those of analogous aromatic azides indicates intensified localisation of bonds in the azide fragment under the influence of the sulphonyl group. Nevertheless, the correlations found between the absorption frequency of the azido-group (in the range 2120–2135 cm^{-1}) and the integral intensity of this band with the Hammett σ constants of substituents in the aromatic ring indicate that these substituents may be conjugated through the sulphonyl group with the π-electron system of the azido-group.

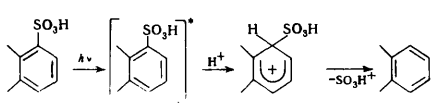
III. PHOTOCHEMICAL PROCESSES INVOLVING THE SULPHUR-CONTAINING GROUP

The simplest photochemical process directly involving the SO_2X group—elimination of the sulpho-group from certain aromatic sulphonic acids—can be accomplished by exposing their weakly acid, neutral, and weakly alkaline

aqueous solutions (pH 1–13) to ultraviolet radiation. The reaction takes place at room temperature, i.e. under conditions under which desulphonation does not take place in the dark. The yields of desulphonation products (III), (V), (VII), 1-sulphonic acids of naphthalene (IVa) and of 4-naphthylamine (VI), and *o*-, *m*-, and *p*-anilinesulphonic acids (IIa–b) increase in this sequence (from 2% to 50%) [64,65].



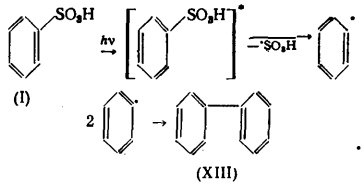
Both acidic and basic properties of aromatic molecules are strengthened by photoexcitation [66]. Which are realised in amphoteric excited states will depend on many factors. The electron affinity of the aromatic system increases in certain electrophilic photosubstitutions, e.g. isotopic hydrogen exchange, acylation, etc. [66,67]. By analogy with these reactions it has been postulated [65] that in acid media photodesulphonation involves hydrolytic detachment of the sulpho-group as a consequence of the enhanced basic properties of the aromatic ring. From the general consideration that, in comparison with the ground state, the basicity of triplet states varies less than that of singlet states, it seems more probable that a singlet excited state of the sulphonic acid takes part in the process [68]. Since the change in the acid–base properties of the π-electron system is very considerable (ΔpK_a may reach 25–30 [66]), it is quite likely that this increase in basic properties covers the decrease in hydrogen-ion concentration on passing from acid to neutral and weakly alkaline media in the pH range investigated [64] and, to all appearances, a mechanism of hydrolytic desulphonation



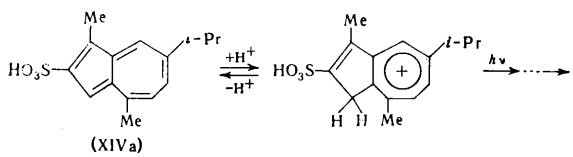
may operate not only in acid but also in neutral and even weakly alkaline media.

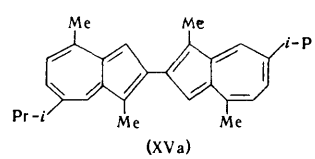
In alkaline aqueous solutions, on the other hand, reductive photodesulphonation with the hydroxide ion as electron donor is also possible [64]. It is interesting that the *meta*-isomer (IIb) is most readily desulphonated when alkaline solutions of the *o*-, *m*-, and *p*-sulphonic acids of aniline (IIa–c) undergo photolysis [64], as well as in the electrolytic detachment of the sulpho-group [69]. The reductive properties of the hydroxide ion in photochemical reactions with aromatic compounds have been discussed [70,71].

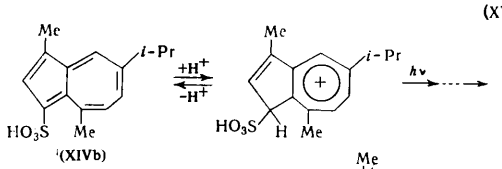
Elimination of the sulpho-group from benzenesulphonic acid (I) has a different mechanism [72]. Photolysis of its aqueous solutions produces biphenyl (XIII); the yield of the latter (up to 6%) is independent of pH (over the range 1–13 investigated) under identical conditions of irradiation, and the quantum efficiency of the process is below 10^{-4}. Desulphonation probably involves homolytic cleavage of the Ar–S bond in the photoexcited molecule of (I):

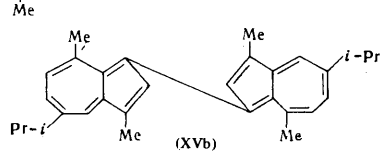


A similar result— the coupling of residues from the starting materials—is produced by photolysis of the protonated forms of guaiazulene-2- and -3-sulphonic acids (XIVa) and (XIVb). In 96% sulphuric acid they give respectively 2,2′- and 3,3′-biguaiazulyls (XVa) and (XVb) in up to 40% yield [73]:

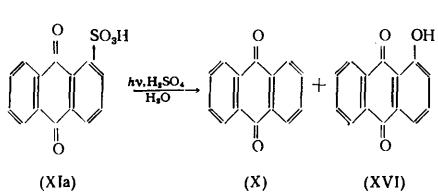








Only traces of anthraquinone (X) are formed by the irradiation of weakly acid (pH 1–7) aqueous anthraquinone-1-sulphonic acid (XIa). The efficiency of desulphonation is increased (up to 20%) by photolysis in 11 *N* sulphuric acid, and a small quantity (~3%) of 1-hydroxyanthraquinone (XVI) is obtained:



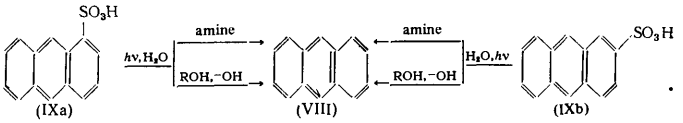
The sulpho-group of other anthraquinonesulphonic acids investigated—the 2-, 1,5-, and 1,8-acids (XII), (XIb), and (XIc)—remains unchanged under these conditions [74].

Considerable yields of anthraquinone (15–90%) have been obtained [64,65,75] by the irradiation of aqueous solutions of a sulphonate of (XIa) containing hydrazine, an aliphatic amine, or an alcohol with added alkali (the efficiency of photodesulphonation is lower with branched-chain alcohols [65]). Under identical conditions of photolysis the efficiences of complete desulphonation of anthraquinone-1,5- and -1,8-disulphonic acids (XIb) and (XIc) were substantially lower, not exceeding 10%; anthraquinone-2-sulphonic acid (XII) is not desulphonated.

Preliminary results indicate [65] that the rate of photodesulphonation is variable in the region of absorption by sulphonated anthraquinones: the maximum rate is obtained by photolysis in the far ultraviolet and decreases significantly with increase in wavelength of the exciting light.

Although elimination of the sulpho-group is effected in an alkaline medium, the initial compounds do not undergo hydroxylation (see beginning of this Section) [64], since alkoxide ions act as the main electron donor; furthermore, hydroxyl radicals, formed in considerably smaller quantity (than alkoxyl radicals), are removed by reaction with the alcohol.

Only traces of anthracene (VIII) are formed by the prolonged photolysis of aqueous solutions (in the presence of an amine) or alkaline aqueous–alcoholic solutions of anthracene-1- and -2-sulphonic acids (IXa) and (IXb) [75]:



Thus both the structure of the aromatic system and the position of the sulpho-group play important roles in this process.

When an anthraquinone-1-sulphonic acid undergoes photodesulphonation in alkaline aqueous–alcoholic and aqueous amine media, no component other than the acid is excited, and the formation of atomic hydrogen or a solvated electron as reductant is improbable. It has therefore been postulated [76] that electron transfer to the acid molecule, resulting from the enhancement of the electron-accepting properties of the latter on excitation, takes place in an excited complex of the sulphonic acid and the alkoxide ion or the amine [77]. Subsequent breakdown of the excited complex was assumed to yield the sulphite ion and an anthraquinone radical; detachment by the latter of a hydrogen atom from the alcohol or the amine yields anthraquinone.

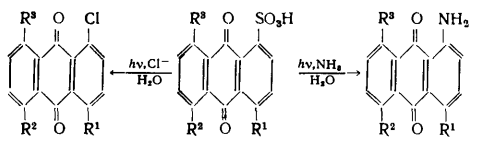
The photolysis of sulphonated anthraquinones (AS) in the above reducing media results in the corresponding products of their one- and two-electron reduction (the latter arise in secondary dark processes)—radical-ions ($AS^{\cdot -}$) and mono- and di-anions of anthraquinolsulphonic acids (ASH^-, AS^{2-})—which might have been intermediates in photodesulphonation, since in certain cases compounds of similar structure are able to eliminate electron-accepting substituents without excitation [78,79]. However, investigation of the effect of oxygen on photodesulphonation, together with the kinetics of the accumulation and destruction of the radical-anions and the formation of anthraquinone (A), has shown that the photodesulphonation of 1-sulphonated anthraquinones is actually a two-stage process with absorption of a light quantum at each stage. Absorption of the first quantum causes photoreduction of the substrate to the corresponding radical-anions with the appearance of products of their secondary dark reactions; absorption of the second quantum by one or all of the reduced forms yields anthraquinone as a result of the photochemical process and subsequent chemical reactions [80]:

$$AS \xrightarrow{h\nu} AS^*$$

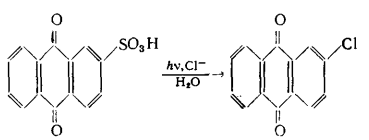
$$AS^* \xrightarrow{H_2O,ROH,\ NaOH} AS^{\cdot -} \longrightarrow ASH^- \ (AS^{=})$$

$$[AS^{\cdot -} \text{ and/or } ASH^-, AS^{=}] \xrightarrow{h\nu} [AS^{\cdot -} \text{ and/or } ASH^-, AS^{=}]^* \xrightarrow[[O_2]]{H_2O,RCH_2OH,\ NaOH} A$$

Irradiation of anthraquinone-1-sulphonic acids (XIa–g, l, m) in aqueous solutions containing chloride ions or ammonia entails replacement of the sulpho-group by a chlorine atom [81] or an amino-group [64]. Chlorination goes in quantitative yield, but the yields from photoamination do not exceed 20%, and the rate of formation of the corresponding amino-derivative decreases as the duration of exposure is increased. Such slowing down is due to secondary nuclear hydroxylation and amination of the initial anthraquinonesulphonate (see Section IV for these reactions), as the resulting water-soluble hydroxy- and amino-anthraquinonesulphonic acids inhibit substitution of the sulpho-group by filtering out the photochemically active light [82]. Special experiments on the effect of additions of such water-soluble acids on photoamination have shown that the assumed energy transfer from excited substrate molecules to by-product molecules [65] plays no appreciable part. Replacement of the sulpho-group in anthraquinone-2-sulphonic acid (XII) by a chlorine atom has a low yield (2%), but the sulpho-group in anthracenesulphonic acids (IXa) and (IXb) is replaced neither by chlorine nor by an amino-group.



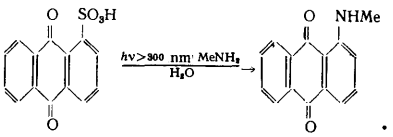
(XVIIa–g, l, m) (XIa–g, l, m) (XVIIIa–g, l, m)



(XII) (XIX)

a: $R^1=R^2=R^3=H$; (b) $R^1=R^3=H$, $R^2=SO_3H$; (c) $R^1=R^3=H$, $R^3=SO_3H$; (d) $R^1=SO_3H$, $R^2=R^3=H$; (e) $R^1=Cl$, $R^2=R^3=H$; (f) $R^1=R^3=H$, $R^2=Cl$; (g) $R^1=R^2=H$, $R^3=Cl$; (h) $R^1=NH_2$, $R^2=R^3=H$; (j) $R^1=R^3=H$, $R^2=NH_2$; (k) $R^1=R^2=H$, $R^3=NH_2$; (l) $R^1=R^3=H$, $R^2=NO_2$; (m) $R^1=R^2=H$, $R^3=NO_2$.

A 1-sulpho-group in anthraquinone does not undergo substitution by an alkylamino- or an arylamino-group: photodesulphonation occurs in the presence of aliphatic amines, as already mentioned, and no photoreaction takes place in the presence of aromatic amines. Methylamine is the only aliphatic amine in whose aqueous solutions both photodesulphonation and photosubstitution of the 1-sulphogroup in (XIa) takes place [65], the former process predominating on exposure to the complete spectrum from a mercury lamp. The second process predominates on exposure to light of wavelength exceeding 300 nm (the yield of 1-methylaminoanthraquinone (XX) is ~1%):



(XIa) (XX)

Photosubstitution of the 1-sulpho-group in (XIa) by a chlorine atom or an amino-group is not prevented by the presence of electron-accepting substituents (sulpho, chloro, nitro) at positions 4, 5, and 8 in the anthraquinone ring system, but the nature of the substituent and its position determine the rate of the process. Photosubstitution does

not take place when an electron-donating group (e.g. amino) is present at any of these three positions [74].

Light throughout the range of absorption is photochemically active in photosubstitution of the sulpho-group in anthraquinonesulphonates [82]. Photoamination and photochlorination of (XIa) have similar quantum efficiencies, which are independent of the wavelength of the exciting light over the range 250–435 nm. They vary between 10^{-4} and 10^{-3} depending on the reactant concentration: the quantum efficiency increases with the ammonia or chloride-ion concentration up to around molar, and then falls with further increase in concentration, probably owing to the concentration quenching of reactive excited states. In both cases photosubstitution is a one-photon process, as is confirmed by the linear dependence of its rate on the intensity of the light flux. The activation energy of photosubstitution (2.2–2.3 kcal mole^{-1} [83]) is typical of diffusion-controlled reactions [84]. Both photosubstitutions obey the simple Stern–Volmer equation on the addition of quenching agents (sodium iodide), with superposition of the straight lines corresponding to the observed relations when conducted simultaneously as competing reactions. Together with the equality of activation energy and closely similar quantum efficiencies of photoamination and photochlorination, this suggests that the processes have the same mechanism and involve a single excited state, probably $n\pi^*$.[65,82]

On the postulate that only the $n\pi^*$ level of the substrate is reactive, the inactivity of anthraquinonesulphonic acids with strong electron-donating substituents in reactions involving the sulpho-group can be explained by inversion of the energy levels on introduction of a donor substituent into the anthraquinonesulphonate ring system, as a consequence of which the unreactive $\pi\pi^*$ state becomes the lowest excited state of the molecule.

Two hypotheses have been put forward on the nature of the interaction between an excited substrate molecule and the reactant. According to the first the photochemical step in photochlorination is formation of a chlorine radical by electron transfer from a chloride ion to an excited molecule of anthraquinonesulphonic acid [65] (the possibility of such a process has been proved—Section IV); subsequent replacement of the sulpho-group by chlorine occurs as a dark radical process [85] with formation of the corresponding chloroanthraquinone (ACl):

$$AS \xrightarrow{h\nu} AS^* ,$$

$$AS^* + Cl^- \rightarrow AS^{\cdot-} + Cl^{\cdot} ,$$

$$Cl^{\cdot} + AS \rightarrow ACl .$$

Another possible radical substitution path does not involve formation of a chlorine radical as a kinetically independent species. On formation of the complex of the chloride ion and an excited molecule of anthraquinonesulphonic acid, almost simultaneously with the act of electron transfer, the resulting chlorine radical is trapped in a solvent cage by a sulphonate molecule in the ground (or an excited) state:

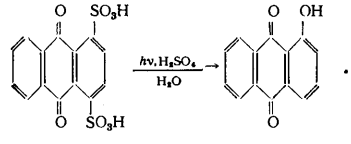
$$AS + \overset{\overset{AS}{+}}{Cl} \xrightarrow{h\nu} ([AS \ldots Cl^-]^*, AS, AS^*) \longrightarrow ACl .$$

The second possible mechanism of photochlorination is nucleophilic substitution (in the classical sense of intermediate formation of a σ-complex) of the sulpho-group by a chloride ion in a photoexcited molecule of anthraquinonesulphonic acid [65]:

$$Cl^- + AS^* \rightarrow ACl .$$

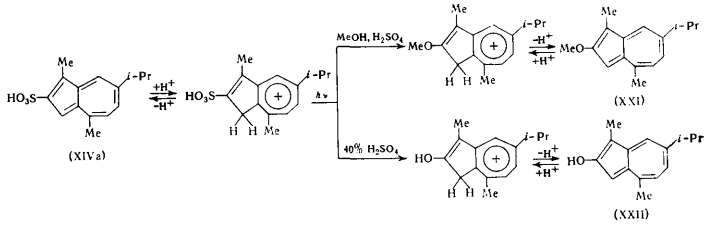
Analogous mechanisms may be suggested for the formation of aminoanthraquinones from anthraquinonesulphonic acids.

A sulpho-group in the anthraquinone ring system can sometimes be replaced photochemically by hydroxyl, as already noted. Whereas anthraquinone-1-sulphonic acid (XIa) yields only traces of 1-hydroxyanthraquinone (XVI), the latter is the main product (in 60% yield) of the photolysis of anthraquinone-1,4-disulphonic acid (XId) in 11 *N* sulphuric acid [74]:

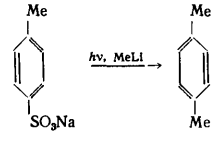


(XId) (XVI)

Considerably less study has been made of photosubstitution of the sulpho-group in systems other than anthraquinone. However, data have been published indicating that this group can be replaced also by hydroxyl, methoxyl, methyl, and the nitro-group. The first of these reactions occurs when guaiazulene-2-sulphonic acid (XIVa) is illuminated in 40% sulphuric acid, and the second on its photolysis in a mixture of methanol and sulphuric acid (3 : 2), with 40–50% yields [73]:

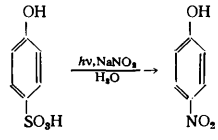


The action of light on sodium toluene-*p*-sulphonate (XXIII) in the presence of methyl-lithium gives a yield of *p*-xylene (XXIV) reaching 4.5% as a result of nucleophilic substitution:



(XXIII) (XXIV)

hardly any reaction occurs in the dark (yield <1%) [86]. Photosubstitution of the sulpho-group in phenol-*p*-sulphonic acid (XXV) gives a not very high yield (~4%) [87]:



(XXV) (XXVI)

Compounds $ArSO_2X$ other than sulphonic acids are able to undergo nucleophilic photosubstitution. This has been shown for derivatives of sulphanilic acid and related compounds, such as *p*-aminobenzenesulphonamide (XXVIIa), *p*-trifluoromethylsulphonylaniline (XXVIIb), and *p*-methylsulphonylaniline (XXVIIc) subjected to photolysis in aqueous

solutions containing cyanide, nitrite, and thiocyanate ions [87]:

$$p\text{-}NH_2C_6H_4SO_2X \xrightarrow[H_2O]{h\nu,Nu^-} p\text{-}NH_2C_6H_4Nu + PhNH_2$$
(XXVIIa-c) (XXVIII) (III)

X=NH_2 (a), CF_3 (b), CH_3 (c); Nu=CN, NO_2, SCN .

The action of the cyanide ion gives 60–65% yields of photosubstituted products from compounds (XXVIIa) and (XXVIIc), but only 12–15% from (XXVIIb) and benzenesulphonamide. Compounds (XXVIIa) and (XXVIIc) react less vigorously with the nitrite ion: yields of the corresponding nitro-compounds are 2–4%. A still lower yield is obtained from (XXVIIa) with sodium thiocyanate. The photoreaction of (XXVIIc) with sodium methoxide in methanol forms only traces of *p*-anisidine (XXIX), the main product being aniline (III):

$$p\text{-}NH_2C_6H_4SO_2Me \xrightarrow{h\nu,MeOH,MeONa} p\text{-}NH_2C_6H_4OMe + (III) .$$
(XXVIIc) (XXIX)

Attempts to replace the SO_2X group by a fluorine atom by exposing aqueous solutions of (XXVIIa) and (XXVIIc) containing fluoride ions were unsuccessful. The relative unreactivity of the fluoride ion in photosubstitutions was attributed [87] to its high redox potential.

In all cases of photolysis of the compounds (XXVIIa)–(XXVIIc) photoelimination of the SO_2X group, leading to formation of aniline, competes with photosubstitution. As with halogenobenzenes, the latter process itself is activated by electron-donor substituents in the aromatic ring. The relative immobility of the SO_2X group on reaction with the nitrite ion is due to the low energies of the singlet and triplet levels of the latter, so that it can act not only as a nucleophilic reagent but also as an acceptor of the energy of excitation of the substrate.

As with sulphonic acids (see e.g. the photolysis of benzelesulphonic acid in aqueous solution, above) substitution of the SO_2X group (X ≠ OH) may begin with homolytic cleavage of the Ar–S bond. Thus *SS*-dimethyl-*N*-arenesulphonylsulphoximines (XXX) on exposure in aromatic hydrocarbons to light of wavelength 254 nm generate radicals which arylate the solvent [88]:

$$ArSO_2N{=}\overset{\overset{O}{\uparrow}}{S}Me_2 \xrightarrow{h\nu,C_6H_6} [Ar^\cdot] \xrightarrow{C_6H_6} ArPh .$$
(XXX) (XXXI)

Diaryl sulphones (XXXII) behave similarly on photolysis in benzene. The processes involved can be represented by the scheme [89]

$$ArSO_2Ar \xrightarrow[C_6H_6]{h\nu\,(254\ nm)} Ar^\cdot + ArSO_2^\cdot ,$$
(XXXII)

$$Ar^\cdot + C_6H_6 \longrightarrow Ar\text{-}C_6H_6^\cdot ,$$

$$Ar\text{-}C_6H_6^\cdot + ArSO_2^\cdot \text{ or } Ar^\cdot \longrightarrow ArC_6H_5 + ArSO_2H \text{ or } ArH ,$$

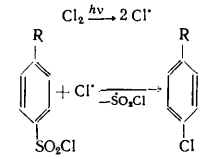
$$ArSO_2^\cdot + C_6H_6 \longrightarrow ArSO_2\text{-}C_6H_6^\cdot ,$$

$$ArSO_2\text{-}C_6H_6^\cdot + ArSO_2^\cdot \text{ or } Ar^\cdot \longrightarrow ArSO_2C_6H_5 + ArSO_2H \text{ or } ArH .$$

The suggested mechanism is supported by data on the distribution of carbon-14 in the products of photolysis of a labelled model compound—diphenyl sulphone [90].

Another type of radical photosubstitution of the SO_2X group is also possible, when the reagent—not the $ArSO_2X$ molecule—is excited, and forms radical species on photodissociation. This occurs when benzenesulphonyl and *p*-bromobenzenesulphonyl chlorides (XXXIIIa) and (XXXIIIb) in carbon tetrachloride containing excess of chlorine are exposed to the light from a tungsten lamp. The chlorosulphonyl group is replaced by a chlorine atom, and in (XXXIIIb) the bromine atom is also exchanged, the yields being 97% [91]:

$$Cl_2 \xrightarrow{h\nu} 2\,Cl^\cdot$$



(XXXIII a, b) (XXXIV a, b) .

$$^\cdot SO_2Cl \rightarrow SO_2 + {}^\cdot Cl$$

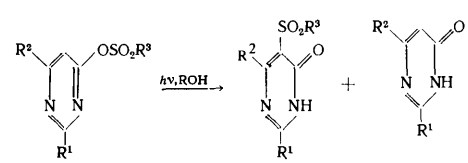
R=H (a), Br (b)

Phenyl and methyl benzenesulphonates do not undergo this reaction, but diphenyl sulphone (XXXV) gives a quantitative yield of chlorobenzene (XXXIVa) [91]:

$$Cl_2 \xrightarrow{h\nu} 2\,{}^\cdot Cl$$
$$PhSO_2Ph + {}^\cdot Cl \rightarrow PhCl + PhSO_2^\cdot$$
(XXXV) (XXXIVa)
$$PhSO_2^\cdot + Cl_2 \rightarrow PhSO_2Cl + {}^\cdot Cl$$
$$PhSO_2^\cdot \rightarrow Ph^\cdot + SO_2$$
$$Ph^\cdot + Cl_2 \rightarrow PhCl + {}^\cdot Cl$$
(XXXIVa) .

We have been discussing photochemical reactions of compounds $ArSO_2X$ in which the sulphur-containing group is either eliminated or replaced by another group, i.e. processes involving rupture of the Ar–S bond. These reactions have been most thoroughly investigated in the compounds considered. Nevertheless, we cannot disregard the considerably less studied but quite numerous photoprocesses of aromatic sulphonyl compounds $ArSO_2X$ in which the S–X bond is broken by the action of light, which leads to rearrangement or to stabilisation of the residue of the substrate molecule by interaction with the solvent (reagent).

Certain arenesulphonic esters [93,94] are arenesulphonamides [95] tend to undergo light-induced rearrangements like the Fries photorearrangement [92]. Thus exposure of 5-unsubstituted 2-dialkylaminopyrimid-4-yl arenesulphonates (XXXVI) in alcohols to the far ultraviolet (254 nm) converts them into 20–30% yields of the 5-arylsulphonyl-2-dialkylamino-4-hydroxypyrimidines (XXXVII) accompanied by small quantities of the 2-dialkylamino-4-hydroxypyrimidines (XXXVIII):

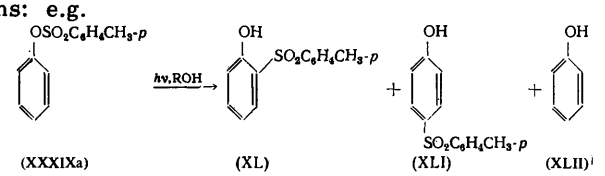


(XXXVI) (XXXVII) (XXXVIII)

R^1=NMe_2, morpholino, pyrrolidino, piperidino;
R^2 = H, Me; R^3=C_6H_5, *p*-MeC_6H_4, *p*-BrC_6H_4, *p*-ClC_6H_4, 2,5-$Me_2C_6H_3$

Phenyl and 1-naphthyl toluene-*p*-sulphonates (XXXIXa) and

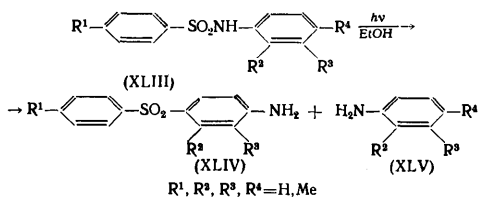
(XXXIXb) undergo photorearrangement under similar conditions: e.g.



(XXXIXa) (XL) (XLI) (XLII)

The reaction is assumed[96] to result from $\pi\pi^*$-excitation of the phenolic portion of the ester molecule.

Arenesulphonamides (XLIII) are converted photochemically into *p*-arylsulphonylarylamines (XLIV) in 6–25% yield and primary aromatic amines (XLV) in 25–70% yield:

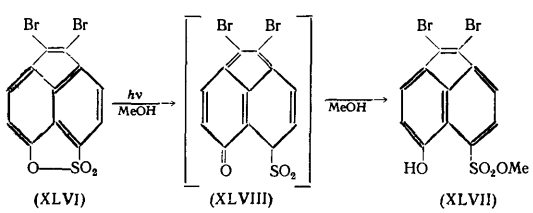


(XLIII) (XLIV) (XLV)

R^1, R^2, R^3, R^4=H, Me

The relatively low yields of rearranged products are explained[95] by filtration of the light by the resulting sulphones (XLIV) and by unidentified coloured by-products of the reaction.

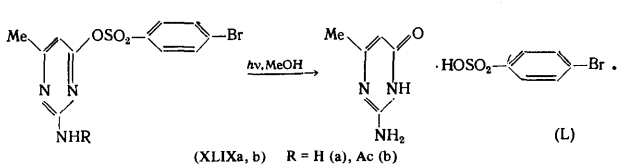
The acenaphthene sultone (XLVI), on illumination in methanol through a Pyrex filter, is converted into the corresponding methyl sulphonate (XLVII)[97] with intermediate formation of the sulphene (XLVIII):



(XLVI) (XLVIII) (XLVII)

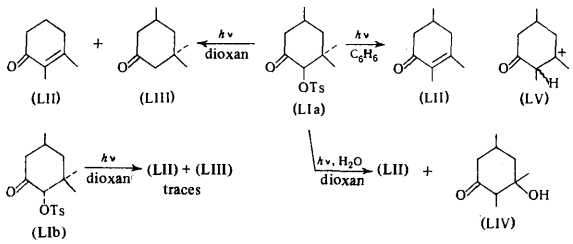
A singlet excited state of (XLVI) is assumed to take part in the photoreaction, but no strict proof of this is given.

In several cases light detaches the ester group from arenesulphonates, e.g. from 2-aminopyrimid-4-yl and 2-acetamidopyrimid-4-yl *p*-bromobenzenesulphonates (XLIXa) and (XLIXb) in ethanol. Instead of rearrangement (see above) a salt (L) of 2-amino-4-hydroxypyrimidine and the sulphonic acid is formed[93]:



(XLIXa, b) R = H (a), Ac (b) (L)

Photoelimination occurs stereospecifically in the case of oxocycloalkyl toluene-*p*-sulphonates[98]. Thus exposure of the *cis*-isomer (LIa) in benzene forms an unsaturated ketone (LII), in dioxan a mixture (4 : 1) of (LII) and (LIII), and in aqueous dioxan the ketone (LII) and the β-hydroxy-ketone (LIV); the *trans*-isomer (LIb) in more stable, forming small quantities of the ketones (LII) and (LIII) (1 : 1) only on prolonged photolysis:



(LII) (LIII) (LIa) (LII) (LV)

(LIb) (LII) + (LIII) traces (LII) + (LIV)

Photoreaction evidently requires a sterically accessible conformation of the carbonyl group and the $C_{(\alpha)}$–O bond, which is present in the ester (LIa) but not in its isomer (LIb). The $n\pi^*$ state of these ketones is regarded as reactive. Formation of the αβ-unsaturated ketone (LII) is explained by production of the cation (LV) by heterolytic cleavage of the C–O bond followed by migration of a methyl group and deprotonation of the cation[98].

In contrast to the long known de-O-tosylation of toluene-*p*-sulphonates of sugars by catalytic reduction, it has recently been suggested that this should be effected photochemically in methanolic sodium methoxide (in an inert gas)[99]. The corresponding sugars are formed in yields of 90% or more and, what is especially important, the photoreaction is not complicated by secondary processes, as occurs in the dark reaction.

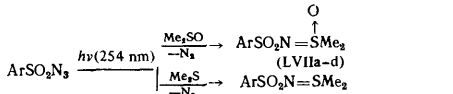
Photochemical cleavage of the sulphur–nitrogen bond (–SO_2NH–) in sulphonylated amino-acids and peptides might also have found practical application[100]. Unfortunately, however, the yields are not yet high enough for this photoreaction to be a serious competitor to the deblocking of tosylated amino-acids achieved in dark chemistry. This is due to the secondary processes of photodecarboxylation and photodeamination, and also to the photodegradation of certain unstable amino-acids (e.g. tryptophan).

We conclude this Section by considering photoreactions of aromatic sulphonyl compounds that do not affect the Ar–S and S–X bonds but involve cleavage of bonds in the X fragment of the molecule. Considerable interest has been taken in reactions of sulphonyl azides, which resemble aryl azides in photochemical behaviour, also being capable of breaking down with evolution of molecular nitrogen and formation of nitrenes—isoelectronic analogues of carbenes—on exposure to light. Like the latter, nitrenes are able to exist in singlet and triplet states $ArSO_2\ddot{N}$ and $ArSO_2\ddot{N}\cdot$. Electron spin resonance investigations have shown that the photolysis of benzenesulphonyl and toluene-*p*-sulphonyl azides (LVIa) and (LVIb) in matrices[101–103] at 77 °C yields the corresponding nitrenes in a triplet ground or excited state (the latter readily attainable by thermal activation).

The photochemical reactions of arenesulphonyl azides are usually regarded as those in which the photolytically generated nitrene undergoes rearrangement or else interacts with the solvent or the reagent. However, a critical attitude has recently been adopted towards this approach, on the assumption that in certain processes elimination of nitrogen is not the primary step (see below). The photolysis of sulphonyl azides in aprotic solvents (benzene, cyclohexane, thiophen, pyridine, etc.) usually yields insoluble resinous or polymeric products; intermediate formation of nitrenes is almost impossible to demonstrate[104,105].

Exposure of arenesulphonyl azides (LVIa–d) in dimethyl

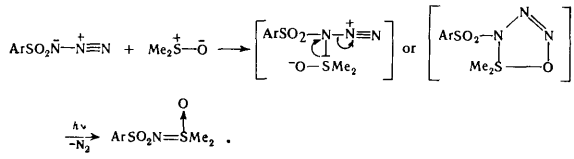
sulphoxide and in dimethyl sulphide produces *N*-sulphonylsulphoximines (LVIIa–d) (15–50%) and *N*-sulphonylsulphidimines (LVIIIa–d) (48–55%) respectively [104]:



(LVIa–d) (LVIIa–d) (LVIIIa–d)

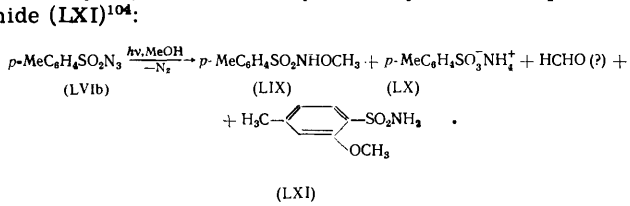
Ar=C_6H_5 (a), *p*-MeC_6H_4 (b), *p*-$NO_2C_6H_4$ (c), *p*-$MeOC_6H_4$ (d).

Whereas a mechanism of intermediate formation of nitrenes is alone assumed for the reaction with dimethyl sulphide, dimethyl sulphoxide also offers the possibility of complex formation between sulphonyl azides and the solvent (DMSO) acting as an electrophile, with expulsion of a nitrogen molecule on excitation of the complex:



The readily occurring photoreactions of sulphonyl azides in alcohols yield various compounds, which can be regarded formally as products of the insertion of nitrenes in the alcohol molecules, reduction of the nitrenes by detachment of a hydrogen atom, and the Curtius rearrangement [104–106]. It is especially difficult to determine in these photoreactions whether or not nitrenes are formed as intermediates.

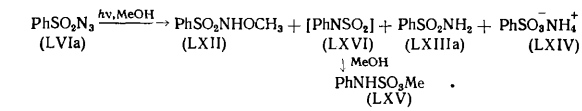
The photolysis of toluene-*p*-sulphonyl azide (LVIb) in methanol gives a 44% yield of O-methyl-*N*-toluene-*p*-sulphonylhydroxylamine (LIX) and small quantities of ammonium toluene-*p*-sulphonate (LX), a volatile substance (probably formaldehyde), and 2-methoxy-4-methylbenzenesulphonamide (LXI)[104]:



(LVIb) (LIX) (LX) (LXI)

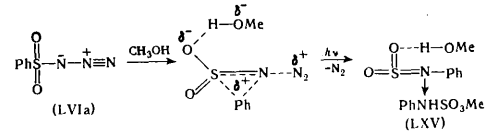
This process has an induction period: evolution of nitrogen begins after fairly long illumination of the reaction solution. If the solution is kept in the dark, however, reaction begins from the moment of exposure.

A more rigorous investigation of this reaction on benzenesulphonyl azide (LVIa) showed [105,107] that methyl *N*-phenylsulphamate (LXV) is formed together with the compounds (LXII)–(LXIV) (in yields respectively of 15, 4.5, and 8%):



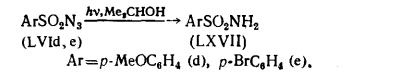
(LVIa) (LXII) (LXVI) (LXIIIa) (LXIV) (LXV)

Compound (LXV) can be assumed to result from rearrangement of the corresponding nitrene into *N*-sulphurylaniline (LXVI) followed by reaction with methanol. An alternative mechanism suggested involves protonation of the initial sulphonyl azide (formation of a hydrogen bond) and the photoinduced concerted rearrangement of such reactive complex with loss of a nitrogen molecule:



(LVIa) (LXV)

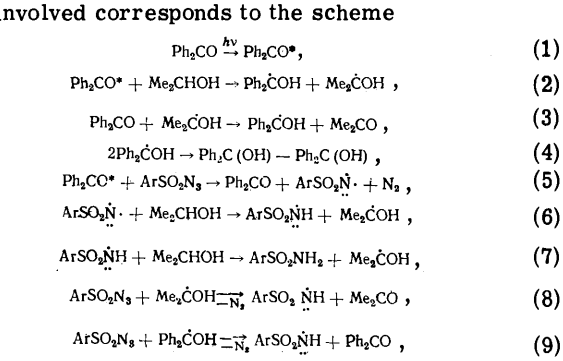
The photolysis of arenesulphonyl azides (LVId) and (LVIe) in propan-2-ol (excited by 254 or 365 nm in the presence of a sensitiser—benzophenone), in contrast to the above processes, gives only the corresponding arenesulphonamides (LXVII) in 85–95% yield [106]:



(LVId, e) (LXVII)

Ar=*p*-$MeOC_6H_4$ (d), *p*-BrC_6H_4 (e).

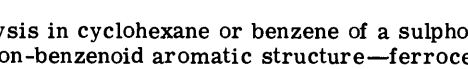
In this case detachment of a hydrogen atom predominates substantially over rearrangement, perhaps becuase of the greater mobility of the hydrogen atom attached to the carbinol carbon of the secondary alcohol. The radical-chain process involved corresponds to the scheme



(1)–(9)

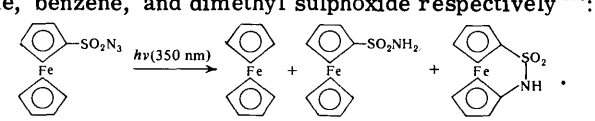
with the possible exclusion of Eqn. (2) or Eqns. (5) and (6).

Free-radical decomposition takes place also in the photolysis of benzenesulphonyl azide (LVIa) in benzenethiol, when benzenesulphonamide (LXIIIa) and diphenyl disulphide (LXVIII) are obtained [108]:



(LVIa) (LXIIIa) (LXVIII)

Photolysis in cyclohexane or benzene of a sulphonyl azide of non-benzenoid aromatic structure—ferrocenesulphonyl azide (LXIX)—results in ferrocene (LXX), ferrocenesulphonamide (LXXI), and a cyclisation product (LXXII), the last in yields of 13.3%, 67%, and 0 in cyclohexane, benzene, and dimethyl sulphoxide respectively [109]:

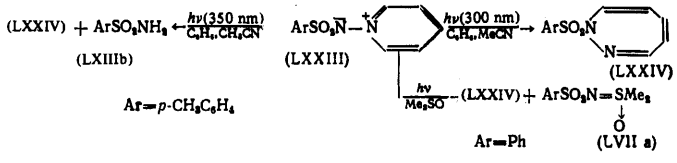


(LXIX) (LXX) (LXXI) (LXXII)

Formation of the free nitrene is postulated [109] on photolysis; cyclisation is probably a singlet reaction, since the yield of (LXXII) is not diminished by the presence of oxygen or quinol.

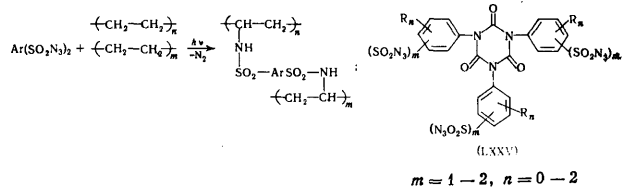
Formation of nitrenes was expected also when pyridinium ylids (LXXIII) were eliminated [110]. However, photolysis of the ylid (LXXIII: Ar = C_6H_5) in a mixture of benzene and acetonitrile by filtered radiation of wavelength 300 nm gave the compound (LXXIV) in 76% yield; compounds

which might have been formed from nitrenes (benzenesulphonamide, *N*-phenylsulphonylazepine) were not detected; in dimethyl sulphoxide the yield of (LXXIV) falls to 12%, and the sulphoximine (LVIIa) is formed in 40% yield:



Photolysis of the ylid (LXXIII: Ar = *p*-$CH_3C_6H_4$) by wavelength 350 nm resulted in low yields of the diazepine (LXXIV: Ar = *p*-$CH_3C_6H_4$) and toluene-*p*-sulphonamide (LXIIIb) (2:1). Thus under certain conditions of photolysis the stable pyridinium ylids of type (LXXIII) are able to produce sulphonylnitrenes.

We note in conclusion the practical value of sulphonyl azides as cross-linking agents for several polymeric materials. This exploits the property exhibited by sulphonylnitrenes formed on exposure of entering into carbon-hydrogen and oxygen–hydrogen bonds: e.g.



Several di- and poly-sulphonyl azides, in particular tris-azidosulphonylphenylhexahydrotrioxo-1,2,5-triazines (LXXV), find application in photographic resins [111-113].

IV. PHOTOREACTIONS NOT INVOLVING THE SO_2X SUBSTITUENT

The chief reactions of this type involve photoreduction of the carbonyl group in compounds containing an SO_2X substituent. The most thoroughly studied among them are the photochemical dehydrogenation of organic compounds by anthraquinonesulphonic acids and the oxidation by the latter of inorganic anions. An impetus to such interest in the photodehydrogenating power of anthraquinone and its sulphonic acids was provided by research on the photodegradation of natural and artificial fibres sensitised by anthraquinone vat dyes [114-126].

The mechanism of the photodehydrogenation of alcohols, which has been studied in detail, is at present regarded as

$$AS \xrightarrow{h\nu} AS^*$$

$$AS^* + R^1R^2CHOH \rightarrow ASH^{\cdot} + R^1R^2\dot{C}OH$$

$$R^1R^2\dot{C}OH + AS \rightarrow R^1R^2CO + ASH^{\cdot} \qquad ASH^{\cdot} + O_2 \rightarrow AS + HO_2^{\cdot}$$

$$2\,ASH^{\cdot} \rightarrow AS + ASH_2 \qquad R^1R^2\dot{C}OH + O_2 \rightarrow R^1R^2CO + HO_2^{\cdot}$$

$$ASH_2 + O_2 \rightarrow H_2O_2 + AS$$

$$2\,HO_2^{\cdot} \rightarrow H_2O_2 + O_2\,.$$

absent oxygen present

The hydrogen atom is abstracted from the carbinol carbon atom by an excited anthraquinonesulphonate molecule (AS*) with formation of the semiquinone (ASH$^{\cdot}$) and the radical $^{\cdot}CR^1R^2OH$. A second hydrogen atom is detached, from the hydroxy-group of the radical, this time by an unexcited substrate molecule (AS), with formation of a second semiquinone molecule (ASH$^{\cdot}$) (per light quantum absorbed) and the ketone or aldehyde respectively. The product of complete reduction of the quinone (AS)—the anthraquinolsulphonic acid (ASH_2)—is obtained by disproportionation of the semiquinones (ASH$^{\cdot}$). If oxygen is present in the reaction mixture, it oxidises the semiquinone (ASH$^{\cdot}$) and the anthraquinol (ASH_2) to the initial quinone (AS), so that the final reaction products are in effect only the ketone or aldehyde. For this reason the process has been termed a "photosensitised oxidation of alcohols". It can quite rightly be termed also "photocatalytic" or—more correctly, in the Reviewers' opinion— a "chemically sensitised process", since the role of the quinone is not to transfer energy to the carbinol radical but, as an excited molecule, to interact chemically with the alcohol.

Table 1. Ratio of rate constant of detachment of a hydrogen atom to rate constant of all other processes effecting deactivation of excited states of anthraquinone-2-sulphonate k_1/k_0 during photodehydrogenation [116,117].

Compound to be dehydrogenated	k_1/k_0	Compound to be dehydrogenated	k_1/k_0
Methanol	0.054	Ethane-1,2-diol	0.258
Ethanol	0.445	Propane-1,2-diol	0.56
Propan-1-ol	0.682	Propane-1,2,3-triol	0.374
Propan-2-ol	0.921	Cyclohexanol	2.31
Butan-1-ol	0.952	Diethyl ether	2.14
Butan-2-ol	1.270	Di-isopropyl ether	1.80
2-Methylpropan-2-ol	0.01	Acetone	0

Besides alcohols (monohydric and polyhydric), ethers and ketones can also be photodehydrogenated by sulphonated anthraquinones. The comparative reactivities of all these compounds towards photodehydrogenation has been studied [116,117] as the ratio of the photodehydrogenation rate constant to the total rate constant of the other processes by which the excited state of the substrate is deactivated (Table 1). The reactivity of alcohols towards photodehydrogenation by anthraquinone-2-sulphonic acid (XII) increases with the length and the degree of branching of the hydrocarbon chain, which is attributed to increasing mobility of the hydrogen atom attached to the carbinol carbon atom resulting from increase of the positive inductive effect of the alkyl group in the alcohol molecule [116]. The absolute rate constants of detachment of the hydrogen atom from certain alcohols, measured by flash photolysis, are around $10^6\ M^{-1}\ s^{-1}$. [120,127]

The above reactivity sequence of alcohols towards photodehydrogenation by anthraquinone-2-sulphonic acid (XII) indicates that the primary photochemical step consists in detachment of a hydrogen atom, not in transfer of an electron. An energetic assessment of photodehydrogenation leads to the same conclusion, showing that energies of excitation of anthraquinonesulphonic acids are insufficient to abstract an electron from an alcohol molecule [127]. The above results apply to alcoholic or neutral aqueous–alcoholic solution. In alkaline aqueous–alcoholic media and in alcoholic solutions of the corresponding sodium alkoxide, however, electron transfer from the alkoxide ion to the excited sulphonic acid

$$AS^* + RO^- \rightarrow AS^{\cdot-} + RO^{\cdot}$$

predominates. The possibility of this process has been confirmed [128,129] by a detailed study of the photoreduction

of sulphonated anthraquinones by electronic and electron spin resonance (e.s.r.) spectroscopy.

In ethers a hydrogen atom is abstracted from a carbon atom forming the ether bond. Increase in the length and the degree of branching of the alkyl groups diminishes the reactivity of the ether owing to the shielding effect [117].

The simplest ketone (acetone) shows little tendency to undergo photo-oxidation by anthraquinonesulphonic acids, but the rate of the process is substantially larger in alkaline aqueous solutions. This can be attributed either to reaction of acetone as the enolic form [117] $CH_3.CH(OH):CH_2$ or to involvement of the hydroxide ion in the reaction (see below).

Alcohols (and other organic compounds) undergo considerably less photo-oxidation in the presence of 1-sulphonates than of 2-sulphonates of anthraquinone (Table 2), so that less study has been made of the behaviour of the 1-isomers in this process. Thus the introduction of a sulpho-group into the anthraquinone molecule, which might be expected to influence only the solubility in organic and aqueous media, leads to substantial differences in the photodehydrogenating power of the quinonoid group depending on the position of the sulpho-group.

Table 2. Quantum efficiencies of the formation of anthraquinole in the photodehydrogenation of propan-2-ol [122].

Sulphonated anthraquinone	Quantum efficiency	Solvent
Anthraquinone	0.81	benzene–propan-2-ol (4 : 1)
2-Sulphonated	1.06	propan-2-ol
2,6-Disulphonated	1.07	
2,7-Disulphonated	1.14	
1-Sulphonated	0.05	
1,5-Disulphonated	0.015	

For a long time the spectral sensitivity of the photoreduction of anthraquinone and its sulpho-derivatives remained an unsolved problem. Investigation of anthraquinone-1-sulphonic acids in alkaline aqueous–alcoholic solutions merely showed [128] that the quantum efficiency of photoreduction was the same throughout the range of absorption of the substrate, whence it may be concluded that conversion to a reactive state with higher energy levels takes place with equal probability.

The involvement of the triplet state of anthraquinone [122] and its sulphonated derivatives [127] in the photodehydrogenation of alcohols has been shown by triplet–triplet energy transfer. Not only the 2-sulphonates, which actively dehydrogenate alcohols, but also the less active 1-isomers take part in this process in an excited triplet state [126]. Of the two possible triplet states of anthraquinones only the $n\pi^*$ state possesses dehydrogenating power, when excitation is localised in a carbonyl group, and a hydrogen atom may be abstracted by a radical-like oxygen atom. The $T_{\pi\pi^*}$ state of the substrate, characterised by delocalisation of the excitation energy in the π-electron system of the molecule, is inactive in these processes. Such an approach makes it obvious that substances in which the lowest triple level is an $n\pi^*$ level are good acceptors of hydrogen [130,131]. With compounds which hardly dehydrogenate alcohols at all—hydroxy- and amino-anthraquinones (and also anthraquinonesulphonic acids containing these electron-donor groups)—the energy levels are inverted, and the unreactive $T_{\pi\pi^*}$ state becomes the lowest [55]. Certain authors attribute the low reactivity of anthraquinone-1-sulphonates (compared with the 2-isomers) in photodehydrogenation to the low probability of the interconversion $S \rightarrow T$: with the 2-sulpho-derivatives this probability is approximately unity [132].

Anthraquinonesulphonic acids can be reduced photochemically not only by organic compounds but also by inorganic anions, e.g. hydroxide ions [133–137]. The reaction entails in effect the transfer of an electron from the ion to an excited acid molecule with formation of a hydroxyl radical and a radical-anion ($AS^{\cdot -}$), the latter being fairly stable in alkaline media. These radical-anions have been recorded by e.s.r. [133] (for the structure of the spectra see Ref. 124) and by electronic [137] spectroscopy. Use of these methods to study the kinetics of formation of the radical-ions as a function of the hydroxide-ion concentration confirmed [133,137] that the hydroxide ion—not a water molecule, as postulated previously [135]—is actually the electron donor:

$$AS^* + {}^-OH \rightarrow AS^{\dot{-}} + {}^{\cdot}OH \ .$$

The radical-ions ($AS^{\cdot -}$) interact vigorously with oxygen

$$AS^{\dot{-}} + O_2 \rightarrow AS + O_2^{\dot{-}},$$

with a rate constant $k = \simeq 10^8\ M^{-1}\ s^{-1}$. Hence accumulation of these radical-ions is observed only in deaerated media [121].

Alkaline solutions contain hardly any semiquinone ($ASH^{\cdot}$)—the protonated form of the radical-anion ($AS^{\cdot -}$)—since the pK is small (e.g. 2.3–3.2 for the radical-anion obtained from anthraquinone-2,6-disulphonic acid [127,138]). In contrast to the semiquinone, whose disproportionation rate constant lies in the range 10^8–$10^9\ M^{-1}\ s^{-1}$, the ionised form ($AS^{\cdot -}$) disproportionates far more slowly ($k_{dispr} < 10^2\ M^{-1}\ s^{-1}$) [127]. In alkaline solutions, therefore, the equilibrium

$$2AS^{\dot{-}} \rightleftarrows AS^- + AS$$

is displaced to the left, which enables a nearly quantitative yield of the radical-anions to be obtained.

The formation of hydroxyl radicals in these reactions could not be detected by physical methods, because of their great reactivity and the frequent ambiguity of their identification by characteristic reactions [136]. Direct evidence of the photochemical generation of hydroxyl radicals in alkaline aqueous solutions of anthraquinonesulphonic acids was the detection of $CO_3^{\dot{-}}$ radical-anions in the reaction mixtures on illumination by flash photolysis in the presence of added carbonate ions. This radical-ion is formed by the interaction of a hydroxyl radical and a carbonate ion [134]:

$$HO^{\cdot} + CO_3^{2-} \rightarrow HO^- + CO_3^{\dot{-}} \ .$$

The Stern–Volmer relation gave the value $k_T\tau \simeq 2000$–$3000\ M^{-1}$ for the photoreaction of the hydroxyl ion with anthraquinone-2,6-disulphonic acid (quenched by iodide, thiocyanate, thiosulphate, and hexacyanoferrate(II) ions) [132]. From this it was found that the lifetime of the reactive state of the substrate lay within the limits $\tau = 10^{-7}$–10^{-5} s depending on the value of $k_T = 10^8$–$10^{10}\ M^{-1}\ s^{-1}$ used in the calculations. Such a lifetime is more typical of a T than of an S state, from which it was concluded that a triplet state of the anthraquinonesulphonates is active in the present process as in photodehydrogenation. Flash photolysis has since been used to record the triplet states of anthraquinone-2-sulphonates and determine their absorption spectra (λ_{max} = 480–500 nm). Their deactivation

obeys a first-order kinetic equation (k_{des} = 34 000 s^{-1} for anthraquinone-2,6-disulphonic acid at pH 6.5). Deactivation is accelerated considerably by the presence of an acceptor of triplet energy (e.g. anthracene-1-sulphonic acid) because of efficient energy transfer. A similar effect is produced by the introduction of electron donors (hydroxide and carbonate ions): the rate constants of their reaction with excited anthraquinone-2,6-disulphonic acid are respectively 7.1×10^6 and 1.8×10^6 M^{-1} s^{-1}. These results finally confirmed that a triplet state of anthraquinone-2-sulphonic acids was involved in electron transfer [127].

The quantum efficiencies of the photoreduction of various anthraquinone derivatives have been compared for the photoreaction with the carbonate ion [127]. Efficiencies of around unit are obtained with mono- and di-sulphonic acids containing a 2-sulpho-group; with anthraquinone-1-sulphonic acid and hydroxyanthraquinones the quantum efficiencies are respectively 0.32 and 0. Hence compounds whose lowest triplet level is an $n\pi^*$ level are active in processes involving the phototransfer of an electron, as in photodehydrogenation.

The fairly high quantum efficiencies of photoreduction of the anthraquinone-1-sulphonate (XIa) by the carbonate ion in aqueous solution [127] and the limiting quantum efficiency of its photoreduction in a methanolic solution of sodium methoxide (Φ_{lim} = 0.40 [129]) indicate that in these cases $\Phi_{ST} \geqslant 0.3$ for 1-sulphoanthraquinone. Thus the above hypothesis, that the low reactivity of anthraquinone-1-sulphonic acids towards photodehydrogenation is due solely to the extraordinarily low probability of their occupying a triplet level, must be regarded as questionable. However, data are still lacking that would enable us to find the true reason for the low photodehydrogenating activity of anthraquinone-1-sulphonic acids in comparison with the 2-isomers.

Excited anthraquinonesulphonic acids are photoreduced not only by hydroxide and carbonate ions but also by chloride, sulphate, and thiocyanate ions. They are not reduced by fluoride, chlorate, metabisulphite, and bromate ions. This sequence has enabled the redox potential of the $AS_{T,n\pi^*}/AS^{\cdot -}$ pair to be estimated: it lies between those of the pairs $Cl^{\cdot}/Cl^-$ and $F^{\cdot}/F^-$ (2.55 and 3.6 eV) [127].

Radical-anions of sulphonated anthraquinones are formed in low yields on flash photolysis in neutral aqueous solutions containing bromide or iodide ions. Two competing processes—electron transfer and physical quenching—are assumed to occur in the exciplex of the halide ion and the sulphoanthraquinone molecule in an excited triplet state:

$$AS \xrightarrow{h\nu} AS^* \xrightarrow{X^{-n}} [AS \ldots X^{-n}]^* ,$$
$$X^{-n} + AS \xleftarrow{k_r} [AS \ldots X^{-n}]^* \xrightarrow{k_p} \dot{X}^{-(n-1)} + AS^{\cdot -} ,$$

where $k_T \gg k_P$ for iodide and bromide ions, but $k_P \gg k_T$ for carbonate, sulphate, and other ions [127].

However, the above scheme probably does not fully represent the processes occurring in the reaction system. Thus a study of the photoreduction of sulphonated anthraquinones in alkaline aqueous and aqueous–alcoholic solutions revealed regularities that cannot be explained by this scheme. Whereas with iodide ions the slowing down of the reaction conforms closely with simple Stern–Volmer equation, with chloride and bromide ions such conformity is observed only at low concentrations, and increase in the chloride-ion concentration is accompanied by an increase in reaction velocity right up to the original rate in the absence of quenching anions. These facts were explained on the hypothesis [129] that chloride ions are able to form a fairly stable charge-transfer complex with the unexcited anthraquinonesulphonic acid. Absorption of light by the complex leads to the appearance of radical-anions of the sulphonated anthraquinone. Quenching, however, occurs by interaction of a chloride ion with an excited anthraquinonesulphonate molecule:

$$AS_{fr.} + Hal^- \rightleftarrows [AS \ldots Hal^-] ,$$
$$AS_{fr.} \xrightarrow{h\nu} AS^*_{fr.} ,$$
$$AS^*_{fr.} \rightarrow AS_{fr.}$$
$$AS^*_{fr.} + Hal^- \rightarrow AS^{\cdot -} + Hal^{\cdot} ,$$
$$AS^*_{fr.} + X^- \rightarrow AS^{\cdot -} + X^{\cdot} ,$$
$$[AS \ldots Hal^-] \xrightarrow{h\nu} [AS \ldots Hal^-]^* ,$$
$$[AS \ldots Hal^-]^* \rightarrow [AS \ldots Hal^-] ,$$
$$[AS \ldots Hal^-]^* \rightarrow AS^{\cdot -} + Hal^{\cdot}$$
$$X = OH, OAlk .$$

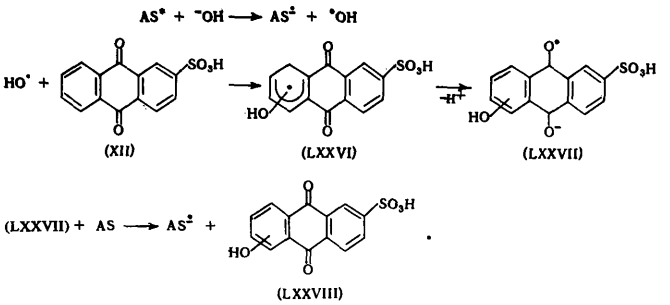
Calculation based on the kinetic scheme of photoreduction taking into account the above assumptions provides a qualitative explanation of the observed regularities [129].

The forward (photochemical) electron-transfer reaction is always accompanied by the reverse (dark) reaction of radical-anions of sulphonated anthraquinones with products of the one-electron oxidation of inorganic ions. In some cases the rate constants of such reverse reactions are extremely large: e.g. $k = 10^9$ M^{-1} s^{-1} for the reaction [127]

$$AS^{\cdot -} + CO_3^{\cdot -} \rightarrow AS + CO_3^{2-}$$

The disappearance of $CO_3^{\cdot -}$ radical-ions after the flash is due solely to the above process, since they hardly interact at all among themselves or with the initial anthraquinonesulphonic acids. Under steady illumination their yield in solutions containing carbonate ions will be extremely small (even if the reaction is conducted under conditions such that the radical-anions ($AS^{\cdot -}$) are stable, i.e. do not disproportionate).

Sometimes the reverse reaction is comparatively slow, and the photochemical electron transfers from anions to excited sulphoanthraquinone molecules are then accompanied by secondary dark processes. This occurs in the photo-oxidation of hydroxide ions, for example, when the resulting hydroxyl radicals interact mainly with the initial sulphonated anthraquinone [137]. The hydroxyl radical is weakly electrophilic [139], so that it enters only the unsulphonated ring [132]. This gives the adduct (LXXVI) or the radical-anion (LXXVII), which are oxidised by the original quinone (AS) to the corresponding hydroxyanthraquinonesulphonates (LXXVIII):



Hydroxylation actually takes place by a radical mechanism, which is confirmed by the diminished yield of hydroxy-derivatives (LXXVIII) on the introduction of acceptors of hydroxyl radicals into the reaction mass and by the fact that the same compounds are obtained by the action of Fenton's

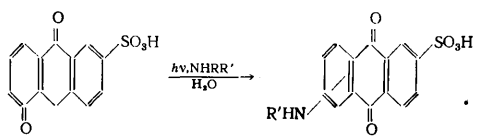
reagent on anthraquinonesulphonates as by the photochemical reaction[135,136].

The position entered by the hydroxy-group depends on the pH: at pH = 7–12 the main products of the photoreaction are 6- and 7-hydroxyanthraquinone-2-sulphonates, and these are the sole products at pH > 12; in neutral solutions hydroxylation occurs both at positions 6 and 7 and at positions 5 and 8.[136,139] Since hydroxyl radicals are able to undergo the dissociation

$$\cdot OH \rightleftarrows O^{\cdot -} + H^+,$$

with pK = 11.9,[140] the formation of different products is probably due to different hydroxylating agents according to the pH—the hydroxyl radical in neutral and weakly alkaline media and the oxide radical-anion $O^{\cdot -}$ in strongly alkaline media. All these assumptions require experimental confirmation, of course, but nevertheless the selective addition of such active radicals as these is a noteworthy fact.

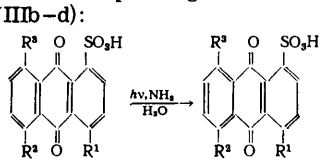
Not only anthraquinonesulphonates but also other compounds added to the solutions to be illuminated can be hydroxylated in this way. For example, phenol was obtained on the addition of benzene, which was also evidence of the formation of a hydroxyl radical in the photoreaction of the hydroxide ion with anthraquinonesulphonic acid[134]. When photohydroxylation takes place in the presence of an oxidant (molecular oxygen or potassium hexacyanoferrate(III)[133], the oxidation of hydroxide ions to hydroxyl radicals will be a cyclic process, so that the reaction may evidently be of value for the preparation of aromatic hydroxy-derivatives, especially as under certain conditions addition of a hydroxyl radical is a directed process. The photolysis of aqueous–ammoniacal solutions of anthraquinone-2-sulphonic acids probably resembles photohydroxylation. The 2-sulphonic acid (XII) forms amino-, diamino-, and amino-hydroxy-derivatives (principally 6(or 7)-aminoanthraquinone-2-sulphonates (LXXIX: R′ = H)): i.e. as in the preceding process, the unsulphonated ring undergoes substitution (amination). Photolysis of an aqueous solution of the sulphonated quinone (XII) in the presence of hydrazine (which breaks down into amino-radicals on exposure to ultraviolet radiation[141]) yields the same aminoanthraquinonesulphonic acids (LXXIX: R′ = H) as does photolysis in the presence of ammonia. The photochemical reaction of methylamine with anthraquinone-2-sulphonic acid (XII) gives the methylamino-derivatives (LXXXIX: R′ = CH_3)[142]:



(XII) (LXXIX)

R = H, NH_2; R′ = H, CH_3

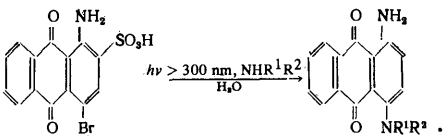
Not only hydrogen but also halogen can be replaced by an amino(or alkylamino)-group. Thus the photolysis of chloroanthraquinonesulphonic acids (XIe–g) in aqueous ammonia yields the corresponding aminoanthraquinonesulphonic acids (XVIIIb–d):



(XIe–g) (XVIIIb–d)

(XI : R^1, R^2, R^3 = H, Cl) (XVIII : R^1, R^2, R^3 = H, NH_2)

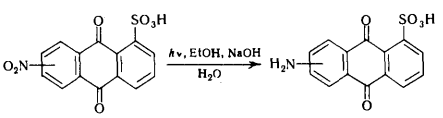
Although the yields are smaller (up to 6%), they are comparable with those of the simultaneously formed aminochloroanthraquinones (Section III)[74]. Bromine in the aminobromo-sulphonic acid (LXXX) is exchanged considerably better (probably because of the activating effect of the donor substituent). The process is conducted in aqueous solution; additions of aliphatic alcohols, dioxan, or acetonitrile increase significantly the yield of substitution products (LXXXI), which varies between 10% and 55%. Necessary conditions for the reaction are exposure to light of wavelength exceeding 300 nm and the presence of an oxidant (air or Fe^{3+} ions): only photodecomposition of the sulphonic acid (LXXX) takes place if these conditions are disrupted[143]:



(LXXX) (LXXXI)

R^1R^2NH=NH_3, $MeNH_2$ $EtNH_2$, $PrNH_2$, $BuNH_2$, piperidine

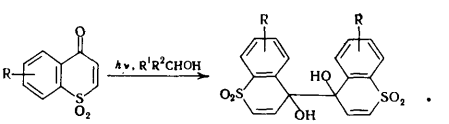
An amino-group can be formed also by photochemical reduction of a nitro-group. An attempt to effect the photodesulphonation of 5- and 8-nitroanthraquinone-1-sulphonic acids (XIl) and (XIm) in alkaline aqueous–ethanolic solution gave only a low yield (<5%) of the aminoanthraquinonesulphonic acids (XVIIIb) and (XVIIIc)[74]:



(XII, m) (XVIIIb, c)

Reduction of the nitro-group accompanied by loss of capacity for photodesulphonation is evidently due to the fact that the lowest reactive excited state of nitroanthraquinonesulphonic acids is the $T_{n\pi^*}$ level of the nitro-group, which is responsible for its photoreduction.

An example of photoreactions of non-quinonoid aromatic sulphonyl compounds that do not involve the SO_2X group is the photoreduction of 4-oxothiachroman 1,1-dioxides (LXXXII) in alcohols, when the yields of the pinacols (LXXXIII) reach 30%:



(LXXXII) (LXXXIII)

The electronic effect of the substituent is assumed to have little effect on the course of the process, with steric factors playing a considerably larger role[96].

The above account shows that the photochemistry of aromatic sulphonyl compounds is at present in an initial state of development. Future investigations of their photochemical reactions will undoubtedly provide answers to the problems examined in the present Review and to many others of importance not only for the present group of compounds but also for organic photochemistry in general.

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Paramagnetic Reagents for the Investigation of the Structures of Organic Ligands

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This review illustrates the effectiveness of the methods for the investigation of the structures of organic ligands based on the characteristics of the NMR spectra of paramagnetic complexes.
The bibliography includes 109 references.

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1. Complexes of elements in the first transition group
2. Lanthanide complexes

I. INTRODUCTION

Despite the fact that the first study on nuclear magnetic resonance (NMR) in paramagnetic systems was published in 1949,[1] the most fruitful investigations in this field were made in the last ten years concurrently with general progress in the technique of NMR spectroscopy. Studies carried out outside the Soviet Union by McConnell, Eaton, and others and in the Soviet Union by Molin and coworkers significantly extended our ideas concerning the mechanism of the electronic-nuclear (hyperfine) interaction in paramagnetic systems. Moreover, studies published in 1968 to 1972 showed that the specific features of the NMR of paramagnetic complexes can be used successfully to investigate the structures of organic ligands.

II. NUCLEAR MAGNETIC RESONANCE IN PARAMAGNETIC SYSTEMS

The use of NMR for the investigation of the electronic and geometrical structures of organic ligands is based on the characteristics of the NMR spectra of paramagnetic compounds[2,3]. If the resonating nucleus (for example a proton) forms part of a paramagnetic molecule, i.e. a molecule having a non-compensated electronic spin moment, it is subjected to an additional magnetic influence by the electron spin. The leads to a broadening and also to paramagnetic shifts (contact and pseudocontact) of the resonance lines in relation to the widths and positions of the lines in the NMR spectra of diamagnetic compounds. A contact shift is observed in those cases where the probability that the unpaired electron is located at the site of the resonating nucleus is non-zero. This shift is proportional to the proton–electron interaction constant and (when the spin–orbital interaction is slight) is defined by the expression[2]

$$\omega_k = -A \cdot \frac{\gamma_e}{\gamma_p} \cdot \frac{g\beta S(S+1)}{3kT}, \qquad (1)$$

where γ_e and γ_p are the gyromagnetic ratios for the electron and proton, g is the g-factor of the paramagnetic compound, S the spin of the complex, β the Bohr magneton, T the absolute temperature, and k the Boltzmann constant.

A, which can be both positive and negative, is determined by the magnetic moment of the unpaired electrons of the paramagnetic species and the orientation of the unpaired electron at the given proton. According to the Fermi formula,

$$A = \frac{4}{3}\pi g\beta g_n\beta_n\rho(N),$$

where g_n is the nuclear g-factor, β_n the nuclear magneton, $\rho(N)$ the unpaired electron spin density at the given nucleus defined by the expression

$$\rho(N) = \int \psi^* \sum_k 2S_{zk}\,\delta(N)\,\psi\,d\tau,$$

and ψ the wave function of the electrons in the molecule; the remaining symbols in the last expression have the usual significance[2,3].

The pseudocontact shift† is due to the fact, that when the g-factor of the paramagnetic compound is anisotropic, the dipole–dipole interaction between the magnetic moments of the unpaired electron and the nucleus does not average out to zero[2]. This shift is defined by the following expression in an implicit form:

$$\omega_p = \frac{\text{const}}{T} \cdot f(g)\, f(\varphi, r).$$

Here the multipliers $f(g)$ and $f(\varphi, r)$ are determined by the anisotropy of the g-factor and the geometry of the complex respectively. The explicit form of these functional relations and hence the magnitude and sign of ω_p depend on the type of symmetry of the paramagnetic complex. For a paramagnetic ion moving at random in solution, the electric field around which has a tetragonal symmetry, the pseudocontact shift is given by the expression[2]

$$\omega_p = \frac{\beta^2 S(S+1)(3\cos^2\varphi - 1)(g_\parallel - g_\perp)(g_\parallel + 2g_\perp)}{27kTr^3}, \qquad (2)$$

where φ is the angle between the symmetry axis and the radius-vector directed from the centre of the coordinating ion to the proton, r the radius-vector, and $g_\parallel$ and $g_\perp$ are the electronic g-factors in directions parallel and perpendicular to the symmetry axis.

For molecules containing different protons (i, j, ...), the pseudocontact shifts for different nuclei i and j are

† Studies on contact interaction in paramagnetic complexes with organic ligands based on NMR spectra have been described[2,4-30].

linked by the relation

$$\omega_i : \omega_j = \frac{3\cos^2\varphi_i - 1}{r_i^3} : \frac{3\cos^2\varphi_j - 1}{r_j^3} , \qquad (3)$$

which makes it possible to obviate the difficulties associated with the measurement of the g-tensor components.

The pseudocontact interaction described by Eqn.(2) was introduced by McConnell and Robertson for an anisotropic g-factor, i.e. for a paramagnetic ion with degenerate levels in the absence of an external magnetic field when the Zeeman interaction depends on the relative orientation of the external field and the symmetry axis of the paramagnetic complex[31]. Bleaney[32] showed that the pseudocontact shifts in the NMR spectra due to paramagnetic complexes of lanthanides, which are characterised by an isotropic g-factor, are a consequence of the anisotropy of the susceptibility. In this case ω_p for an axially symmetrical complex is defined by the expression[32,33]

$$\omega_p = \frac{\beta^2}{60\,(kT)^2} \times \left(\frac{3\cos^2\varphi - 1}{r^3}\right) \times 2A_0^2 \langle \bar{a}^2 \rangle \times \\ \times g^2 J\,(J+1)\,(2J-1)\,(2J+3) \langle J \| \alpha \| J \rangle \qquad (2\text{–A})$$

where A_0^2 is the crystal field coefficient, $\langle \bar{a}^2 \rangle$ the mean square of the radius of $4f$ electrons, and $\langle J \| \alpha \| J \rangle$ a numerical coefficient; the remaining symbols are analogous to those in Eqns.(1) and (2). The first multiplier in Eqn.(2–A), depends on T^{-2} and not on T^{-1} [cf. Eqn.(2)]. However, the dependence on φ and r of the second multiplier is the same as for the anisotropic g-factor of axially asymmetric complexes. The third and fourth multipliers characterise the state of the paramagnetic ion. When Eqn.(2–A) is employed in structural studies, the influence of the third multiplier may be taken into account by means of an appropriate procedure, while the fourth multipler has been tabulated for tervalent lanthanides[33]. Since Eqn.(2–A) was obtained taking into account the ground state only, the europium complex should not induce shifts because $J = 0$ for Eu^{3+}. However, Eu^{3+} has an excited level with $J = 1$, which is close to the ground level (the energy of the first excited state is about 300 cm^{-1}). Allowance for this factor leads to a non-zero value of the fourth term in Eqn.(2–A), which accounts for the appearance of shifts in the spectra of europium complexes[32]‡.

The longitudinal (T_1M) and transverse (T_2M) relaxation times of the protons in the coordination sphere are given by the formulae[2]

$$\frac{1}{NT_{1M}} = \left(\frac{2}{15}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\left(3\tau_c + \frac{7\tau_c}{1+\omega_s^2\tau_c^2}\right) + \\ + \left(\frac{2}{3}\right) S(S+1)\,\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\cdot\left(\frac{\tau_e}{1+\omega_s^2\tau_e^2}\right) , \qquad (4)$$

$$\frac{1}{NT_{2M}} = \left(\frac{1}{15}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\left(7\tau_c + \frac{13\tau_c}{1+\omega_s^2\tau_c^2}\right) + \\ + \left(\frac{1}{3}\right) S(S+1)\,\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\left(\tau_e + \frac{\tau_e}{1+\omega_s^2\tau_e^2}\right) , \qquad (5)$$

where n_h is the number of nuclei in the sphere of the paramagnetic complex, N_p the molar concentration of the resonating nuclei, N the molar concentration of paramagnetic ions, ω_s the Larmor precession frequency of the electron, and τ_e and τ_c are the correlation times of the contact and pseudocontact interactions respectively, which are defined by the expressions

$$\frac{1}{\tau_e} = \frac{1}{\tau_s} + \frac{1}{\tau_h} ; \quad \frac{1}{\tau_c} = \frac{1}{\tau_s} + \frac{1}{\tau_r} + \frac{1}{\tau_h} . \qquad (6)$$

Here τ_s is the electron spin relaxation time, τ_h the residence time of the resonating nucleus in the coordination sphere, and τ_r the time required for the reorientation of the paramagnetic species. τ_h and τ_s must satisfy the condition $\tau_h^{-1} \gg A$; $\tau_s^{-1} \gg A$.

Since τ_e and τ_c are characteristics of random processes, each specific situation must be considered separately. However, in the general case τ_e and τ_c are determined by the fastest molecular processes. Moreover, τ_e^{-1} and τ_c^{-1} may differ appreciably from ω_s, which results in different contributions by dipole and contact interactions to T_1M and T_2M. This follows from Eqns.(4) and (5) containing the products $\omega_s\tau_e$ and $\omega_s\tau_c$, which satisfy different inequalities in the case of a significant different between τ_e and τ_c. For example, at a proton resonance frequency of 30 MHz, it is found that for Mn^{2+}

$$\omega_s\,\tau_e \gg 1; \qquad \omega_s\,\tau_c \ll 1 . \qquad (7)$$

When inequalities (7) hold, Eqns.(4) and (5) are replaced by other expressions:

$$\frac{1}{NT_{1M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c , \qquad (8)$$

$$\frac{1}{NT_{2M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c + \left(\frac{1}{3}\right) S(S+1)\cdot\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\tau_e . \qquad (9)$$

Consequently contact interaction (the second term in the last equation) will contribute to line width. This contribution may be reduced if

$$\omega_s\,\tau_c \ll 1 \quad \text{и} \quad \omega_s\,\tau_e \ll 1 . \qquad (10)$$

In this case

$$\frac{1}{NT_{1M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c + \left(\frac{2}{3}\right) S(S+1)\,\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\tau_e , \qquad (11)$$

$$\frac{1}{NT_{2M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c + \left(\frac{2}{3}\right) S(S+1)\,\frac{A^2}{\hbar^2}\left(\frac{n_h}{N_p}\right)\tau_e , \qquad (12)$$

or

$$\frac{1}{T_{1M}} = \frac{1}{T_{2M}} .$$

Like the preceding expression, the last equation for $1/T_2$M contains a second term, but its contribution is significantly smaller. Inequalities (10) hold where the characteristic relaxation times τ_e and τ_c are equal or differ insignificantly, which can happen, in particular, when the electron spin relaxation is fast[34] ($\tau_s \ll \tau_h, \tau_r$). At a proton resonance frequency of 100 MHz, $\omega_s\tau_e \ll 1$, provided that τ_e is of the order of magnitude of 10^{-12} s. A significant enhancement of the inequality $\omega_s\tau_e \ll 1$ (i.e. a narrowing of the resonance lines) occurs also with increase of the temperature of the test specimen.

It follows from a comparison of Eqns.(1) and (12) that

$$\frac{1}{NT_{2M}} = \left(\frac{4}{3}\right) S(S+1)\, g^2\beta^2\gamma_n^2 \left(\frac{n_h}{N_p}\right)\left(\frac{1}{r^6}\right)\tau_c + \frac{24k^2T^2}{\hbar^2 g^2 S(S+1)}\left(\frac{n_h}{N_p}\right)^2 \tau_e^2\omega_k^2$$

or

$$1/T_{2M} = B\, r^{-6} + C\,(\delta_k')^2 , \qquad (13)$$

where δ'_k is the observed contact shift of the resonance line and B and C are constants for the test specimen at the given temperature. For complexes in which there is no

‡ The nature of the shifts induced by paramagnetic europium complexes has also been discussed by Weissman[109].

contact interaction, the relaxation time of the nucleus is determined by the distance from the coordinating ion:

$$1/T_{2M} = C\ r^{-6}\ . \qquad (14)$$

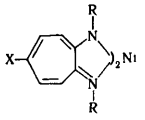
The study of the NMR phenomenon in paramagnetic systems yields important information about the structure of many-electron systems. This becomes evident if one remembers that Eqns.(1), (2), (2—A), and (3), which define the parameters of the NMR spectra of paramagnetic systems, are related to the electronic and geometric structures of molecules. Paramagnetic shifts are much greater than chemical shifts in the spectra of diamagnetic compounds and moreover they exhibit a characteristic temperature variation. A wide variety of relaxation effects are possible for paramagnetic substances and hence a broadening of the spectral lines, which significantly extends the scope of NMR as a research technique. This is because a decrease of the electron spin relaxation time leads to a broadening of the resonance lines in the ESR spectra, while NMR signals become narrower (the conditions governing the recording of the NMR spectra are improved)[4]. This interrelation between the relaxation times of electron and nuclear spins enables one to influence the form of the NMR and ESR spectra of paramagnetic systems (provided that electronic-nuclear interactions occur in them). For example, on dissolution in chloroform (0.001 M), bishexafluoroacetylacetonatocopper and bistrifluoroacetylacetonatocopper give rise to satisfactorily resolved ESR spectra in which a hyperfine structure is observed. When the stable di-t-butyl nitroxide (DBNO) radical is added to the solution to give a concentration as low as 0.01 M, the ESR spectra are broadened, so that their hyperfine structure is not resolved and the ^{19}F NMR spectra of these complexes in chloroform cannot be observed. However, when they are dissolved in DBNO [solution?], the ^{19}F NMR spectra can be recorded. This is because the spin exchange between the free radicals and the copper complexes reduces the electronic relaxation time and permits the detection of the NMR signal[35].

III. ANALYSIS OF NUCLEAR MAGNETIC RESONANCE SPECTRA USING THE NMR PHENOMENON IN PARAMAGNETIC COMPLEXES

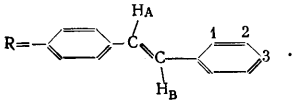
Nowadays NMR is a powerful tool for the investigation of many-electron systems, since the parameters of the NMR spectra carry valuable information about the electronic and geometric structures of the molecules[36]. However, the assignment of the resonance lines in NMR spectra on the basis of the simple rules for the analysis of the spectra (in the first-order perturbation theory) is impossible. On the other hand, it follows from Eqns.(2) and (2—A) that in the coordination of the molecules to a paramagnetic ion the resonance lines may shift unequally relative to their positions in the spectrum of the free ligand. This should make the difference between the proton chemical shifts greater than the spin—spin coupling constant between them and the analysis of the spectrum is significantly simplified.

1. Complexes of Elements in the First Transition Group

The factor noted above was apparently used for the first time to determine the spin—spin interaction constants J for substituted aminotroponeiminatonickel coordination complexes I. Eaton et al. examined this problem in detail[37]. They assumed that the spin—spin interaction in aromatic and unsaturated compounds is transmitted, predominantly by σ-electrons, over distances not greater than that corresponding to three bonds[38]. On the other hand, in paramagnetic nickel complexes (I) the contact shifts are due to the perturbation of the π-electron system of the ligand molecule[7]. Therefore one may expect that J found from the ^1H NMR spectrum of the paramagnetic complex will be close to the value of J for a diamagnetic molecule. The complex has the structure



where X = H or Br and R are different aliphatic and aromatic groups. Fig. 1B illustrates part of the spectrum of the paramagnetic complex due to the protons of the ligand molecule:



For comparison, the ^1H NMR spectrum of *trans*-stilbene taken from the catalogue of the Varian Company is also included[39]. The olefinic protons in *trans*-stilbene are chemically equivalent so that the spin—spin interaction between them is not observed and their signal in the spectrum consists of a singlet (δ = 7.10 p.p.m.). The aromatic protons form an unresolved multiplet. In a paramagnetic complex the resonating nuclei of the same molecule become significantly non-equivalent (Fig. 1*B*). The nickel complex (I) in solution is characterised by a rapid intramolecular equilibrium of the type

$$\underset{\text{(square)}}{\text{diamagnetic form}} \rightleftharpoons \underset{\text{(tetrahedron)}}{\text{paramagnetic form.}}$$

This leads to a narrowing of the resonance lines in the ^1H NMR spectra of the complexes to such an extent that it is possible to observe the spin—spin interaction characterised by J = 2—3 Hz.[7]

The high-resolution spectrum of a paramagnetic complex cannot usually be recorded owing to the considerable width of the resonance lines. However, this difficulty can be obviated by recording the spectra of specimens in which the metal/ligand ratio is much less then unity. As a result of the rapid exchange of molecules between the coordination sphere of the complex and the free ligand, an average spectrum is observed. Its form depends particularly on the nature of the electron—nuclear interaction in the paramagnetic complex. The use of this method becomes evident from an examination of the influence of exchange effects on the form of the NMR spectrum[36]. Evidently, when the proton H is involved in rapid exchange of the type HA + B $\rightleftharpoons$ HB + A, the observed shift of its signal is defined by the expression

$$\delta_H = P_A\ \delta_A + P_B\ \delta_B\ ,$$

where P_A and P_B are the mole fractions of H_A and H_B, and δ_A and δ_B are the chemical shifts of the proton signal in the environments of A and B. In our case A and B are the free molecule (P_C, δ_C) and the molecule coordinated (P_M, δ_M) to the paramagnetic ion, whence

$$\delta_H = P_C\,\delta_C + P_M\,\delta_M = \delta_C + (\delta_M - \delta_C)P_M = \delta_C + \omega\ P_M\ , \qquad (15)$$
$$\delta_M - \delta_C = \omega;\quad P_C + P_M = 1\ .$$

In order to assign the resonance lines in the spectra of specimens containing paramagnetic complexes, it is necessary that the solution should contain only one complex when the metal/ligand ratio is varied; if there are several complexes, their proportions must remain fixed. It is readily seen that the linear relation between δ_H and P_M is a criterion of the characteristics of complex formation in the test specimen. Moreover, Eqn.(15) can be used to determine ω when $P_M = 1$ and δ_C when $P_M = 0$ by the graphical extrapolation of the $\delta_H = f(P_M)$ relation. This method was used to assign the signals in the ^{1}H NMR spectra of pyridine, quinoline, and isoquinoline N-oxides[5,8].

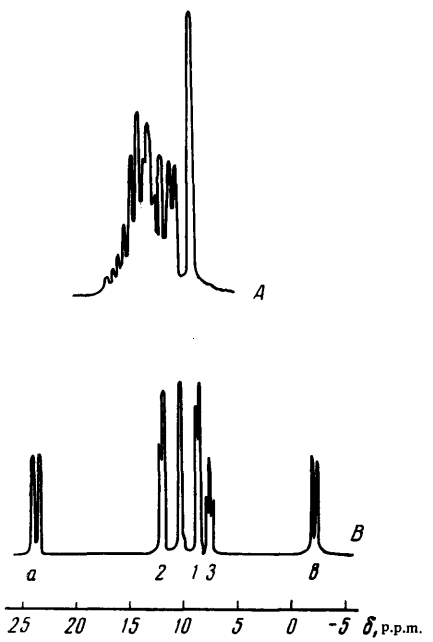


Figure 1. *A*) The ^{1}H NMR spectrum of *trans*-stilbene; *B*) part of the ^{1}H NMR spectrum of a paramagnetic complex due to the protons of *trans*-stilbene.

A method has been proposed[40] for the determination of the functional groups in organic compounds capable of forming paramagnetic complexes, which is also based on the employment of the characteristics of the NMR spectra of paramagnetic compounds. Its application is illustrated by the interpretation of the ^{1}H NMR spectra of certain methyl derivatives of pyrazole. The same method has been used also to assign the resonance lines in the spectra of N-vinylimidazole(II) and N-ethylimidazole(III).[41] The assignment was based on an estimate of the broadening (Δ) and shifts (δ) of the resonance lines due to the influence of the non-compensated electron spin of the paramagnetic complex. The estimation of Δ and δ' for labile complexes reduces to the solution of the Bloch equations modified by McConnell. For a two-component system, analysis of the Bloch–McConnell equations leads to the following expressions defining the observed Δ and δ' relative to the widths and positions of the lines in the spectrum of a diamagnetic compound[42]:

$$\Delta = \frac{P_M[(1/T_{2M})^2 + 1/T_{2M}\cdot\tau_M + \omega^2]}{\tau_M[(1/T_{2M} + 1/\tau_M)^2 + \omega^2]}, \quad (16)$$

$$\delta' = \delta'_c + \delta'_p = -\frac{P_M\cdot\omega}{\tau_M^2[(1/T_{2M} + 1/\tau_M)^2 + \omega^2]}, \quad (17)$$

where τ_M is the lifetime of the ligand molecule in the first coordination sphere of the complex, P_M the mole fraction of the complex in the specimen, $\omega = \omega_C + \omega_p$ the shift of the resonance line of the nucleus entering into the composition of the paramagnetic complex§, and T_{2M} the transverse relaxation time of the resonating nucleus in the complex.

Evidently, depending on the relative values of τ_M, T_{2M}, and ω, Eqns.(16) and (17) may be simplified[42].

1) Slow exchange:

$$\Delta = \frac{P_M}{\tau_M}, \quad (18)$$

$$\delta' = -P_M\ \omega\ \frac{T_{2M}^2}{\tau_M^2}, \quad \text{or} \quad \delta' = -\frac{P_M}{\tau_M^2\cdot\omega}. \quad (19)$$

2) Fast exchange:

$$\Delta = P_M\cdot\tau_M\cdot\omega^2 \quad (20)$$

or

$$\Delta = \frac{P_M}{T_{2M}}, \quad (21)$$

$$\delta' = -\omega\cdot P_M. \quad (22)$$

3) Intermediate case:

$$\Delta = \frac{P_M}{T_{2M}} + P_M\cdot\tau_M\cdot\omega^2, \quad (23)$$

$$\delta' = -\omega\cdot P_M. \quad (24)$$

The simplification of Eqns.(16) and (17) involves the derivation of the relations

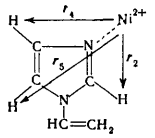
$$\Delta = f(T), \quad (25)$$

$$\delta' = f(T), \quad (26)$$

where T is the absolute temperature of the test specimen. Here it is necessary to note the importance of the fact that Δ and δ' are functions of the same variables. Therefore, depending on the nature of the complex and the experimental conditions, it is possible to obtain both Eqns.(25) and (26) or one of them. The above considerations were used to assign the ring proton signals in the ^{1}H NMR spectra of compounds (II) and (III). The experiments were performed in the presence of an excess of the ligand in the specimen. Fig. 2 presents the temperature variation of the broadening of the ring proton signals in the spectrum of compound (II) with the added paramagnetic complex $NiCl_2.4L$ [L = (II)]. The plots show that up to 313°K the broadening Δ is determined by Eqn.(18). In order to find approximate expressions for Eqns.(16) and (17) in the range 313–370°K, account was taken of the temperature variation of δ'. Moreover, the ratios $(r_5/r_2)^6$, $(r_5/r_4)^6$, and $(r_4/r_2)^6$ were estimated from data for the geometry of imidazole[43] and

§ One should note here that in a number of studies[6,10,12] the pseudocontact shifts were found to be insignificant in those cases where the nickel atom was the coordinating species.

also the ionic radius of Ni^{2+} and the van der Waals radius of nitrogen



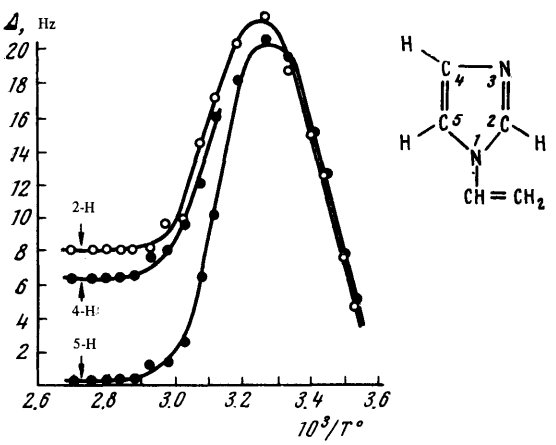


Figure 2. Temperature variation of the broadening of the signals of the imidazole ring protons.

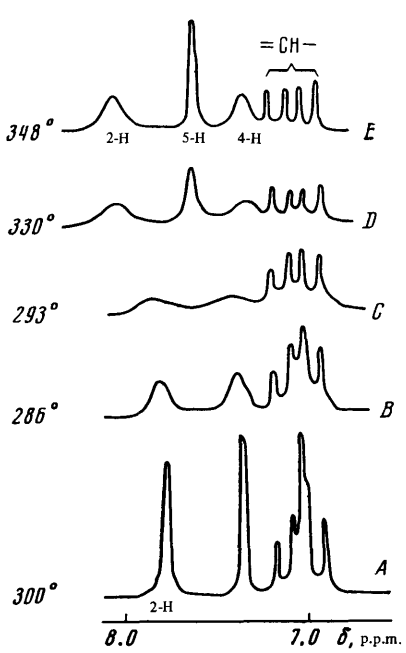


Figure 3. The positions of the ring and CH proton signals in the spectrum of *N*-vinylimidazole without the addition (*A*) and with addition (*B* –*E*) of the paramagnetic complex at different temperatures.

By comparing Δ and δ′ and taking into account the fact that the 2-H proton of imidazole resonates in a lower field than the 4-H and 5-H protons, it was found that the signals of the imidazole ring protons in the spectrum of compound (II) are in the sequence $\delta_2 > \delta_5 > \delta_4$. When the temperature of the test specimen with the added complex $NiCl_2.4L$ is altered, the signals of the vinyl protons hardly shift in relation to their positions in the spectrum of the specimen without the paramagnetic additive. Since these protons are quite far (compared with 2-H and 4-H) from the coordinating ion, their resonance lines are hardly broadened, i.e. over the entire range of variation of temperature Δ is determined by the first term of Eqn.(16). The positions of the signals of the 2-H, 4-H, 5-H, and CH protons in the spectrum of compound (II) with and without the addition of the paramagnetic complex at different temperatures are illustrated in Fig. 3. The ^{1}H NMR spectrum of compound (III) was analysed similarly. The following two examples illustrate the results of Zaev and coworkers' study [40]. Fig. 4 presents the spectrum of 1,3,5-trimethylpyrazole (IV) without the addition (*A*) and with addition (*B*) of the salt $NiBr_2.3H_2O$, which forms a paramagnetic complex with compound (IV). Fig. 4*A* shows that the assignment of the 3-CH_3 and 5-CH_3 signals is not unambiguous, since their protons resonate at high field and are responsible for the appearance of two singlets with an insignificant difference between the chemical shifts (0.03 p.p.m.).

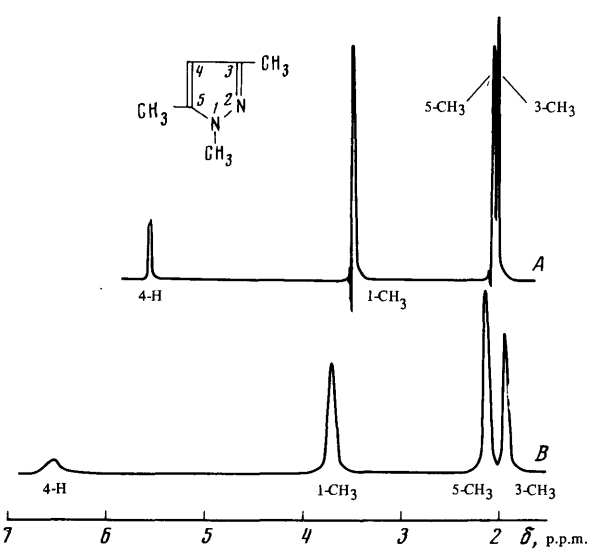


Figure 4. ^{1}H NMR spectrum of 1,3,5-trimethylpyrazole without the addition (*A*) and with addition (*B*) of $NiBr_2.3H_2O$.

The formation of complexes leads to a shift of the singlets in opposite directions and to different degrees of broadening. Comparison of the values of Δ and δ′ with the distances from the coordinating ion to the resonating nuclei showed that in the spectrum of compound (IV) without $NiBr_2.3H_2O$ the singlet in the high field is due to the protons of the 3-CH_3 group. Fig. 5 presents the spectra of one of the isomers of dimethylpyrazole without the addition (*A*) and with addition (*B*) of the same nickel salt. Since Δ for the signal of the 4-H proton, the position of

which in the spectrum is known, is significantly smaller than Δ for the signal of the other proton of the pyrazole ring, the above isomer is 1,5-dimethylpyrazole in which $r^6_{3\text{-H}} \ll r^6_{5\text{-H}}$. In the above investigations[40,41] the mole fraction of the paramagnetic complex did not exceed $10^{-2}-10^{-3}$, which ensures constancy of the composition of the complex and a linear relation between δ′ and P_M. Carbon tetrachloride, chloroform, and nitromethane were used as solvents. Any substance can be used for this purpose, provided that it does not displace the ligand molecules from the paramagnetic complex.

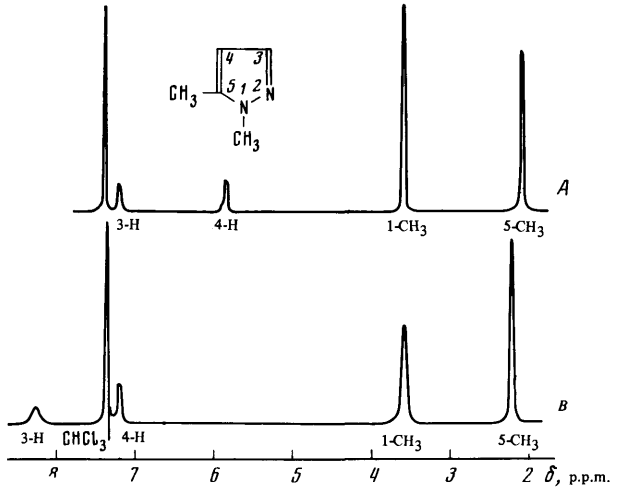


Figure 5. ^{1}H NMR spectrum of 1,5-dimethylpyrazole without the addition (*A*) and with addition (*B*) of $NiBr_2.3H_2O$.

Other investigators[13,44-46] also used the addition of salts of metals of the first transition group in order to analyse the ^{1}H NMR spectra. In particular, the relative positions of the NH_2 and NHR groups and the aromatic ring were established[13] in aniline derivatives coordinated to $Ni(AA)_2$¶ and $Co(AA)_2$. The conformation of the tropane ring was refined[44]. Account was taken of the effect of the orientation of the nitrogen atom lone pair and the paramagnetic shifts in the spectra of piperidines induced by $Ni(AA)_2$.[47] A study was made of the effect of $Co(AA)_2$, $Ni(AA)_2$, and $Cu(AA)_2$ on the ^{1}H NMR spectra of various alcohols and amines at room temperature[45].

To conclude this section, we may mention that, for different ligands and coordinating ions, which can form complexes differing in the values of ω and T_{2M}, Eqns. (16) and (17) can be represented approximately by Eqns. (18) to (24) at different temperatures of the test specimens. Since the complexes formed by elements of the first transition group are characterised by different values of τ_S (τ_S^{Mn} and $\tau_S^{Cu} \gg \tau_S^{Ni}$, τ_S^{Co}, τ_S^{Fe}),[34] it follows that comparison of the values of Δ and δ′ for the purpose of the assignment of the resonance lines is also possible at different temperatures of the test specimens. This fact is illustrated in Fig. 6.[48] A similar behaviour may be shown for the same coordinating ion with different ligands.

¶ AA = acetylacetonato-group.

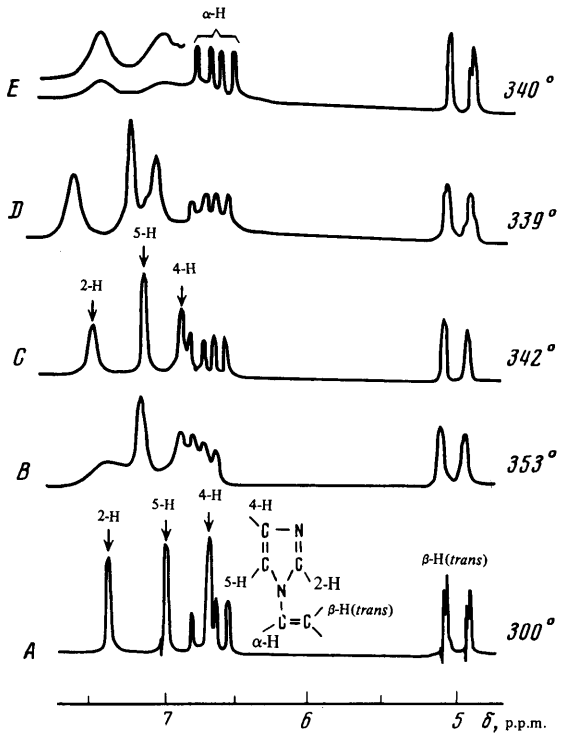


Figure 6. ^{1}H NMR spectrum of *N*-vinylimidazole without the addition (*A*) and with addition of a paramagnetic complex at different temperatures: *B*) $NiCl_2.4L$; *C*) $FeCl_3.4L$; *D*) $CoCl_2.4L$; *E*) $CuCl_2.4L$.

2. LANTHANIDE COMPLEXES

The vast majority of studies in which the ^{1}H NMR spectra were simplified using the spectra of paramagnetic systems were made after the publication of Hinckley's paper[49], which reported a comparison of the ^{1}H NMR spectrum of a cholesterol solution with and without the addition of the paramagnetic complex $Eu(DPM)_3.2Py$ (DPM = dipivaloylmethane or 2,2,6,6-tetramethylheptane-3,5-dione[50] and Py = pyridine). The author justifies the use of the europium complex by the very short electronic relaxation time (τ_S) of lanthanide ions. Therefore (see Section II) the formation of a complex with tris(dipivaloylmethane)europium lead to only a slight broadening of the resonance lines, while their paramagnetic shifts are significant. Fig. 7 illustrates the spectrum of cholesterol (V) in carbon tetrachloride solution without addition (Fig. 7*A*) and with addition of $Eu(DPM)_3.2Py$.[49] In the free ligand the protons of the methyl and also methylene and methine groups, which are not bound to an oxygen atom, resonate in a high field, forming an unresolved multiplet in the spectrum. The remaining protons resonate in the weaker field. The coordination of cholesterol to the europium ion leads to an appreciable shift of the signals in the spectrum. The greatest paramagnetic shifts are observed for the signals of the vinyl proton *f* and the proton *e*, which indicates coordination via the hydroxy-group. The signals of the methyl groups *a*, *b*, and *c* are also displaced. Moreover, new resonance lines *g*, *h*, and *i* appear in a weak field. The assignment of the resonance

line was based on a comparison of the spectra at different $Eu(DPM)_3.2Py$ concentrations in the test specimen with allowance for the integrated signal intensities. Moreover, account was taken of the fact that, when the coordinating centre is the lanthanide ion, the paramagnetic shift is due to a pseudocontact interaction[4]. The paramagnetic shifts were therefore compared with the corresponding values of r. For this purpose, the possible structure of the complex was examined using a model of cholesterol. It was found that the metal ion is in the *trans*-position relative to the proton *e*, i.e. that the configuration of the complex depends significantly on the steric factor, determined by the mutual orientations of the proton and the hydroxy-group. The dependence of the observed paramagnetic shifts on r^{-3} shows that the paramagnetic shifts are mainly determined by the distance from the coordinating ion to the resonating nuclei. This analysis of the ^1H NMR spectra of cholesterol led to the conclusion that $Eu(DPM)_3.2Py$ can be used for the conformational analysis of steroids and similar compounds. The capacity of $Eu(DPM)_3.2Py$ to induce relatively large paramagnetic shifts, which depend on the concentration of the complex in the test specimen, without a significant broadening of the resonance line shows that this complex can be used as a shift reagent[49].

In his next paper[51] Hinckley reported the use of a paramagnetic europium complex for the assignment of the signals of the methyl protons in the ^1H NMR spectrum of (+)-camphor, since there had been no unanimous view in the literature concerning this problem. Hinckley preceded the spectrum analysis by the following justification of the use of paramagnetic additives.

When a complex $M(DPM)_3.2Py$ (M is a lanthanide element) is dissolved in carbon tetrachloride, its molecule dissociates in accordance with the equations

$$M(DPM)_3.2Py \rightleftharpoons M(DPM)_3.Py + Py,$$
$$M(DPM)_3.Py \rightleftharpoons M(DPM)_3 + Py.$$

If an organic compound B with a coordinating group is added to the solution, association of the following type will take place:

$$M(DPM)_3.Py + B \rightleftharpoons M(DPM)_3.Py.B.$$

The paramagnetic shifts in the spectrum of B are then a consequence of such association.

According to Hinckley[51], the use of lanthanide complexes must involve the following procedures: 1) the recording of the ^1H NMR spectrum of compound B dissolved in carbon tetrachloride without an additive and then with one or several additions of $Eu(DPM)_3.2Py$; the determination of the concentration variation of the observed shifts is necessary in those cases where it is difficult to analyse the spectrum at one concentration; 2) the construction of a model of compound B and the measurement of the distances r from the coordinating metal ion to the resonating protons (the ionic radius of Eu^{3+} is 0.950 Å). The spectrum of B is interpreted accordingly.

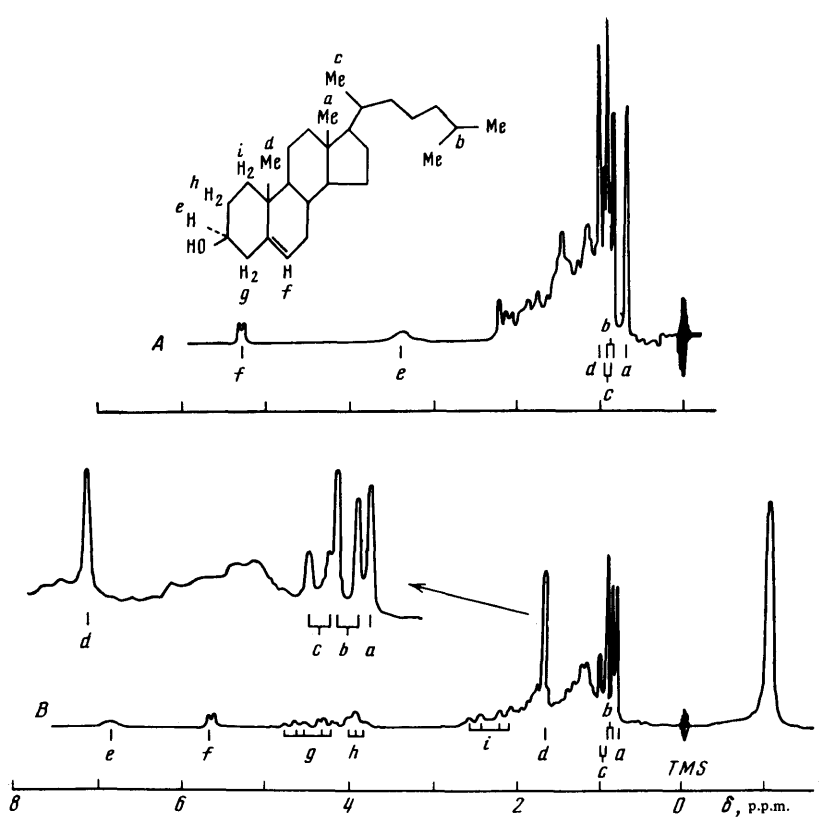
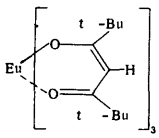


Figure 7. *A*) ^1H NMR spectrum of cholesterol in carbon tetrachloride; *B*) the spectrum of cholesterol after the addition of the complex $Eu(DPM)_3.2Py$. The high-field signal is due to the methyl protons of DPM.

Although Hinckley's paper[49] was published in the middle of 1969, more than 200 reports of the use of shift reagents for the analysis of NMR spectra have already been published. These studies, illustrating the scope of the method of analysing NMR spectra with the aid of lanthanide complexes, are described below.



After Hinckley[49], Sanders and Williams reported that Eu(DPM)$_3$ is an excellent shift reagent[52]. This europium compound induces considerable paramagnetic shifts by coordinating the lone electron pair of the functional group. For example, the aromatic protons in the ^{1}H NMR spectra of benzyl alcohol give rise to a broad spectrum. When Eu(DPM)$_3$ is added to the solution (0.39 M), the spectrum becomes susceptible to a first-order analysis (Fig. 8).

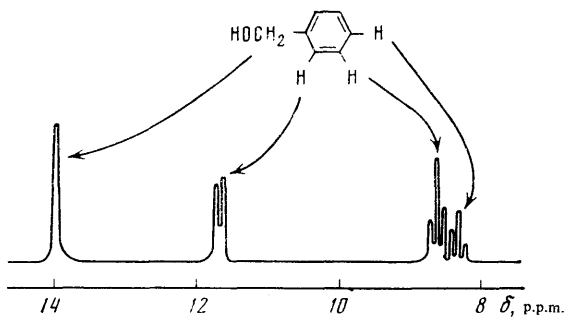


Figure 8. The ^{1}H NMR spectrum of benzyl alcohol in the presence of Eu(DPM)$_3$.

The induced shifts decay rapidly with increase of the number of bonds separating the hydroxy-groups and the corresponding protons. When Eu(DPM)$_3$ is added to a solution of 1-hexanol, the analysis of its spectrum in accordance with the first-order rules is also possible. The signal of the OH group is then broadened to such an extent that it cannot be recorded. However, the broadening of the resonance lines of the other protons is much smaller. It was found that Eu(DPM)$_3$ induces paramagnetic shifts also in the ^{1}H NMR spectra of ketones, ethers, esters, and amines. Ketones form complexes (to an extent of about 35–40%) less effectively than alcohols, and ethers and esters are less effective still. However, amines behave similarly to alcohols. Sanders and Williams believe that Eu(DPM)$_3$ can be extremely effective in the determination of the structures of natural products and supported this view by an analysis of the changes in the ^{1}H NMR spectrum of lupeol recorded after the addition of Eu(DPM)$_3$. They discussed[52] the conditions governing the employment of Eu(DPM)$_3$. In particular, they noted its high solubility in carbon tetrachloride. One of the first studies was that of Wahl and Peterson[53], who employed Eu(DPM)$_3$ for the analysis of the ^{1}H NMR spectra of adamantan-1-ol and adamantan-2-ol.

The effectiveness of Eu(DPM)$_3$ was illustrated by Demarko et al.[54] in the analysis of the spectra of *trans*- and *cis*-4-butylhexanol, isoborneol, and borneol[54]. The signals in the spectra of these compounds were assigned on the basis of a comparison of the paramagnetic shifts with the corresponding distances r' from the resonating nuclei to the oxygen of the hydroxy-group and not to the coordinating ion†. This approach was justified by postulating that the values of $3\cos^2\varphi_i - 1$ for the protons of the test compounds would be significantly different. It is impossible to calculate them owing to the lack of information about the geometry of the paramagnetic complex in solution. It was established that a relation between the shift‡ and the distances from the protons to the oxygen atom can be expressed by a straight line on a logarithmic scale with a slope of -2.3. This is evidence of a correspondence between the induced shifts and r': $\lg(r')^{-3} = (-3)\lg r'$. The replacement of r by r' must be regarded as justified, since it implies a shift of the origin of the readings of the power base r in the functional relation $y = r^3$, the shape of the plot of which is determined by the cube of the distance. Evidently for small values the use of r' in comparing the paramagnetic shifts will yield less satisfactory results. Therefore the replacement of r by r' should be most successful for protons remote from the europium atom. Fig. 9 illustrates the results of Demarko et al.[54]. Only two signals may be assigned in the spectrum of a solution of *cis*-butylhexanol (Fig. 9*A*) without Eu(DPM)$_3$. However, for a molar ratio alcohol/Eu(DPM)$_3$ = 0.7, the recorded spectrum meets the requirements for a first-order interpretation (Fig. 9*E*). The signals were assigned on the basis of the spin–spin interaction constants taking into account double resonance experiments. Demarko et al. also illustrated the efficiency of the shift reagent method in the study of the structures of steroids and triterpenes by a detailed analysis of the ^{1}H NMR spectra of 5α-androstan-2β-ol and friedelan-3-β-ol.[56] The possibility of employing the shift reagent method for the determination of the numbers and positions of the methyl groups in molecules of natural products was demonstrated by comparing the shifts induced by Eu(DPM)$_3$ in the ^{1}H NMR spectra of 22 triterpenes[57]. In order to obtain spectra with non-overlapping signals, account was taken in the above study of both the concentration and temperature variation of the observed shifts. The compared values of the latter were normalised in relation to the low-field signal of the protons in the 4-CH$_3$ group, the chemical shift of which was assumed to be 10 p.p.m.

Briggs et al.[58] were the first to report that Pr(DPM)$_3$ induces, like Eu(DPM)$_3$, paramagnetic shifts in ^{1}H NMR spectra. It is striking that these shifts are approximately three times greater than the shifts due to Eu(DPM)$_3$ and are of opposite sign. Briggs et al.[58] quote the paramagnetic shifts induced by complexes of the type M(ClO$_4$)$_3$·{OP[N(CH$_3$)$_2$]$_3$}$_4$ in the ^{1}H NMR spectrum of a solution of acetonitrile (the shifts are quoted relative to the acetonitrile complex in which M is lanthanum; the minus sign

† The r' were calculated by determining the distances between non-linked atoms[55].

‡ The paramagnetic shifts compared with the r' were calculated subject to the condition that the molar ratio alcohol/Eu(DPM)$_3$ = 1.

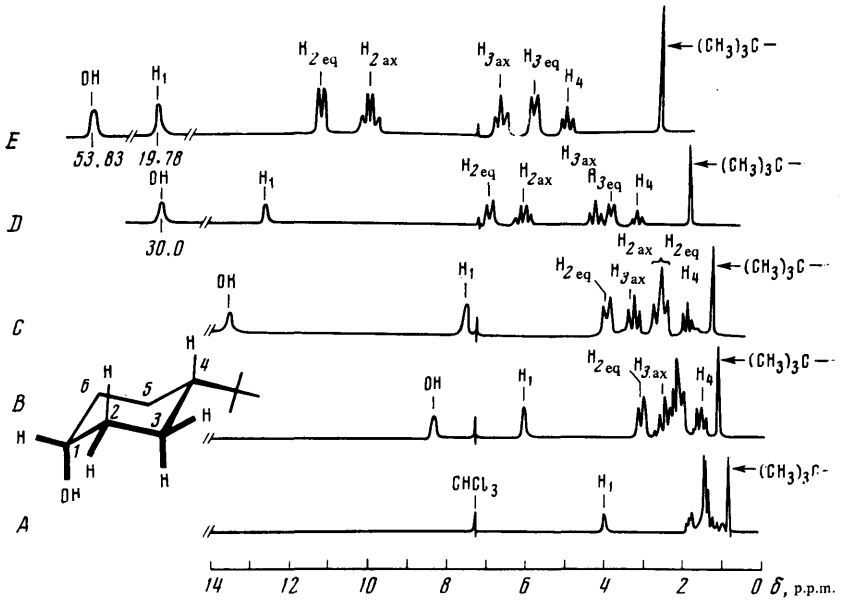


Figure 9. The ^{1}H NMR spectrum of *cis*-4-t-butylcyclohexanol (20 mg) in $CDCl_3$ (0.4 ml) with different contents of $Eu(DPM)_3$ (mg): *A*) 0.0; *B*) 10.3; *C*) 16.0; *D*) 33.1; *E*) 60.2. (The signal of the methyl protons was recorded with a lower amplification than the other signals.)

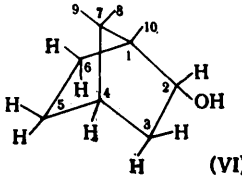
corresponds to a shift to high field:

Metal	Paramagnetic shift, p.p.m.
Ce	−1.5
Pr	−3.0
Nd	−1.75
Sm	−0.27
Eu	+1.33
Gd	not observed
Tb	−19.2
Dy	not observed
Ho	−17.0
Er	+4.4
Tm	+6.9
Yb	+6.66
Lu	0

The above example shows that complexes of other lanthanides, together with $M(DPM)_3$, can be used as shift reagents. At the same time there are important limitations to the use of these complexes, which are determined in particular by the following causes[58].

1. The $M(DPM)_3$ form complexes with a coordination number of 6, which is suitable for the coordination of organic molecules.
2. The shift reagent method is based on the use of nonpolar solvents.
3. One must bear in mind that (a) the test substance may not be coordinated to the lanthanide compound due to steric hindrance and (b) that the signals of the resonating nuclei may not be affected significantly by complex formation. For example, it has been found that $Pr(NO_3)_3(OPPh_3)_3$, $Pr(ClO_4)_3\{OP[N(CH_3)_2]_3\}_4$, $Eu(NO_3)_3(OAsPh_3)_4$, $Ce(NCS)_3 \cdot (OPPh_3)_4$, and lanthanide perchlorates induce insignificant paramagnetic shifts in the spectra of alcohols and ketones (the signal of α-protons is displaced only by approximately 0.5 p.p.m.).

Briggs et al. were the first to compare the observed and calculated paramagnetic shifts induced by $Pr(DPM)_3$.[59] They used borneol (VI), which has a fixed conformation, as the ligand

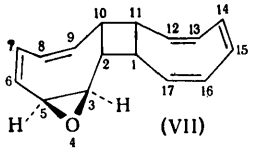


(VI)

An unambiguous assignment of the observed paramagnetic shifts was achieved by a preliminary analysis of the ^{1}H NMR spectrum of borneol recorded at three frequencies (60, 100, and 220 MHz) using the double resonance and deuteriation techniques. It was assumed (1) that the paramagnetic shifts are due to a pseudocontact interaction and (2) that the complex is axially symmetric in solution.

This implied that the induced shift must be proportional $(3\cos^2\varphi - 1)r^{-3}$. The orientation of the resonating nuclei was specified by the Pr—O distance, the Pr—O—(2-C) angle, and the Pr—O—(2-C)—(H-2)-dihedral angle. The values of these parameters in the initial model (2.6 Å, 109°, and 33°) were then varied until agreement was reached between the calculated and experimental shifts to within a constant factor. This agreement was found for the following values: 3 Å, 126°, and 25°. The authors concluded that the problem of the orientation of the hydroxy-groups in various lanthanide complexes should probably be solved separately in each specific case. The importance of the $3\cos^2\varphi - 1$ contribution to the paramagnetic shifts was also demonstrated (particularly for resonating nuclei close to the coordinating ion). This conclusion is confirmed by the ^{1}H NMR spectrum of a

tetracyclic epoxide (VII) recorded in the presence of $Eu(DPM)_3$.[60]



(VII)

It was found that, in contrast to the signals of other protons, those of 15-H and 16-H are displaced to high field. The explanation is that $\varphi_{15\text{-H}} = 58°$ and $\varphi_{16\text{-H}} = 55$, i.e. is greater than 54.7° (if $\varphi < 54.7°$, then $3\cos^2\varphi - 1 < 0$). Therefore complex formation leads to additional screening of the 15-H and 16-H protons and displaces their signals to high field. The shifts to high field induced by $Eu(DPM)_3$ were also reported in other investigations[61-63]. It is noteworthy that Tjan and Visser[62] believe that the hypothesis of a contact and pseudocontact mechanism for the interaction of unpaired electrons and resonating nuclei constitutes the most acceptable explanation of the paramagnetic shifts to high field which they observed. These two mechanisms lead to the appearance of paramagnetic shifts with opposite signs, which is in fact reflected in the ^1H NMR spectra.

Bélanger[64] examined the shifts induced by $Pr(DPM)_3$ in the spectra of certain ketones and found that the shifts are greater by a factor of 1.4 than the shifts induced by $Eu(DPM)_3$.

Wolkowski and coworkers[65,66] used addition of the ytterbium compound $Yb(DPM)_3$ for the analysis of ^1H NMR spectra. In the first study they investigated primary, secondary, and tertiary amines and established that the induced paramagnetic shifts depend on the steric factor and on the charge of the nitrogen atom. They compared the paramagnetic shifts and r for pyridine and quinuclidine, which have a characteristic orientation of a lone electron pair orbital available for coordination. The N...Yb distance was varied from 1 to 5 Å. It was found that, for a N...Yb distance of 3 ± 0.3 Å, the graphical relation between the shifts and r (on a logarithmic scale) is linear.

Wolkowski[66] illustrated the effectiveness of $Yb(DPM)_3$ for the assignment of the signals in the ^1H NMR spectra of ketones and aldehydes. A significant influence of steric factors and of the charge of coordinating atoms on the shifts induced by lanthanides was observed also by Ernst and Mannschreck[67] who found, in particular, a linear correlation between the basicity of the substitutent and the paramagnetic shifts of the signals of the *ortho*- and *meta*-protons in the ^1H NMR spectra of substituted anilines. The application of the shift reagent method to compounds having more than one coordinating centre was examined in a number of studies. It was found, for example, that *trans*- and *cis*-1-hexyl-2-phenylazetidin-3-ol is coordinated to $Eu(DPM)_3$ via the oxygen of the hydroxy-group and not via the nitrogen atom of the four-membered ring[68]. Details of the analysis of the paramagnetic shifts in the spectra of compounds with several coordination centres can be found in studies by Hinckley[69] and Sanders and coworkers[70].

The dependence of the pseudocontact interaction not only on r_i but also on φ_i complicates the assignment of the signals on the basis of a comparison of the observed paramagnetic shifts. At the same time, in the case of rapid exchange the difference between the broadening of the resonance lines at the given specimen temperature depends only on r^{-6}. Therefore, when the broadening can be determined as the signals are displaced, the values of Δ can be used for the same purpose as δ'.

This was taken into account by Morallee et al.[71] who reported that not only the shift but also the broadening of the resonance lines, due to the lanthanide ions, permits their use as excellent NMR probes for the investigation of biological systems. This was specifically illustrated in a study of the ^1H NMR spectrum of lysozyme in the presence of europium(III), holmium(III), and gadolinium(III) ions. Comparison of the broadening of the signals due to gadolinium enabled the distances from the coordinating ion to the protons of the acetamide and glycosidic methyl groups to be determined. The effectiveness of the joint analysis of δ' and Δ in the ^1H NMR spectra of pyridine and quinoline was demonstrated by Reuben and Leigh[72].

It is noteworthy that, in assigning the resonance lines in the spectra, some investigators compared the induced paramagnetic shifts with $(r')^{-2}$, motivating this approach by the uncertainty of the relative positions of the resonating nuclei and the centra ion. Rafalski et al.[73] compared the following two correlations: (1) between δ' and r^{-n} or $(r')^{-n}$ ($n = 2, 3$) and (2) between $\lg\delta'$ and $\lg r^{-n}$ or $\lg(r')^{-n}$. The values of n calculated from the experimental data of different workers served as a criterion for the comparison. The following remarks are appropriate to the study of Rafalski et al.[73].

1. The replacement of δ' and r (or r') by their logarithms implies only a change in the scale of the quantities compared. Therefore the above correlations must not be contrasted with one another.

2. The above investigations showed that the magnitude of the induced paramagnetic shifts is determined by the relative positions of the resonating nuclei and the central atom and also by the nature of the electron-nuclear interaction in the complex. Therefore the problem of choice of n is not fundamental, particularly since the pseudocontact shifts depend on $n = -3$.

Examination of NMR in paramagnetic systems showed that the observed values of Δ and δ' are determined, in particular, by the nature of the coordinating ion. Therefore Crump et al.[74] made a comparative study of complexes of the type $M(DPM)_3$, where M = Pr, Sm, Eu, Tb, Ho, or Yb§. The criteria of this comparison were (a) the position of the signal due to the protons of the t-butyl groups of DPM, (b) the slopes of the linear plot of $\delta' = \delta'(X_M)$, where X_M is the molar ratio $M(DPM)_3$/ test substance, (c) the relative shifts in the spectra of complexes of the type $M\{OP[N(CH_3)_2]_3\}_4(ClO_3)$ taken from the study of Briggs et al.[58], and (d) the ratio of the broadening (Hz) to the shift (Hz) of the signal due to the protons of the methyl groups of t-butyl alcohol in the presence of the complexes $M(DPM)_3$. The comparison showed that, in order to obtain first-order ^1H NMR spectra with retention of multiple structure, it is best to employ $Eu(DPM)_3$. The signal of the t-butyl groups of this salt appears in high field relative to tetramethylsilane and is therefore not superimposed on the signals of the test substances. Moreover, the paramagnetic shifts to low field induced by $Eu(DPM)_3$ are more suitable from the experimental standpoint. $Pr(DPM)_3$ should be used in addition to $Eu(DPM)_3$, particularly for the assignment of the signals of the t-butyl groups in the spectra of steroids. One must note that the signal of the t-butyl groups of $Pr(DPM)_3$, which

§ See also Refs. 75–77.

appears in the region of 3–5 p.p.m. (δ), may be superimposed on the signals of the test compounds. Conditions governing the use of $M(DPM)_3$ (solubility¶, effect of H_2O, etc.) have been described [74,78]. The stoichiometry in the solute (test substance)–shift reagent system has been analysed in a number of publications. It has been established [80] that, when the ligand concentration is much higher than that of the shift reagent, the paramagnetic complexes have the 1 : 2 composition and not 1 : 1, as believed by Armitage et al. [81] Shapiro and Johnston [80] also examined in detail the use of the relation between the observed paramagnetic shifts and the ratio of the ligand and lanthanide concentrations. Careful analyses of the application of the $M(DPM)_3$ complexes as displacing agents and also of the scope of the method have been made [75,82].

The investigations showed that the paramagnetic shifts induced by lanthanides depend significantly on the structure of the diketone [82–84]. It was established that the tris-[3-t-butylhydroxymethylene-(+)-camphorato]europium can be used to determine the degree of enantiometric purity [85]. However, its applicability proved to be limited [86,87] Tris-[3-heptafluoropropylhydroxymethylene-(+)-camphorato]europium proved to be a more effective optically active displacing agent [86]. At the same time the use of $Eu(DPM)_3$ for similar purposes can also be successful [87]. A comparison of $Eu(DPM)_3$, $Eu(FOD)_3$ [FOD = tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato)europium], and $Eu(FND)_3$ [FND = tris-(1, 1, 1, 2, 2, 6, 6, 7, 7, 7-decafluorheptane-3,6-dionato]europium has been made [76].

It was noted in Section II that in the general case the paramagnetic shifts δ′ and the broadening Δ of the resonance lines observed in the NMR spectra are defined by Eqns. (16) and (17). On the other hand, the practical employment of δ′ and Δ is based on Eqns. (18)–(24) the validity of which is determined by the nature of the paramagnetic complex and the temperature of the test specimens. For lanthanide complexes, this problem has been hardly discussed in the literature. Only the effect of varying temperature has been reported [57,71,77,88–92]. In this connection the effect of the specimen temperature on the paramagnetic shifts induced by $Eu(FOD)_3$ in the ^1H NMR spectra of limonoids is of interest [88]. It was found that, with increase of temperature, the δ′ for the signals of certain protons increase. This finding was regarded [88] as unexpected on the grounds that the paramagnetic shifts are inversely proportional to the temperature of the test specimen (Section II). However, in the case of a slow exchange an increase of temperature leads to a decrease of τ_M and therefore δ′ in the NMR spectra should increase. In particular, when the spectrum of the ligand molecule contains signals with significantly different values of ω, cases are possible for which Eqns. (16) and (17) can be represented approximately by different expressions from the set of Eqns. (18)–(24). Therefore the determination of the $\delta' = \delta'(T)$ relation may be not only desirable but also essential.

NMR studies on other nuclei (other than the proton) with addition of lanthanide complexes have already been published. The effect of $Eu(DPM)_3$ and $Yb(DPM)_3$ on the ^{14}N NMR spectra of pyrrolidinone, n-propylamine, pyridine, *N*-methylimidazole, acetonitrile, and dimethylformamide has been examined [93]. Briggs et al. demonstrated the effectiveness of the interpretation of ^{13}C NMR spectra with the aid of tris(dipivaloylmethane)lanthanides [94]. Duggan and Urry [95] used the paramagnetic shifts induced by $Eu(DPM)_3$ in the ^{13}C NMR spectra for structural investigations. A method of assignment of the ^{13}C NMR signals based on the joint use of $M(DPM)_3$ and $^{13}C-\{^1H\}$ heteronuclear double resonance has also been proposed [96]. Mention should be made of the work by Sanders and Williams [97] concerning the nature of the shift induced by lanthanides in the ^{31}P NMR spectra. In particular they established that $Eu(NO_3)_2{\cdot}6H_2O$ is an effective shift reagent in polar solvents for compounds with a $X-O^-$ (X = R–CO, $R_3\overset{+}{P}$, or $R_3\overset{+}{A}s$) functional group. Interesting results were obtained in studies [98,99] in which the isotope effect of deuterium on the paramagnetic shifts induced in NMR spectra by lanthanide complexes was considered. Mention should also be made of the work by Willcott and coworkers [100,101] who considered a statistical method for the analysis of paramagnetic shifts induced by lanthanide complexes. Finally a fairly complete list of publications in 1969–71 and also some of the publications in 1972 can be found in studies [102,103] on the use of shift reagents.

The following remarks must be made in conclusion. Firstly, the change in the relative contents of the ligand and the lanthanide within wide limits can influence significantly the constancy of the composition of the complex in solution. Secondly, X-ray diffraction analysis of the complexes† $Ho(DPM)_3{\cdot}(VIII)_2$ [104] and $Eu(DPM)_3{\cdot}(IX)$ [105] showed that the paramagnetic lanthanide complexes used as shift reagents can have a symmetry other than axial‡. For example, Uebel and Wing [105] found agreement between the experimental and calculated (for axial symmetry) paramagnetic shifts only for a signal assignment known to be incorrect. Thirdly, the nature of the electron-nuclear interaction in lanthanide complexes with organic ligands has been comparatively little investigated, in contrast to the complexes of the first transition series. The majority of investigators do not think it obligatory to resort to a contact mechanism in order to account for the nature of the paramagnetic shifts induced by lanthanide complexes. However, according to one view, the contribution of the contact interaction to the paramagnetic shifts induced by lanthanide complexes may be significant [20,21,72]. Therefore, caution must be exercised in using the paramagnetic shifts induced in the NMR spectra by lanthanide complexes for structural investigations. If the paramagnetic complex is used only to increase the ratio of the difference between the chemical shifts and the spin–spin interaction constants, it is sufficient to record the NMR spectrum of the test substance with one or several additions of the shift reagent. However, one must bear in mind that coordination to the lanthanide may influence the spin–spin interaction constants for the nuclei in the ligand molecule [107]. The suggestion that germanium–porphyrin systems be employed as shift reagents is interesting [108]. Maskasky and Kenney [108], who described a method for the formation of such systems, note, in particular, that they are diamagnetic, and, in contrast to the paramagnetic displacing agents, do not broaden the resonance lines in the NMR spectra.

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The paramagnetic complexes of lanthanides can be used to facilitate significantly the interpretation of NMR spectra,

¶ For the use of carbon disulphide as a solvent, see Walters [79].

† (VIII) = 4-picoline; (IX) = 1,2-epoxy-3,3-dimethylethane.

‡ See also Honeybourne [106].

which extends the scope of the NMR method in the study of the structures of organic ligands. Further progress in the use of shift reagents requires a more profound study of the nature of the electron-nuclear interaction in the paramagnetic lanthanide complexes. The name of the method (the shift reagent method), which has become common in the literature outside the Soviet Union, reflects exactly the consequences of the use of lanthanides. However, bearing in mind the nature of the shifts and the broadening of the resonance lines, the method based on the characteristics of the NMR spectra of paramagnetic systems should be logically termed the method of paramagnetic additives.

The NMR spectrum analysed frequently satisfies the requirements for first-order spectra but its interpretation is ambiguous owing to the uncertainty of the molecular geometry. In such cases the use of complexes of elements in the first transition series for the structural determination of organic ligands may also prove to be effective.

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Non-empirical Calculations of the Geometry and Conformations of Polyatomic Molecules

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Non-empirical methods for the calculation of the geometry, barriers to internal rotation, and conformation energies of polyatomic molecules are discussed. It is shown that the geometry can be predicted with adequate accuracy by calculations with "moderate" basis sets. Reliable estimations of barriers to internal rotation and of conformational energies require in general considerably larger basis sets. Several procedures for combining quantum-mechanical integrals are considered and the "nature" of the barriers is analysed from this standpoint.
The bibliography includes 174 references.

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I. BASIS SETS EMPLOYED IN *AB INITIO* CALCULATIONS

The previous review[1] dealt with the self-consistent field approximation and the Roothaan equations of the LCAO-MO method, on which modern calculations of the electronic structures of molecules are based, were discussed. These equations will serve as our starting point. However, in the analysis of non-empirical *ab initio* calculations one should note certain factors which are less important in semiempirical theories.

In the Hartree–Fock approximation for a molecule with a closed electronic shell, the wave function Ψ is represented by the antisymmetrised products of the spin-orbitals (SMO) Ψ_i or the Slater determinant

$$\Psi = \frac{1}{\sqrt{N!}} |\psi_1\bar{\psi}_1\psi_2\bar{\psi}_2 \ldots \psi_{N/2}\bar{\psi}_{N/2}| \qquad (1)$$

where N is the number of electrons.

There are of course no conditions under which function (1) can be an exact wave function of the molecule whatever are the exact individual SMO; also the energy defined by this function differs from the true total energy. The difference between the Hartree–Fock energy and the energy corresponding to the exact wave function has come to be called the correlation energy. As a rule, the correlation energy of a molecule is greater than the sum of the correlation energies of its constituent atoms[2,3].

The exact wave function can be approached only by going outside the framework of the single-configuration approximation (one Slater determinant is usually termed a configuration). Thus in the configuration interaction method the molecular wave function is assumed to be

$$\Psi = C_1\Psi_1 + C_2\Psi_2 + \ldots, \qquad (2)$$

where Ψ_i is one of the configurations defined as the antisymmetrised product of the spin-orbitals. The coefficients C_i can be found by the variational method[4,5], but this procedure is extremely laborious, since series (2) converges slowly. For this reason, the exact wave functions are usually sought only for atoms and diatomic molecules. On the other hand, when considering polyatomic molecules the treatment is as a rule confined to the Hartree–Fock approximation.

The second assumption usually made in quantum-mechanical calculations on molecules involves the representation of the molecular orbitals, i.e. the spatial component of the spin-orbitals Ψ_i, by a linear combination of atomic orbitals (LCAO):

$$\varphi_i = \sum_{\nu=1}^{m} c_{i\nu}\varphi_\nu \qquad (3)$$

where φ_ν are the atomic orbitals (AO) the set of which is termed the basis set.

The LCAO approximation imparts to the wave function of the molecule a specific analytical form and in addition the Hartree–Fock formulation presupposes that the best molecular orbitals of the Slater determinant are found. However, it has been shown for other examples[5-7] that, when the basis set is sufficiently large (and also flexible), then the LCAO procedure can yield the Hartree–Fock energy to within about 0.5%. The minimum energy attainable by increasing the basis set has come to be called the Hartree–Fock limit, although in fact this is more correctly the limit of the LCAO-MO approximation and not at all the Hartree–Fock energy of the molecule.

All the calculations discussed below are based on the above two approximations. The LCAO-MO approximation for molecular properties such as geometry and conformational energies, expressed in terms of the Roothaan equation, is quite acceptable. It is shown below that, for a sufficiently large number of atomic orbitals in Eqn.(3), these properties can be calculated with "chemical" accuracy, i.e. with an accuracy characteristic of experimental determinations. The procedures used to go outside the framework of the above approximations are only briefly discussed at the end of the review and the possible limits of the errors are indicated.

We shall now consider the atomic orbitals entering into Eqn.(3). In the course of more than two decades (since the end of the 1920's) Slater type functions (STO≡Slater type orbitals) have been used in all quantum-mechanical calculations on molecules:

$$\varphi = Ar^{n^*-1}e^{-\zeta r}Y_{l,m}(\theta, \varphi) \qquad (4)$$

where n^* is the effective principal quantum number, A a

normalising factor, and $Yl,m(\theta,\varphi)$ are spherical harmonics. In the radial component of the STO r is the distance from the centre and ζ the orbital exponent. The STO are known to be close in form to the true Hartree–Fock atomic orbitals which are in turn obtained by a numerical calculation and have been tabulated long ago for many atoms: at any rate, at short and long distances from nuclei, the STO are virtually identical with the tabulated data. The search for the STO contants most effective in molecular calculations has continued, since the 1930's, i.e. since the time when Slater[7] proposed formulae for the calculation of n^* and the screening constants γ entering into the orbital exponents [$\xi = (Z_e - \gamma)/n^*$, where Ze is the nuclear charge]. Clementi and Raimondi[8] tabulated the STO constants found by minimising the atomic energy up to krypton inclusive. In later studies[9,10] the STO constants were selected by taking into account the properties of the atoms in molecules.

It would appear that the STO should be ideally suitable for calculations on polyatomic molecules, since the use of a slightly extended basis set makes it possible to obtain a wave function close to the true Hartree–Fock function and on energy differing only slightly from the Hartree–Fock limit. However, the application of the STO involves mathematical difficulties associated with the calculation of many-centre integrals. Indeed it has been shown[1] that the matrix elements of the Hartree–Fock operator include the integrals $(\mu\nu/\lambda\delta)$

$$(\mu\nu/\lambda\sigma) = \int\int \varphi_\mu^*(1)\varphi_\nu(1)(r_{12})^{-1}\varphi_\lambda^*(2)\varphi_\sigma(2)\,d\tau_1 \cdot d\tau_2 \qquad (5)$$

in which there are orbitals centred on different atoms. The evaluation of one- and two-centre integrals does not present special difficulties: as a rule, they can be estimated rapidly and accurately[11–13]. However, the evaluation of three- and four-centre integrals is difficult. Although several methods have been proposed for their estimation[14,15], until recently the evaluation of each integral required on average about 1 s even on the most powerful modern computers. Moreover, the number of two-electron integrals arising in the solution of the Hartree–Fock LCAO-MO problem is of the order of N^4, where N is the number of orbitals; for example, in the case of a basis set of 20 orbitals the number of integrals is 22 155 and for a basis set of 50 orbitals the number is 814 725. The total time required for the solution of the Roothaan equations using the STO for polyatomic molecules naturally becomes very long. Therefore in the last decade Gaussian type orbitals, in which the radial component is proportional to $\exp(-\alpha r^2)$ and not to $\exp(-\zeta r)$, have come to be widely used. Namely

$$\varphi = A(\alpha)\, r^{n-1} \exp(-\alpha r^2)\, Y_{l,m}(\theta, \varphi) \qquad (6)$$

where

$$A(\alpha) = 2^{n+1}[(2n-1)!!]^{-1/2}(2\pi)^{-1/4}\alpha^{(2n+1)/4}, \qquad (7)$$

and the functions $Yl,m(\theta,\varphi)$ are in this case exactly the same as in Eqn. (4).

Although the Gaussian type orbitals (GTO Gaussian type orbitals) describe incorrectly the distribution of electron density near the nuclei and at long distance from them, the evaluation of the $(\mu\nu/\lambda\delta)$ integrals no longer presents special difficulties. It is probable that the GTO, introduced into practical molecular calculations by Boys[16] and Meckler[17], have in fact made it possible to achieve in quantum chemistry an approach to the solution of the Hartree–Fock problem for polyatomic molecules, including organic molecules[18].

It is not surprising that generally speaking the Slater basis set gives a more adequate description of molecular properties than the Gaussian basis set because the STO are close in form to the Hartree–Fock orbitals. The use of the minimal Guassian basis set (one function for each electron) results in a difference of 10–20 eV between the total energy of comparatively small molecules and the Hartree–Fock limit, whereas the difference for the minimal STO basis set is only 1–2 eV. Thus much effort has been expended in attempts to approximate the Slater orbitals in terms of the Gaussian orbitals and thereby achieve the best approximation to the Hartree–Fock limit. This idea constitutes the basis of the STO-N G method[19,20], in which each STO is replaced by N GTO.

The expansion of the Slater functions φ_S in terms of the Gaussian functions φ_g can be represented in the form

$$\varphi_s = \sum_{i=1}^{N} c_i \varphi_{g,i}, \qquad (8)$$

where c_i are the expansion coefficients and N is the parameter of the STO-N G method. Huzinaga[21] showed that, for the hydrogen atom, 6–10 GTO of 1s and 2p types yield virtually the same energy as a single STO, and determined the coefficients c_i. Subsequently Stewart[32] obtained the c_i constants also for other atoms.

The choice of N in non-empirical calculations by the STO-N G method constitutes a special problem and depends on the property which must be estimated. Experiment shows that the average time required for the evaluation of many-centre integrals with GTO is approximately 1000 times less than for computation with STO. Thus, on replacing each STO by N Gaussian type orbitals, the time gain is approximately by the factor $1000/N^4$. It is easy to calculate that the STO-2G method leads to a reduction of the time of computation by a factor of 60, the STO-3G method by a factor of 12, and the STO-4G method by a factor of 4. The STO-N G methods with $N = 5, 6, \ldots$ are no longer effective and, in order to obtain the required accuracy, it is necessary to employ the STO or, even better, an extended basis set which can be made up of both STO and GTO. Subsequently it will be shown that, for adequate estimates of many properties of polyatomic molecules including their geometry, it is sufficient to introduce 3–4 GTO for each STO.

However it is absolutely obligatory to select Gaussian basis sets in such a way that they are close to the corresponding Slater basis sets. One can begin with the condition that, provided that the Gaussian basis sets are sufficiently large, they yield a fair approximation to the Hartree–Fock limit and make it possible to predict with satisfactory accuracy the properties of polyatomic molecules. Several methods of formulating such basis sets are discussed below.

Finally one should note that comparatively recently considerable advances have been achieved in the evaluation of many-centre integrals $(\mu\nu/\lambda\delta)$ in which $\varphi\mu$, $\varphi\nu\ldots$ are the STO.[23–25] Therefore in the near future one may expect the resumption of non-empirical calculations of electronic structure, geometries, conformation energies, and other properties of polyatomic molecules with the aid of Slater basis sets. Examples of such calculations already exist[26,27].

We shall now enumerate several methods of formulating the basis set which have become common in calculations of the geometries and energies of polyatomic molecules. The results of their application and the comparative assessment of their effectiveness are discussed in succeeding sections.

1. The Slater basis set. The orbital exponents ζ are optimised with respect to the atomic energies and are assumed to be unchanged in molecular calculations; in the solution of the Roothaan equations only the coefficients $c_{i\nu}$ in Eqn. (3) are varied. Both limited (minimal)[28,29] and expanded[27] basis sets are employed in the calculations.

2. The "double-zeta" basis set. The exponential factor in the STO, $\exp(-\zeta r)$, is replaced by a linear combination of two exponents—$\exp(-\zeta_1 r)$ and $\exp(-\zeta_2 r)$. The optimal values of ζ_1 and ζ_2 have been found[30,31] for atoms with $Z \leqslant 36$ and they are assumed to be fixed in molecular calculations, only the LCAO coefficients being varied.

The basis sets discussed below are constructed from Gaussian type functions.

3. Basis sets of the STO-N G type. The problem of which values of N are to be adopted in order to obtain satisfactory estimates of molecular properties was investigated by Pople and coworkers[32-35] in relation to such properties as the geometry, barriers to internal rotation, dipole moments, and Mulliken populations. It was found that the STO-3G method yields a satisafactory approximation of the STO.

4. The LEMAO-N G basis sets (LEMAO ≡ least energy minimal atomic orbitals)[36,37]. For each atomic orbital, one introduces N GTO, the parameters of which correspond to the minimum energy of the atom. For $N \to \infty$, the energy of the molecule calculated using this basis set must necessarily tend to the Hartree–Fock limit, while in the STO-N G method the Hartree–Fock limit cannot be attained in principle for $N \to \infty$ when the Slater basis set is limited. However, specific calculations have shown[37] that the convergence of the LEMAO-N G method with increase of N is extremely slow: for low values of N (3, 4, 5), the STO-N G method is more effective; on the other hand, there is no point in a further increase of N, since the time required to calculate the total energy increases rapidly and it is then better to employ an extended Slater basis set.

5. The 4-31 G basis set[38,39]. It is constructed as follows: each orbital of the inner shell is represented by the sum of four Gaussian type functions and the valence shell orbitals are divided into two groups. The orbitals of the first group are described by three GTO and those of the second group by one GTO (in particular four GTO are required for the H atom and twenty GTO are required for the C atom). The coefficients of the expansion in terms of GTO are found from the condition for the minimum energy of the atom in the ground state. The 4-31 G basis set is more flexible than STO-3G but at the same time it is much more "expensive". This basis set yields a lower energy and, what is most important, gives satisfactory differences between the energies of various nuclear configurations. Therefore, as shown in Sections II and III, it is entirely suitable for very accurate calculations of molecular geometry, conformational energies, and particularly barriers to internal rotation.

6. The contracted Gaussian basis set. Apart from the 4-31 G basis set, one can of course employ also other extended Gaussian basis sets, and the greater the number of functions introduced for each orbital the greater the accuracy of the prediction of various molecular properties. However, an increase of the basis set entails a sharp increase of computer time. It has therefore been suggested that the Gaussian functions be grouped and that not all the coefficients $c_{i\nu}$ entering into Eqn. (3) be varied, but only those which refer to the given groups of functions[40-43]. The number of Hartree–Fock equations is then significantly reduced.

The employment of contracted basis sets permits the calculation of the structures and properties of large organic molecules. For example, the energies of various conformations of cyclo-octatetraene, whose molecule consists of 8 carbon atoms and 8 hydrogen atoms, have been calculated[44]. The authors employed five s-type and two p-type Gaussian functions for each carbon atom and two s-type functions for each hydrogen atom. This basis set can be naturally designated by (5.2/2). As a result of the "contraction" procedure, this basis set was reduced to (2.1/1) and the number of Hartree–Fock equations was decreased from 72 to 32. The coefficients within each group and the orbital exponents are usually taken from calculations for simpler molecules and are assumed to be fixed. Thus the same group functions were employed for cyclo-octatetraene as for ethylene.

7. The "lobe" GTO basis set. Whitten[40] proposed Gaussian type basis sets the orbitals of which are not centred on atoms but on certain other points in space. The possibility of employing such basis sets depends on the fact that spherically asymmetric orbitals can be imitated with some approximation by a linear combination of spherically symmetrical Gaussian functions. The spherical harmonics $Yl,m(\theta,\varphi)$ in quantum-mechanical calculations then disappear and the calculation of the integrals is significantly simplified. Thus instead of p orbitals it is possible to introduce two s-type "lobes" or two "petals" the centres of which are located on a straight line passing through the nucleus at equal distances from the latter; instead of d orbitals, it is necessary to introduce now at least four "lobes". Calculations with such basis sets then yield a fairly low total energy, provided that the number of "lobes" is fairly large. Examples of the calculation of the geometry of polyatomic molecules using the "lobe" GTO basis sets have been described[45-50].

8. The "floating orbital" basis set. So far we have considered atomic orbitals with fixed exponents and centres and the molecular orbitals were optimised only with respect to the LCAO coefficients. Nevertheless it is clear that, when the molecular orbitals are also optimised in respect of the orbital exponents and the positions of the centres of the atomic orbitals, one can achieve a closer approximation to the Hartree–Fock wave function. However, this complicates the procedure in the adjustment for self-consistency: it is necessary to solve the Roothaan equation separately for various exponents or to carry out a direct minimisation of the Hartree–Fock functional by numerical methods.

Frost[51-53] proposed a model constructed on the basis of a one orbital–one Gaussian function principle. The limitation of the basis set of this model is to some extent compensated by its flexibility, since, together with the LCAO coefficients, the parameters α_i in Eqn. (6) and the positions of the atomic orbital centres are varied. The geometry of the molecule is determined by direct minimisation of the total energy with respect to independent geometrical parameters describing the positions of the nuclei and with respect to the orbital exponents α_i. As

shown in Section II, the model of "floating Gaussian orbitals" leads to surprisingly satisfactory results owing to the "liberation" of the parameter α_i, despite the fact that, in consequence of the vast limitation of the basis set, one is still a long way from the Hartree–Fock limit.

9. Ellipsoidal Gaussian basis sets. If instead of traditional Gaussian functions (6) one employs ellipsoidal Gaussian functions[54,55], then inclusion of a comparatively small number of orbitals will presumably yield even more satisfactory geometry and energy, which do not differ markedly from the Hartree–Fock parameters. Such functions are of the form

$$\varphi_l = x_l^{\lambda_l} \exp[\alpha_l x_l^2 + \beta_l y_l^2 + \gamma_l z_l^2], \quad (9)$$

where x, y, and z are the local cartesian coordinates of the ith function and α, β, γ, and λ are the parameters varied. The ellipsoidal basis set is more flexible than the floating orbital basis set and it can therefore probably find application in conformational problems.

II. CALCULATION OF THE EQUILIBRIUM GEOMETRY OF POLYATOMIC MOLECULES

Among all the molecular properties, geometry is the most "predictable". "Predictability" must be understood in the sense that, even for very small basis sets and for very unsatisfactory orbitals, the solution of the Hartree–Fock problem yields a reasonable agreement with experiment: the deviations rarely exceed 0.1 Å in bond lengths and several degrees in valence angles. The only difficulty is that in the calculation of the geometry the total energy must be calculated more than once. If there are several geometrical parameters, it is either necessary to plot a network of values of a very complex function (total energy) or direct minimisation methods must be employed. The solution of the latter problem for molecules of any complexity is still unrealistic and therefore in non-empirical calculations one must restrict the treatment to the simplest systems. Apart from the multidimensionality of the problems, one must bear in mind that the time required to calculate the energy increases very rapidly with molecular size—much more rapidly than in empirical and semiempirical methods.

Nevertheless it is easier to calculate the geometry than any other molecular property: the total energy may be approached only by very laborious calculations by the method of configuration interaction; even an approach to the Hartree–Fock limit requires calculations with very large and very carefully selected basis sets; nor is it easy to predict with satisfactory accuracy the distribution of electron density and dipole moments; finally, in order to obtain satisfactory energy differences (bond energies, barriers to internal rotation, and conformational energies), large and fairly reliable basis sets are necessary (in estimates of bond energies one must also take into account correlation effects).

The accuracy of the prediction of molecular geometry depends on the type and size of the basis set employed in the Roothaan equations. The use of Slater orbitals permits a greater accuracy of the calculation of the bond lengths and valence angles corresponding to the total energy minimum. Even better results are obtained when one uses an extended Slater basis set taking into account the polarisation of electrons, i.e. $2p$ functions are included in addition to the s functions of the hydrogen atom and d functions are included in addition to the $2s$ and $2p$ functions of the carbon atom. However, both allowance for polarisation and calculations with STO are too "expensive". Therefore the majority of quantum-mechanical calculations on polyatomic molecules have been carried out with Gaussian type basis sets.

In the search for the equilibrium geometry of polyatomic molecules, it is reasonable to try to restrict the treatment to comparatively small basis sets, since the total energy must be calculated many times. Thus Pople and coworkers[36,56] constructed a network of total energy values at 0.05 Å intervals for bond lengths and at 5° intervals for valence angles; they then subdivided the network at 0.01 Å and 0.1° intervals after which they carried out a quadratic interpolation, which resulted in an average error of about 0.001 Å in bond lengths and about 0.1° in valence angles. Frost[52,53] sought the minimum in the Hartree–Fock functional with respect to natural molecular coordinates (bond lengths, valence angles, and angles of rotation) and orbital exponents using the extremely effective Powell method[57]. Minimisation methods designed specially for quantum-mechanical calculations on molecules have been proposed[58,59]. The use of these methods makes it possible to reduce significantly the number of returns to the procedure function (total energy) and thereby reduce computer time compared with the time required to construct the network. The advantage of direct minimisation consists also in the fact that the derivatives of the Hartree–Fock function required for the selection of the direction of the descent contain the same integrals as the function itself and therefore a considerable proportion of the expensive minimisation process is carried out "free".

Table 1. Comparison of the bond lengths and valence angles calculated using different Gaussian basis sets.

Molecule	Bond or angle	Bond length (Å) or valence angle						
		LEMAO-3G[36]	LEMAO-5G[36]	STO-2G[60]	STO-3G[56]	STO-4G[24]	4-31G[38]	expt.
H_2	H—H	—	—	0.74	0.712	—	0.730	0.742
HF	H—F	0.952	0.966	0.93	0.956	0.955	—	0.917
N_2	N—N	—	—	1.10	1.134	—	—	1.094
NH_3	N—H HNH	1.009 112.8°	1.010 115.0°	— —	1.033 104.2°	1.029 104.4°	0.991 115.9°	1.012 106.7°
H_2O	O—H HOH	0.980 107.3°	0.987 109.1°	—	0.990 100.0°	0.987 100.0°	0.951 111.2°	0.957 104.5°
HCCH	C≡C C—H	1.191 1.055	1.197 1.060	— —	1.168 1.065	1.168 1.063	1.316 1.073	1.203 1.061
H_2CCH_2	C=C C—H HCH	1.332 1.063 116.2°	1.339 1.066 116.3°	1.33 — —	1.305 1.079 115.4°	1.307 1.079 115.7°	1.316 1.073 116.0°	1.330 1.076 116.6°
$H_3C—CH_3$	C—C C—H HCH	1.566 1.065 108.6°	1.581 1.068 108.5°	— — —	1.538 1.085 108.2°	1.535 1.083 108.2°	1.529 1.083 107.7°	1.531 1.096 107.8°
H_2CO	C=O C—H HCH	1.281 1.086 118.7°	1.293 1.087 119.9°	1.21 — —	1.217 1.101 114.5°	1.217 1.099 114.8°	1.206 1.081 116.4°	1.203 1.101 116.5°

We shall now consider the results of calculations of the geometries of certain simple polyatomic molecules and shall attempt to determine which basis sets are adequate

for satisfactory estimates of bond lengths and valence angles. Table 1, which is based on a number of literature data [32,36,56,60], compares the geometrical parameters obtained with the aid of various Gaussian type basis sets—LEMAO-3G, LEMAO-5G, STO-2G, STO-3G, STO-4G, and 4-31G. Table 1 shows that the LEMAO-5G method, let alone the LEMAO-3G method, is somewhat inferior to the STO-3G and 4-31G methods in terms of agreement with experiment: the HNH valence angle in the ammonia molecule is unduly high and the C–C bond in the ethane molecule and the C=O bond in the formaldehyde molecule are too long. Consequently preference must be given to the STO expansion compared with the Gaussian type orbitals even when the latter are optimised with respect to the atoms. The convergence of the STO-N G methods with increase of N is very rapid: judging from the few data obtained by Baird [60], even within the framework of the STO-2G method, it is possible to achieve a fairly satisfactory agreement with experiment and with further approximations by the STO-N G method. One can therefore formulate the problem of the calculation of the equilibrium geometry by the relatively rough STO-2G method with the aim of investigating "less predictable" properties for this geometry—the energy, electron density, etc.—by the STO-N G method with $N > 2$ and the very "expensive" 4-31 G method.

Table 2. Bond lengths and valence angles calculated by the STO-3G method [56].

Molecule	Bond or angle	Bond length (A) or valence angle		Molecule	Bond or angle	Bond length (A) or valence angle	
		calc.	expt.			calc.	expt.
CH_4	C—H	1.083	1.085	F_2N_2	N—F N=N FNN φ	1.277 1.373 111.5° 0° (*cis*)	1.384 1.214 114.5° 0° (*cis*)
CH_3F	C—H C—F	1.097 1.384	1.105 1.385				
CH_2F_2	C—H C—F HCH FCF	1.109 1.378 108.8° 108.7°	1.091 1.358 112.1° 108.2°	H_2O_2	O—H O—O HOO φ	1.001 1.396 101.1° 125°	0.950 1.475 94.8° 111.5°
CHF_3	C—H C—F FCF	1.119 1.371 108.6°	1.098 1.332 108.8°	F_2O_2	O—F O—O FOO φ	1.358 1.392 109.5° 88.1°	1.575 1.217 109.5° 87.5°
NF_3	N—F FNF	1.386 102.1°	1.365 102.3°				

We shall consider in greater detail the results obtained with the aid of the STO-3G method. They are presented in Tables 1 and 2, the latter of which is based on the results of Newton et al. [56] In the first place mention must be made of the satisfactory agreement between the calculated and experimental bond lengths and valence angles in hydrocarbon molecules. Consequently, for the prediction of the structures of these molecules, the minimal Slater basis set (or a slightly "degraded" STO-3G basis set) prove to be entirely satisfactory. The situation is worse for molecules containing electronegative atoms or atoms with lone electron pairs. Thus the changes in the C–F bond lengths in fluoroethanes are not quite accurately represented; the bond length in the HF molecule is also excessive. The calculation does not predict the sharp shortening of the O–O bond on passing from H_2O_2 to O_2F_2; the theoretical O–F bond length in the O_2F_2 molecule is much smaller than the experimental value. The calculated valence angles do not nevertheless differ much from the experimental values even in the most unfavourable cases. However, the greatest discrepancies are again characteristic of the fluorine-and oxygen-containing molecules; in particular the calculated HOO angle in the hydrogen peroxide molecule is 6% greater than the experimental value.

The question arises of the causes of the unsatisfactory agreement with experiment for fluorine- and oxygen-containing molecules. The calculations carried out by Allen's group for simple molecules [45–50] have shown that the main reason is the limitation of the basis series: when orbitals for vacant shells are introduced, the agreement with experiment can be greatly improved. Another reason is of course the correlation effects, but these are probably small. Presumably, after the attainment of the Hartree–Fock limit, the calculated molecular geometry, including that of fluorine- and oxygen-containing derivatives, should virtually agree with the experimental geometry.

Yet another confirmation of the above hypothesis is provided by a study [61] in which the Hartree–Fock calculations were carried out for molecules as complex as that of formamide ($HCONH_2$). The basis series of these calculations included eleven s-type and seven p-type Gaussian functions for the C, N, and O atoms (one d orbital was taken into account for each of the three nuclear configurations): five s-type functions and three p-type functions were considered for the hydrogen atom. After carrying out the calculations for 44 nuclear configurations, the authors showed that the minimum total energy does indeed correspond to the observed experimental geometry of the formamide molecule.

Returning now to the assessment of the results obtained by the STO-3G method, we may note that, despite the observed deviations for several molecules, the agreement between the calculation and experiment is very good. For thirty molecules incorporating 75 individual bonds and angles, Pople and coworkers [56] obtained average deviations of 0.035 Å in the bond length and 1.7° in the valence angles. This is of course much better than can be obtained by different versions of the ZDO method [1] and particularly the CNDO method. Yet another evident advantage of the STO-3G method compared with ZDO is the absence of an arbitrary choice of parameters; the *ab initio* calculations employ only the fundamental constants e, m, and h.

Thus the STO-3G method is entirely satisfactory for the prediction of molecular geometries, at least those of hydrocarbons. The STO-2G method is apparently also fairly satisfactory. The question arises whether one could make do with only one Gaussian type function. Frost [51–53,62,63], who investigated this interesting problem, was able to show that the basis constructed from "floating orbitals" leads to a fairly acceptable accuracy of the calculation of the geometries of simple hydrocarbons, despite the fact that the total energy calculated in terms of this approximation amounts to only 85% of the Hartree–Fock energy. Table 3 presents the geometrical parameters of the five molecules found by Frost [53] by direct minimisation of the Hartree–Fock functional. It is readily seen that the calculations with a very small but flexible basis set yield an entirely reasonable agreement with experiment, which is only slightly worse than that obtained by the STO-3G method. Thus an increase of the sensitivity of the basis set achieved by varying the exponent can lead to a no less effective improvement of the calculations than an increase in the size of the basis set. For STO, this procedure is probably not quite so

effective, since the atomic exponents in the STO do not differ markedly from the optimal exponents of the atomic orbitals in molecules.

The use of floating orbitals is particularly promising in studies on the geometries of large hydrocarbon molecules. Nelson and Frost[64] found the optimal parameters of the wave function of propane and, having transferred them to n-butane and isobutane, obtained entirely satisfactory geometries of these molecules: the calculated CCC angle in n-butane was found to be 112.5° compared with the experimental value of 112.2°,[65] the corresponding values for isobutane being 111° and 111.5°.[66] The total energy was minimised only with respect to the natural molecular coordinates and the orbital exponents and even the expansion coefficients of the molecular orbitals in terms of the atomic orbitals were assumed to be fixed.

Table 3. Geometrical parameters of hydrocarbons calculated by the method of "floating Gaussian orbitals"[53].

Molecule	Bond or angle	Bond length (Å) or angle	
		calc.	expt.
Methane	C—H	1.115	1.085
Ethane	C—C	1.501	1.531
	C—H	1.120	1.096
	HCH	108.2°	107.8°
Ethylene	C=C	1.351	1.330
	C—H	1.101	1.076
	HCH	118.7°	116.6°
Acetylene	C≡C	1.214	1.203
	C—H	1.079	1.061
Cyclopropane	C—C	1.533	1.51
	HCH	114.4°	114.4—115.1°

The calculation on cyclobutane, the molecular geometry of which has been the subject of controversy for a long time, is very interesting. Only comparatively recent studies[67-69] demonstrated the non-planar structure of the four-membered ring (according to experimental data, the dihedral angle is 27—35°). Calculation[64] by the floating orbital method showed that, for the non-sectorial disposition of the HCH valence angle (Fig. 1), the planar form is less favourable than the non-planar form and only when the "tilting" of this angle is introduced as an independent parameter does the non-planar form with a dihedral angle of 32° correspond to the minimum total energy. Calculation predicts a 7° tilt (which can be readily seen from the angle shown in Fig. 1), while the experimental value[70] is 4°.

Thus calculations with very small basis sets in many cases yield an approximately correct geometry. One must not of course overestimate the scope of the floating orbital method. This method is virtually unsuitable for calculations on molecules containing lone electron pairs and molecules with conjugated bonds. The barriers and conformational energies are as a rule found to be twice as high as they should be. Thus the planar form of cyclobutane is found to be less stable than the non-planar form by 3.5 kcal mole^{-1}, while the experimental barrier to ring inversion is 1.48 kcal mole^{-1}.[68]

One should note that during the last 2—3 years many non-empirical calculations have been made on the geometry of molecules of moderate dimensions. 1,4-Dioxane[71], the planar structure of which has been predicted by the method of floating Gaussian type orbitals, and also cyclo-octatetraene mentioned above[44] may be quoted as examples. The theoretical equilibrium geometry of cyclo-octatetraene in the boat conformation (D_{2h}) is defined by the following parameters: r(C=C) = 1.340 Å, r(C—C) = 1.507 Å, and $\angle$CCC = 127.37°: these agree extremely well with the experimental parameters[72] 1.340 Å, 1.476 Å, and 126.1° respectively. The planar form of this molecule has an energy higher by 17.8 kcal mole^{-1} than that of the boat form, which is in good agreement with the experimental activation energy for ring inversion (12—15 kcal mole^{-1}).[73-76] Finally, mention should be made of calculations of the geometries of bicyclic and tricyclic hydrocarbon systems[77]: bicyclobutane, tricyclo[1,1,1,0^{1,3}]pentane, and bicyclo[1,1,1]pentane. These systems are interesting because their valence angles are highly deformed and the non-bonded atoms are very close to one another. Within the framework of the molecular force field model, it is impossible to achieve for these systems an adequate agreement between calculation and experiment[78]. Nevertheless, the employment of a contracted Gaussian basis set makes it possible to estimate the equilibrium geometry with a fairly high accuracy.

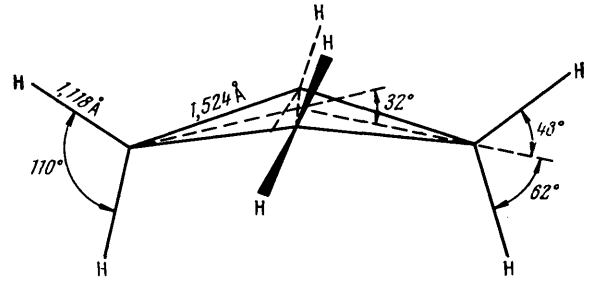

Figure 1. The calculated equilibrium geometry of the cyclobutane molecule.

III. BARRIERS TO INTERNAL ROTATION AND CONFORMATIONAL ENERGIES

Experience gained in quantum-mechanical calculations has shown that the energy associated with a molecular geometry is more sensitive in relation to the choice of the basis than the equilibrium geometry itself. Therefore, generally speaking, a satisfactory prediction of conformational energies and in particular of barriers to internal rotation requires fairly large basis sets. At any rate, the floating orbital method, constructed on the basis of the one orbital—one function principle, is clearly inadequate in this instance. It will be shown in this section that the conformational energy of any molecule can be predicted in very good agreement with experiment, provided that the chosen basis set is fairly large. This means that, when the wave function is such that the total energy is very close to the Hartree—Fock limit, the total energy differences correspond to the experimental conformational energies

and consequently the correlation effects play virtually no role.

We shall consider initially ethane—the "classical" molecule for which non-empirical calculations have been made more frequently than for any other. The complete calculation of the Hartree–Fock energies of the eclipsed and staggered forms of ethane was made for the first time by Pitzer and Lipscomb [28], who employed 16 STO: 1*s* functions for the hydrogen atom and 1*s*, 2*s*, and 2*p* functions for the carbon atom. For this basis set, taking into account the intrinsic molecular symmetry, it was necessary to calculate more than 1200 integrals in each form, a problem which appeared exceptionally difficult at the time. This was the first non-empirical calculation of a barrier to internal rotation and the resulting good agreement with experiment (3.3 compared with 2.93 kcal mole^{-1}) appeared promising.

Clementi and Davis [79] were the first to employ Gaussian type orbitals. After carrying out calculations with various basis sets, they concluded that the barrier is almost insensitive to a change of basis set. After this, it became clear that the agreement with experiment achieved by Pitzer and Lipscomb was by no means fortuitous: the Clementi and Davis basis sets led to a higher total energy (which was reasonable to expect from GTO), but the barrier differed from the experimental value by not more than 20% in all cases.

Table 4 summarises the results of seven computations of the total energies of the staggered and eclipsed forms of ethane. Veillard[84], who employed a very large Gaussian basis set with eleven *s*-type and seven *p*-type orbitals for the carbon atom and six *s*-type functions for the hydrogen atoms, obtained the smallest energy; moreover, $3d_{xz}$ and $3d_{yz}$ correlation functions for carbon atoms with an exponent of 1.5 and $2p_x$, $2p_y$, and $2p_z$ functions for the hydrogen atoms with an exponent of 1.0 were introduced. The resulting basis set, consisting of 122 functions, was contracted to 68 independent functions.

We may note that in all the calculations, except those of Stevens [83] and Veillard [84], experimental bond lengths and valence angles were employed and were seen to be unchanged on rotation. Nevertheless empirical theories predict a slight extension of the C–C bond and a decrease of the HCH angle in the eclipsed conformation. Thus Sovers and Karplus [86] calculated the equilibrium geometry of each form using the atom–atom potentials and spectroscopic deformation functions and minimising the strain energy.

They employed two types of potential: (1) the usual H...H and C...H potentials obtained from molecular beam scattering data or any other physicochemical properties and (2) the "effective" potentials yielding the barrier in ethane without taking into account the torsional term. The calculations showed that the C–C bond length increases in the eclipsed conformation by 0.01 Å when potentials of the first type are used and up to 0.1 Å for potentials of the second type; the HCH valence angle in the eclipsed conformation should be smaller approximately by 0.5° than in the staggered conformation.

In the calculations of Veillard [84] and Stevens [83] account was taken of the change in geometry, i.e. the total energy minimum was found for each conformation. The estimates of Sovers and Karplus were confirmed by non-empirical calculations: according to Veillard, the C–C bond in the eclipsed conformation increases by 0.019 Å (from 1.551 Å in the staggered form to 1.570 Å in the eclipsed form), while according to Stevens the increase is by 0.011 Å (from 1.518 Å to 1.529 Å); the HCH angle is close to the experimental value (107.8°) in both calculations, being reduced by 0.3–0.4° in the eclipsed conformation.

Veillard achieved the closest approach to the Hartree–Fock limit—according to his estimate the remaining distance to the "limit" was only 0.09 a.u. However, Levy and Moireau [87] believe that an infinite basis set would yield a further 0.3–0.4 a.u. Despite the fact that the Hartree–Fock limit has been virtually attained, it is still not clear what should be the "limiting" C–C bond length. Indeed C–C bond lengths of 1.501, 1.581, 1.538, 1.529, 1.518, and 1.551 Å have been obtained respectively by Frost's method, the LEMAO-5G method, the STO-3G method, the 4-31G method, the method based on 16 optimised STO (Stevens), and finally the method of 68 GTO based on 122 GTO (Veillard). If an accuracy of bond length of the order of 0.02–0.03 Å is required, the latter may be provided by the Hartree–Fock method with fairly large basis sets. However the question arises whether correlation effects can alter the "limiting" Hartree–Fock bond lengths by hundredths or thousandths of an Ångstrom. So far an answer to this question has not been obtained.

Table 4. Total energies of the eclipsed and staggered forms of the ethane molecule.

Basis set	Total energy, a.u.		Barrier, kcal mole^{-1}	References
	staggered form	eclipsed form		
16 STO; Slater exponents	−78.9912	−79.9859	3.3	28
16 STO; exponents optimised for CH_4	−79.0980	−79.0923	3.5	80
34 GTO	−78.5090	−78.5044	2.9	81
32 GTO based on 86 GTO	−79.1082	−79.1025	3.6	79
18 GTO based on 110 GTO	−79.1478	−79.1438	2.5	82
16 GTO with optimisation of exponents and geometry	−79.0999	−79.0946	3.3	83
68 GTO based on 122 GTO with optimisation of geometry	−79.2377	−79.2327	3.1	84
Experiment			2.93	85

"Moderate" basis sets lead to an entirely satisfactory agreement with experiment for other hydrocarbon molecules. Hoyland [88–90], who employed Gaussian type function basis sets, made a detailed study of the internal rotation in alkanes. The calculations for propane and n-butane were made with two basis sets: (5,2,2) and (7,3,3). Five *s*-type and six *p*-type orbitals ($2p_x$, $2p_y$, and $2p_z$) for the carbon atoms and two *s*-type orbitals for the hydrogen atoms were used in the (5,2,2) basis sets. [The (7,3,3) basis set yields the same total energy as the basis sets constructed from the STO with optimised exponents.] The Hartree–Fock calculations for alkanes showed that both basis sets, (5,2,2) and (7,3,3), yield virtually indistinguishable results. Consequently it is reasonable to restrict the treatment to comparatively small basis sets for estimating the conformational energies and barriers to internal rotation of hydrocarbons.

Table 5, which is based on Hoyland's results [89], presents the results of the calculation of the conformational

energies of n-butane using two Gaussian type basis sets—(5,2,2) and (7,3,3). The most striking fact is the identity of the results obtained with different basis sets. The agreement with experiment is so good that it is impossible to say which of the two basis sets is better in this sense. Therefore the calculated values of certain properties can actually be regarded as more accurate than the experimental values. Hoyland's results constitute an undoubted achievement of theoretical methods, especially when one remembers that the n-butane molecule is by no means a trivial object for empirical schemes (the conformations of n-butane were considered in particular by Borisova and Vol'kenshtein [96] and Scott and Scheraga [97]).

Table 5. Results of the non-empirical calculations of the conformational energies of the n-butane molecule.

Property	Calc. (5,2,2) basis set	Calc. (7,3,3) basis set	Expt.	References
Barrier to rotation of methyl group, kcal mole^{-1}	2.92	2.94	3.2—3.4	91
Trans-gauche barrier, kcal mole^{-1}	3.536	3.619	3.6	91
Barrier to interconversion of two *gauche*-forms, kcal mole^{-1}	6.824	6.834	5.3	92
			6.5—6.7	93
ΔE (*gauche-trans*), kcal mole^{-1}	0.822	0.761	0.770±0.09	94
Equilibrium angle of *gauche*-form	70.9°	71.3°	72.5±1.1°	95

The calculations of the conformational energies of cycloalkanes carried out by Hoyland in another study [90] are also of considerable interest. Using the experimental bond lengths and valence angles and calculating the total energies with the (5,2,2) basis set, Hoyland obtained approximately identical energies for the envelope and half-chair cyclopentane conformations, in agreement with both experimental data [98] and with the results of empirical calculations [99]. According to the calculation, the twist conformation of cyclohexane is less stable than the chair conformation by 6.05 kcal mole^{-1} and the boat conformation is less stable by 7.19 kcal mole^{-1}; the transition state is less stable by 11.22 kcal mole^{-1} relative to the chair form. These figures are also close to various experimental estimates (about 5.6, about 6.6, and about 11 kcal mole^{-1} respectively [100]).

We shall now consider molecules containing heteroatoms or lone electron pairs. Calculations of the conformational energies and barriers to internal rotation of such molecules generally speaking require larger basis sets than hydrocarbons [101]. Table 6 presents the results of the calculation of the barriers to internal rotation in several molecules of this type. The total energies of propene and its fluoro-derivatives [102] were calculated with two basis sets (A and B); basis set B was constructed by a linear combination of the orbitals of basis set A, i.e. it was less flexible. Table 6 shows that the agreement with experiment leaves something to be desired. Even the direction in which the barrier changes in the fluoro-derivatives is not reflected by the calculation: the calculated barrier in 2-fluoropropene is too small and that in *cis*-fluoropropene (with the A basis) is too large.

The reason for the not entirely satisfactory agreement with experiment is probably inadequacy of the basis set. As we have already seen for fluorine- and oxygen-containing molecules, the smallness of the basis set leads to inaccurate estimates of molecular geometries. However, such smallness affects the barriers even more. Therefore reliable calculations of the barriers to internal rotation (to within about 20%), since the remaining discrepancy may be due to correlation effects) require larger basis sets than do calculations of the geometry.

Table 6. Barriers to internal rotation in molecules with a favourable eclipsed conformation.

Molecule	Barrier, kcal mole^{-1}		Expt.
	A basis set	B basis set	
Propene	1.48	1.25	1.98
cis-Fluoropropene	1.58	1.07	1.06
trans-Fluoropropene	1.53	1.34	2.20
2-Fluoropropene	1.20	—	2.45
Acetaldehyde		1.09[82,103]	1.16

In connection with the question of the role of the basis set and the need to improve accuracy, it is interesting to examine non-empirical calculations of the energies of internal rotation in the hydrogen peroxide molecule. Table 7, which presents the results of calculations by different workers, shows that the agreement with experiment depends in a very unusual manner on the completeness of the basis set: small basis sets predict a reasonable *cis*-barrier; then, as the basis set is improved, the calculated barrier becomes too large, becoming reduced to an acceptable value only in Veillard's very exact calculation [105]. On the other hand, the *trans*-barrier is predicted only by the most accurate calculations; in other cases the energy minimum corresponds to the *trans*-form (admittedly the $E-\varphi$ curve, where φ is the angle of rotation reckoned from the *cis*-form, acquires a very low slope for $\varphi > 100°$).

Table 7. Non-empirical calculations of the barriers to internal rotation in the hydrogen peroxide molecule.

Basis set	Total energy in *trans*-form, a.u.	Barrier, kcal mole^{-1} *cis*	Barrier, kcal mole^{-1} *trans*	References
12 STO with Slater exponents	—150.1457	9.4	0	104
12 STO with exponents optimised in relation to H_2O	—150.2232	13.1	0	104
12 STO with total optimisation	—150.2353	9.4	0	83
26 GTO	—149.2641	15.9	0	81
14 "lobe" GTO	—150.7078	13.7	0	82
Extended GTO basis set	—150.7224	13.2	0.3	82
Extended GTO basis set with optimisation of geometry	—150.7992	10.9	0.6	105
22 GTO based on 40 GTO with optimisation of geometry	—150.8202	8.34	1.09	106
32 STO	—150.8319	10.9	0.72	27
Experiment		7.0	1.1	108

The optimisation of the geometry for hydrogen peroxide is more important than for ethane. Veillard's calculation showed that, on passing from the *trans*-form of H_2O_2 to the *cis*-form, the O—O bond length increases by 0.025 Å and the HOO valence angle increases by 5.35°. The angle $\varphi = 123°$ corresponds to the equilibrium concentration, which is quite close to the experimental value [107] (111.5°).

Similar results were obtained by Dunning and Winter[106], who employed an even larger Gaussian type basis set and obtained the equilibrium value $\varphi = 113.7°$. It is remarkable that the calculation carred out with 52 STO,[57] which yielded the lowest total energy, did not give rise to entirely satisfactory barriers. The reason for this is failure to optimise the geometry.

The problem of internal rotation in yet another simple molecule—disulphane (H_2S_2)—is also interesting. The study of microwave spectra[108] showed that in this molecule there should be two barriers of approximately equal height (the *cis*- and *trans*-barriers), the equilibrium angle of rotation being $\varphi = 90°36'$. The calculation[109] performed with an extended and subsequently contracted Gaussian type basis set (58 GTO based on 106 GTO) gave 9.33 kcal mole^{-1} for the *cis*-barrier, 5.99 kcal mole^{-1} for the *trans*-barrier, and an equilibrium angle of 91°16'.

Non-empirical calculations have not been made solely for molecules with "small" barriers. Various Gaussian type basis sets (with and without *d*-type functions) lead to a barrier in formamide[61] ranging from 19.4 to 21.7 kcal mole^{-1}, while the experimental values obtained from NMR spectra are in the range from 16.8 to 21.3 kcal mole^{-1} (see the previous review[1]).

Lehn et al. investigated the mechanism of inversion in aziridine and oxaziridine[110] and also in methyleneimine and the vinyl anion[111]. Using fairly large Gaussian type basis sets, they estimated the barrier to inversion of nitrogen in aziridine CH_2-CH_2-NH as 18.3 kcal mole^{-1} and in oxaziridine CH_2-O-NH as 32.4 kcal mole^{-1}. These figures agree extremely well with the enthalpies of activation obtained from the analysis of the NMR spectra of substituted aziridines and oxaziridines: 16–19 kcal mole^{-1} [112-114] and 32 kcal mole^{-1} [115] respectively.

Methyleneimine ($H_2C=NH$), which was examined in another study by Lehn[111], can undergo inversion in two ways—by rotation about the C=N bond and by the "bending" of the N–H bond. Calculations[111] carried out with a large Gaussian type basis set showed that saddle point for the "tilting" mechanism corresponds to an energy of 26 to 28 kcal mole^{-1} and the saddle point for the rotation mechanism corresponds to 57 kcal mole^{-1}. The first of these figures is virtually identical with the barriers found experimentally for similar compounds (25–27 kcal mole^{-1} [116-119]).

Finally a few words should be said about the simplest molecule in which the inversion phenomenon occurs—the ammonia molecule. Since non-empirical calculations with limited basis sets yielded low or altogether unlikely values of the barrier[120-128], it was believed for a long time that at least half of the barrier is due to correlation effects. However a recent calculation by Rauk et al.[129], taking into account the *d* orbitals of the nitrogen atom, yielded a value very close to the experimental barrier (5.08 kcal mole^{-1} compared with the experimental value of 5.8 kcal mole^{-1} [130]). This demonstrates yet again that not only rotation barriers but also inversion barriers can be fairly satisfactorily predicted within the framework of the Hartree–Fock approximation, provided that the chosen basis set is sufficiently large.

The question arises whether it is possible to make any recommendations concerning the desirability of employing particular basis sets by analysing the results of quantum-mechanical calculations. Naturally the larger the basis set the better and basis sets of the type (11.7/6), including eleven *s* and seven Gaussian *p*-type functions for each carbon or oxygen atom, which were employed by Veillard[84,124], are best in this sense. Even better is the (13.8.2/8.1) basis set, which includes three *d*-type polarisation functions of the nitrogen atom and two *p* functions of the hydrogen atom. The above calculation of the barrier to ammonia inversion was in fact performed with this basis set[129]. However the computer time at the disposal of investigators is limited and therefore a compromise must be resorted to—it is necessary to employ "moderate" basis sets and accept a reduced accuracy of the calculations.

The 4-31G basis set is regarded as a "moderate" basis set of this type.

Pople and coworkers[131] recently employed this basis set to calculate the conformational energies of twenty organic molecules containing methyl, carbonyl, and carboxy-groups and showed that in the vast majority of cases this basis set yields results close to the experimental values. Several examples of the comparison of the calculated and experimental values of the barriers to internal rotation are given below (the experimental data in kcal mole^{-1} are indicated in brackets): ethane 3.26 (2.93); methanol 1.12 (1.07); acetaldehyde 0.74 (1.16); formamide 24.7 (19); methyl ether 3.0 (2.7); acetone 0.75 (0.78–0.83). Evidently the agreement between the calculation and experiment is moderately satisfactory and therefore basis sets of this type may be recommended for large-scale estimates of conformational energies of small molecules and for conformational analysis in organic chemistry. Admittedly, as we have already seen for the ammonia molecule, one cannot always be certain that the error of the calculation is sufficiently small. However, "moderate" basis sets in all probability yield entirely satisfactory results for hydrocarbon molecules.

Table 8. Bond separation energies.

Molecule	Reaction	Bond separation energy, kcal mole^{-1}	
		calc.	expt.
Propane	$CH_3CH_2CH_3 + CH_4 \rightarrow 2C_2H_6$	1.0	1.5
Propene	$CH_3CHCH_2 + CH_4 \rightarrow C_2H_6 + C_2H_4$	4.1	5.0
Propyl	$CH_3CH + CH_4 \rightarrow C_2H_6 + C_2H_2$	8.0	7.2
Allene	$CH_2CCH_2 + CH_4 \rightarrow 2C_2H_4$	−4.6	−4.0
Cyclopropane	$C_3H_6 + 3CH_4 \rightarrow 3C_2H_6$	−30.4	−23.5
Cyclopropene	$C_3H_4 + 3CH_4 \rightarrow 2C_2H_6 + C_2H_4$	−58.0	−45.2

The differences between the energies of rotational isomers are probably just as sensitive to the basis set as the barriers to internal rotation; admittedly few calculations of this kind have been made. We shall mention in particular the work of Pople and coworkers[132], who calculated the energies of two or several conformers with two basis sets—STO-3G and 4-31G. Thus the *gauche*-form of substituted methylamines (XCH_2-NH_2) was found to be more favourable than the *trans*-form (the C–X bond in the *trans*-form is located in the same plane as the bisector of the HNH angle), when X = CH_3, while the *trans*-form is more favourable for X = OH and F. Spectroscopic data, which are available only for ethylamine[133], show that the two forms are in equilibrium. In substituted hydrazines (NH_2-NHX), the "outer" form (the N–X bond is rotated 180° relative to the bisector of the HNH angle) is more favourable than the "inner" form when X = CH_3 and less favourable for X = OH and F. Indeed infrared spectra[134] show the advantage of the "outer"

form for methylhydrazine—it constitutes more than 90% of the mixture. Calculations predict that in compounds of the type Y=N−O−H the *trans*-form is more stable for all Y (Y = CH_2, NH, or O). The experimental data on nitrous acid (Y = O) [135,136] demonstrate the preponderance of the *trans*-form. Finally, we may mention substituted di-imides (X−N=N−H) whose *trans*-form is more favourable than the *cis*-form for all X except OH. Experimental data demonstrating the advantage of the *trans*-form are available only for di-imide itself [137].

The thermochemical properties of substances are known to bear a definite relation to molecular structure and to steric hindrance. However, absolute values cannot be obtained with adequate precision within the framework of the Hartree−Fock model: the correlation corrections to the total energies are too large. However, if we are interested in the comparative thermochemical properties of a series of molecules with similar structures, such properties can be estimated assuming mutual cancellation of the correlation corrections.

Pople and coworkers [138] introduced the concept of the "bond separation" energy: these are the heats of reactions occurring with retention of the total number of formal bonds. The "bond separation" energies are a measure of the intramolecular interactions including steric strains (on the assumption of exact additivity of the bond energies, the "bond separation" energies should be zero).

Table 8 presents several examples of reactions and the results achieved by the STO-3G and 4-31G methods are compared with experimental data adjusted to 0°K and corrected for zero point vibrations. Bearing in mind that the Hartree−Fock limit is far from being attained when using Gaussian type basis sets, the agreement between the calculations and experiment must be recognised as satisfactory (the correlation corrections can indeed cancel out in systems with identical formal bonds). The "bond separation" energies are particularly large in absolute magnitude in cyclopropane and cyclopropene in consequence of the large angular deformations.

IV. THE NATURE OF THE BARRIERS TO INTERNAL ROTATION

The "nature" of the barriers to internal rotation has been the subject of discussion for a long time at the level of empirical and semi-empirical theories. Since the interatomic potentials "do not explain" the barrier in a simple molecule such as ethane, yielding an unduly low value, many theories in which one factor or another is emphasised have been put forward. Thus the breakdown of the cylindrical symmetry of electron density in rotation about the C−C bond has been treated [139,140] as the cause of the inhibiting potential [139,140]. Pauling [141,142] attributed the barrier to the presence of hybrid orbitals of the *d*- and *f*-types assuming that pure sp^3 hybridisation does not give rise to a barrier; however, 4% of *d*-states and 2% of *f*-states give rise to a barrier of about 3 kcal mole^{-1}. Calculations of the barrier on the basis of the classical electrostatic model [143−145] taking into account the interactions between the dipole and higher moments of the C−H bond also did not yield unambiguous results.

From the standpoint of modern computational methods, these theories appear naive and can be readily criticised. Actually the fact that the correct value of the barrier to internal rotation in ethane is obtained with minimal STO basis sets or extended GTO basis sets but not including vacant orbitals is sufficient to demonstrate the lack of validity of Pauling's theory.

However, despite the considerable achievements of non-empirical methods, the problem of the nature of the inhibition of internal rotation in molecules can still not be regarded as finally elucidated. The ambiguity of the interpretation of the nature of the interactions is primarily related to the fact that the integrals arising in the Roothaan equations can be reasonably combined into certain groups in several ways. Nevertheless only two fundamentally different approaches exist.

1. The repulsion energy of the nuclei V_{nn}, the repulsion energy of the electrons V_{ee}, the kinetic energy of the electrons T, and the attraction energy between the electrons and the nuclei V_{ne} are considered separately. The total repulsion energy is written in the form

$$V_{rep} = V_{nn} + V_{ee} + T \tag{10}$$

and the attraction energy in the form

$$V_{att} = V_{ne}. \tag{11}$$

After calculating in this way the attraction and repulsion energies, one can conclude that V_{rep} and V_{att} change on passing from one conformation to another, and particularly on passing from the staggered to the eclipsed form: if ΔV_{rep} is large and ΔV_{att} is small, repulsion predominates; on the other hand, if ΔV_{att} is large and ΔV_{rep} is small, attraction predominates. One cannot rule out the possibility that both terms play equally important roles.

Apart from the above resolution of the total energy, the resolution into one- and two-electron components is also of interest. $V_{nn} + T + V_{ne}$ may be regarded as the one-electron component and V_{ee} as the two-electron component. Such representation makes it possible to understand, in the first place, the role of the repulsion of electrons and, in the second place, the possibility, scope, and disadvantages of the semi-empirical one-electron approximations, in particular the extended Hückel method.

2. Instead of investigating the interelectronic and electron−nucleus interactions, the individual contributions to the total energy from the localised bond orbitals are analysed. Thus, in discussing the nature of the barrier in ethane, one speaks of the repulsion of the localised orbitals of the C−H bond (when the calculations are carried out with such orbitals) or of the repulsion of the *p* orbitals of the carbon atoms in the eclipsed conformation [146]. This approach can be naturally referred to as the "orbital" approach. It is of course less objective than the "electronic-nuclear" approach, but the degree of involvement of particular interactions is determined to a considerable degree by the choice of the basis set; however, this approach is frequently used to justify various semi-empirical and empirical theories.

Allen, who investigated both the competition between attraction and repulsion [102,103,147] and the relative effects of the one- and two-electron components [82], has been a consistent adherent of the first approach. Table 9 presents the individual components of the total energy of ethane (V_{nn}, V_{ee}, T, and V_{ne}), whence one can also see their relative changes on passing from the eclipsed to the staggered conformation (the values of the total energy components for $\varphi = 90°$, i.e. in the intermediate conformation, are also indicated). Fig. 2, which is based on data of Fink and Allen [82], presents the ΔV_{rep} and ΔV_{att} curves (*a*), the skew conformation being adopted as the starting point of the readings ($\varphi = 0$) and also curves characterising the changes in the one- and two-electron components (*b*). It is interesting that in both representations the individual components vary with different phases

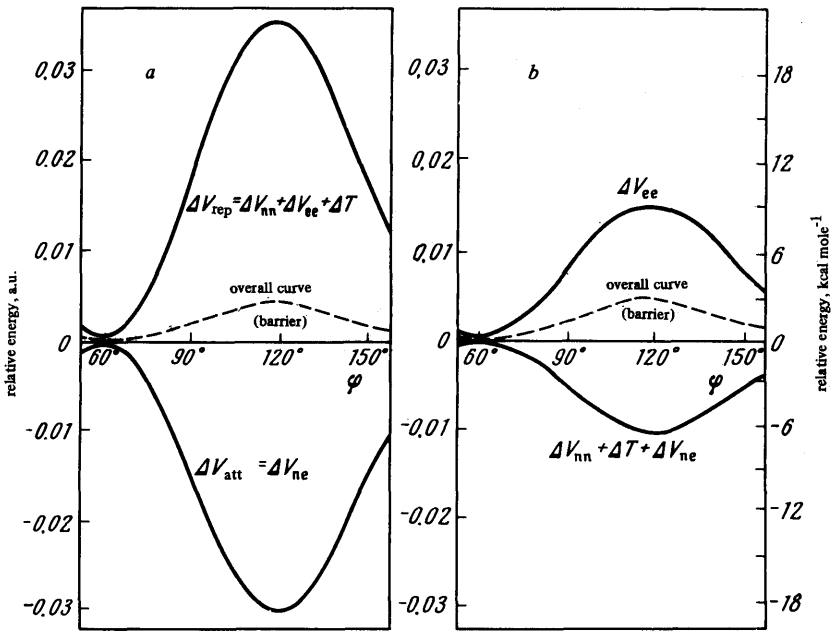

Figure 2. Variation of various components of the total energy of ethane with the internal rotation angle φ.

and the true barrier, illustrated in Fig. 2 by the dashed line, is given by a small difference between fairly large quantities. This situation is characteristic not only of ethane but also of the vast majority of molecules. This is why the experimental barriers to rotation are frequently unexpected and it is by no means always possible to make them fit any empirical rules.

The origin of the barrier in ethane can be most readily understood by examining the repulsion and attraction (Fig. 2*a*). Both terms increase markedly in absolute magnitude in the eclipsed conformation but the repulsion is nevertheless stronger. A detailed study[147] has shown that, in the space between the hydrogen atom, the electron density is significantly reduced. This leads, on the one hand, to an increase of the repulsion of nuclei in consequence of their descreening and, on the other hand, to enhanced attraction of the electrons to the nuclei. On the other hand, the repulsion of atoms constitutes a pure effect. Thus the nature of the barrier in ethane is ultimately the same as the nature of the repulsion of helium atoms at short distances[148].

Evidently the nature of the barriers in propane, n-butane, and cycloalkanes is the same (indeed, in the empirical conformational calculations used to describe these systems, one employs "ethane-like" torsional potentials). However, in molecules with a favourable eclipsed conformation, attraction is more likely to be responsible for the barrier than repulsion. In fact, it has been shown[147] that in the eclipsed conformation of the acetaldehyde molecules (CH_3CHO) the distribution of electron density between the methyl group and the oxygen atom resembles the distribution for a weak chemical bond; but on passing to the staggered form the bond is weakened.

Component-by-component analysis makes it possible to refer the barriers to internal rotation and inversion of molecules to one of two groups—R (repulsive dominant) or A (attractive dominant): if on passing from the state corresponding to the energy minimum to one corresponding to the saddle point on the energy surface, $|\Delta V_{rep}| > |\Delta V_{att}|$, then the barrier refers to group R; for opposite inequality sign, the barrier belongs to group A. In terms of this property, the barriers to rotation in methanol, methylamine, ethyl fluoride, hydrazine, ammonia, etc. belong to group R and the barriers in hydroxylamine, aziridine, hydrogen peroxide, di-imide, etc. belong to group A.[101]

Table 9. Contributions of the individual components to the total Hartree–Fock energy of ethane (in a.u.).

Conformation	V_{nn}	V_{ee}	T	V_{ne}
Eclipsed	41.93845	67.22699	79.00441	−267.3136
Intermediate ($\varphi = 90°$)	41.93469	67.21900	78.99798	−267.2972
Staggered	41.93098	67.21208	78.99142	−267.2823
Δ (eclipsed–intermediate)	0.00376	0.00799	0.00643	−0.0164
Δ (eclipsed–staggered)	0.00747	0.01491	0.01299	−0.0313

Unfortunately it is impossible to say that the component-by-component analysis does indeed reveal the "nature" of the barriers, at least in the sense which would satisfy the chemist who is unable to carry out the calculations *ab initio*. In fact having looked at the structural formula of the compound and even knowing many of its properties, the chemist is hardly able to guess whether the barrier in the given compound belongs to group R or A, let alone being able to predict the magnitude of the barrier. Component-by-component analysis is useful *aposteriori*, i.e. when the quantum-mechanical calculation has already

been performed. However, in this case too it is not always unambiguous, since the sign of the above inequality has been shown to depend for H_2O_2, H_2S_2, and PH_3 on the basis set and on whether or not the geometry has been optimised [101].

The second, "orbital" approach can also be hardly recommended, at least at the present time, since the interpretation of the results depends significantly on the choice of the basis set. We may note, in particular, that Veillard and Demuyck [109], who investigated internal rotation in disulphane (58 independent GTO based on 106 GTO), found that the cause of the *trans*-barrier is the interaction of the electrons of the S–H σ bond with the π electrons of another S atom, which may be classified as hyperconjugation. It may be that this kind of interpretation will find many supporters in the future and will even acquire some predictive power but for this it is necessary that the calculations of the barrier and the analysis of the overlap populations for a large set of molecules are carried out with equivalent basis sets.

Thus the elucidation of the nature of the barriers *aposteriori* is still hardly likely to be of serious interest to the chemist. However, accumulation of new data from quantum-mechanical calculations as well as new experimental data makes it possible to refine and in many cases reformulate the concepts established previously. An attempt to formulate rules which help to predict the least stable conformations has been made [149]: (1) the lone electron pair–lone electron pair, lone electron pair–polar bond, and polar bond–polar bond interactions lead to a considerable increase of the barrier and (2) if the lone electron pairs are located at neighbouring pyramidal atoms (or the polar bonds adjoin these atoms) then the *syn*- and *anti*-periplanar orientations are energetically unfavourable compared with the structure having the maximum number of *gauche*-interactions.

It is possible to quote many examples concerning rule (1): these are the conformations of almost all the halogenoethanes, bis-1,3-dioxolane, [150] etc. However, contrary to expectation, 1,1,2-trichloro- and tribromoethanes exist in the *gauche*-form and not the *trans*-form [151,152]. Rule (2), which Wolfe [153] called the *gauche*-effect, is confirmed both by experimental data and by non-empirical calculations on H_2O_2, H_2S_2, H_2N_2, [154] and H_2P_2. [155,156] The electron pairs in these molecules can be regarded as ligand, which are just as important as the substituents.

The so called anomeric effect [157–160], which is known in the chemistry of carbohydrates and consists in the fact that axial orientations are preferred for electronegative substituents at the anomeric 1-C centre of the pyranose ring, is an exception to rule (2). However, if one supposes that the lone electron pairs of the oxygen atom have the form of "rabbit ears" and "deviate" from one another by an angle of 120°, then the anomeric effect can be readily explained and is no longer an exception to rule (2) but provides conformation of it.

Evidently the state of affairs in this field is by no means satisfactory: despite the fact that non-empirical calculations make it possible to estimate with good precision the conformational energies and barriers to internal rotation in simple molecules, sufficiently convenient methods for the interpretation of the results have not yet been found. Neither have theories satisfactory from the chemist's point of view, whereby one can predict stable and unstable conformers without resorting to laborious computer calculations, yet been established. This is why each new calculation and each new experimental fact are valuable.

V. CALCULATIONS WITH LOCALISED ORBITALS

The ideas of the theory of localised valence bond orbitals (LVBO = localised valence bond orbitals) rest on fundamental empirical chemical postulates. Since the bond energies in molecules are additive with fair accuracy, presumably carefully selected LVBO can be transferred from one molecule to another. This implies that the wave functions for molecules of homologous series can be constructed from the same LVBO. However, the main difficulty of this approach consists in the fact that the transferred orbitals are generally speaking non-orthogonal and when account is taken of the non-orthogonality, the mathematics of the Hartree–Fock method becomes much more complicated [161]. The unitary transformation of molecular orbitals, which does not alter the Slater determinant, makes it possible [162–164] to obtain the localised orbitals b_k from the atomic orbitals φ_i:

$$b_k = \sum_i t_{ki}\varphi_i \,. \qquad (12)$$

The localised orbitals of the C–H bonds in the methane molecule are determined by symmetry considerations. However, for molecules whose symmetry is not quite so high, the localised orbitals cannot be found unambiguously and therefore in choosing the localised orbitals it is necessary to resort to particular criteria [165,166]. The criterion, examined in detail by Edmiston and Ruedenberg [166] and consisting in the fact that the b_k orbitals must correspond to the maximum in the function $\Sigma(kk/kk)$, has found the widest practical application.

Pitzer [167] used the criterion of Edmiston and Ruedenberg to calculate the LVBO for the staggered and eclipsed conformations of ethane. The localised C–C, C–H, and inner shell orbitals obtained by an iterative procedure proved to be not entirely identical for the two conformations: the greatest changes occur on internal rotation in the C–H orbitals.

The principal disadvantage of the localised orbitals determined in this way is that it is difficult to use them to explain the nature of the interactions responsible for the nature of the interactions responsible for the barrier, since the localised orbitals of the staggered conformation of ethane differ from the corresponding orbitals of the eclipsed conformation. Therefore, in order to elucidate the nature of the interactions and to prove the validity of additive empirical schemes, it appears more promising to employ orbitals transferred from one molecule to another.

Hoyland [168] attempted to apply the idea of the transferability of orbitals to hydrocarbon molecules—those of methane, ethane, propane, n-butane, and propene. The localised orbitals of the C–H bond in methane were sought in the form

$$b^{(i)}_{C\text{-}H} = N(t_i + \lambda h_i) \qquad (13)$$

where t_i are hybrid tetrahedral functions on the carbon atom directed towards the ith hydrogen atom, h_i are the 1s orbitals centred on the same hydrogen atom, and N is a normalising factor. The parameter λ was determined from the condition of the correspondence of the calculated and experimental C–H bond lengths: $\lambda = 1.097$ for the (5,2,2) Gaussian basis set and $\lambda = 1.056$ for the (5,3,3) basis set.

The orbital of the C–C bond in ethane was defined thus:

$$b_{C\text{-}C} = N(t_1 + t_2) \qquad (14)$$

where t_1 and t_2 are the hybrid orbitals on the two carbon

atoms directed to the central point in the molecule. The b_{C-H} orbitals were assumed to be exactly the same as in methane.

Calculation of the total energy of ethane using the LVBO yielded −78.493 a.u. for the (5,2,2) basis set and −78.696 a.u. for the (5,3,3) basis set, which are a little higher than the values quoted in Table 4. The calculated barrier amounts to 2.66 kcal mole^{-1} for the (5,2,2) basis set and 2.83 kcal mole^{-1} for the (5,3,3) basis set.

The results for the barrier to internal rotation in propene were not so satisfactory: 0.46 kcal mole^{-1} for the (5,2,2) basis set and 0.80 kcal mole^{-1} for the (5,3,3) basis set (the experimental value is 1.98 kcal mole^{-1}). The reason for the poor agreement between the calculation and experiment becomes understandable if one takes into account the fact that each term V_{ee} and V_{ne} in Eqn. (10) for propene changes on passing from the eclipsed to the staggered conformation by 12−26 kcal mole^{-1} (only ΔT is small), which is a factor of ten greater than the barrier. The errors associated with the inadequacy of the orbitals are fairly large for each total energy component and there is no reason to expect their mutual cancellation.

In another study[169] Hoyland employed the extended (7,3,3) Gaussian basis set and sought the localised orbitals of the C−H bond in methane in the form

$$b^{(i)}_{C-H} = N(2s + \lambda 2p_i + \delta h_i) \qquad (15)$$

where $2p_i$ are linear combinations of the $2p_x$, $2p_y$, and $2p_z$ orbitals. Instead of the single parameter (λ), two parameters (λ and δ) were varied. After transferring the localised orbitals b_{C-H} from methane to ethane, Hoyland obtained for the latter a total energy of −79.093 a.u. and a barrier to internal rotation of 2.40 kcal mole^{-1}. The author explains the comparatively low barrier by the fact that in the eclipsed conformation the wave function constructed from the LVBO is closer to the LCAO-MO wave function for the eclipsed conformation than for the staggered conformation.

Table 10 compares the calculated conformational energies of propane obtained by the LCAO-MO and LVBO methods. In the LVBO method the b_{C-H} orbitals were transferred from methane and the b_{C-C} orbitals from ethane. The closeness of the results obtained by the two methods shows that in many respects the LVBO are entirely satisfactory. However, it is clear that from a quantitative standpoint a better approximation to experiment can be achieved with delocalised LCAO-MO. This is not in fact surprising, since in using the orthogonalised valence bond orbitals one does not take into account satisfactorily the weak interactions which determine the conformational energies and the isomerisation energies of alkanes. However, the agreement with experiment for alkanes may be improved by distinguishing the C−C and C−H bonds as a function of the immediate environment as is done in Tatevskii's method[170,171]. But in this case the non-empirical calculations are reduced to the level of empirical schemes: in fact this is equivalent to postulating the desired result.

VI. CONCLUDING REMARKS

As shown in the previous sections, molecular geometry and conformational energies are quite satisfactorily predicted within the framework of the Hartree−Fock method, provided that one employs delocalised orbitals and fairly large basis sets. Since the Hartree−Fock limit has been approached for only 2−3 molecules, it is still difficult to say what corrections are introduced by allowance for correlation effects; it is only clear that these corrections are small for delocalised orbitals and very large when localised valence bond orbitals are employed.

Table 10. Barriers to internal rotation in propane calculated with delocalised and localised orbitals.

Angles of rotation, deg		ΔE, kcal mole^{-1}	
φ_1	φ_2	LCAO-MO[83]	LVBO[167]
60	60	0	0
60	0	3.134	2.616
0	0	6.971	6.097

The Hartree−Fock model, in which the electrons are considered to move in the effective field due to other electrons and nuclei, does not take into account the "collisions" of electrons, which, as shown by Gruninger et al.[172], makes the average kinetic energy too low and the average electron repulsion energy too high. The correlation energy, which is by definition[173] that difference between the exact non-relativistic energy and the Hartree−Fock energy, amounts on average to 1% of the total energy of the molecules (for example, it is 230 kcal mole^{-1} for the ammonia molecule[126]). Apart from correlation, one could also take into account relativistic corrections, but in calculations on molecules, at least those with fairly light atoms, such corrections are quite insignificant. Thus the relativistic correction for the ammonia molecule is 15 kcal mole^{-1}; however, it is determined mainly by the motion of electrons in atoms and one must suppose that it is the same for different conformations and in general for different relative positions of the nuclei.

In the calculation of the correlation energy, the many-configuration approximation or perturbation methods are employed. In the many-configuration approximation the wave function of the molecule Ψ is represented by a linear combination of functions made up of Slater determinants.

For the function to be exact, it is necessary to employ an infinitely large number of expansion terms. However, one usually restricts the treatment to finite sums and the expansion coefficients are determined from the condition for the energy minimum. The methods of perturbation theory are less accurate, but they make it possible to estimate a considerable proportion of the correlation energy by a relatively simple procedure[174].

It has been known for a long time that the second-order correlation energy $E^{(2)}$, found using perturbation theory, is small for delocalised orbitals and large for localised orbitals (although no one has found a simple explanation for this finding). Levy and Moireau[87], who investigated the effect of the correlation energy on the barrier to internal rotation in ethane, found that $E^{(2)}$ is of the order of 0.01 kcal mole^{-1} for the Slater basis set employed by Pitzer and Lipscomb[28], about 0.1 kcal mole^{-1} for the basis set constructed from the LVBO satisfying the minimal exchange conditions[167], and 0.6−0.8 kcal mole^{-1} for the basis set constructed from hybrid molecular orbitals.

Thus allowance for correlation corrections is important only for localised orbitals. Incidentally, it is precisely in this case that the correlation corrections are most

readily applied and the main idea of the semi-empirical PCILO method discussed in the author's previous review[1] does in fact consist in applying perturbation theory to localised orbitals. The correlation corrections in the non-empirical methods based on atomic orbitals should probably be small and a further approach to the Hartree–Fock limit by extending the basis set and optimising the STO or GTO exponents may serve as the main means of achieving the required accuracy.

The question arises of the prospects for the non-empirical conformational analysis. In the first place one must say that calculations of the electronic structures of molecules with average dimensions, such as those of benzene or pyridine, require several hours of computer time for a single nuclear configuration. It is also significant that such calculations require a large set of programs available hitherto only to individual specialists working in this field. Nevertheless examples are already appearing of predictions of the geometries of complex molecules such as those of bicyclobutane and bicyclopentane. Presumably in the immediate future the number of such examples will increase significantly and towards the end of the 1970's and the beginning of the 1980's, when the speed of computers is increased to 10^9 operations per second, theoretical conformation analysis of organic molecules with average dimensions will become an important instrument in the hands of chemists and physical chemists. However even then, as long as significantly new methods are not devised, the non-empirical calculations of the conformations of complex systems such as steriods, alkaloids, peptides, sugars, nucleic acids, etc. will be hardly possible. Therefore empirical models based on atom–atom potentials and semi-empirical quantum-mechanical methods retain their importance.

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Polymerisation of αβ-Unsaturated Sulphur-containing Compounds

A.V.Sviridova and E.N.Prilezhaeva

The review deals with the present state of the problem of the polymerisation of unsaturated sulphur-containing monomers with sulphide, sulphoxide, and sulphone groups in the immediate vicinity of the double bond. The mechanisms of polymerisation reactions involving various catalytic systems and the effect of the heteroatom on the polymerisation of the above monomers as well as the fields of practical application of the polymers based on them are discussed.
The bibliography includes 167 references.

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I. INTRODUCTION

Numerous studies dealing with the polymerisation of unsaturated sulphur-containing compounds have now been published. However, these investigations have not been discussed from a single standpoint and brief reviews [1-3] on this problem in certain monographs cannot claim to cover the literature completely.

Nevertheless, examination of the polymerisation of such compounds is important from both theoretical and practical points of view. For example, many polymers with enhanced thermal stability and resistance to ozone [4], organic solvents, radiation, and ageing [5] are known to contain in sulphur atoms their structure. Moreover, the problem of the polymerisation of unsaturated sulphur-containing compounds has a direct bearing on the elucidation of the nature of the interaction between the sulphur atom and the π-electron system.

The aim of the present review was to give a general and systematic account of the available data and to draw the attention of research workers to this interesting and hitherto inadequately investigated field. The review deals with the polymerisation of unsaturated compounds with sulphur-containing functional groups in the immediate vicinity of the double bond. The polymerisation of ethylenesulphonic acids and their esters will not be considered, since a fairly complete review on this subject has already been published [4].

II. POLYMERISATION AND COPOLYMERISATION OF VINYL MONOMERS CONTAINING BIVALENT SULPHUR

1. Polymerisation of Vinyl Sulphides, Divinylmercaptals, and Divinylmercaptols

A comprehensive study of the physical and chemical properties of unsaturated sulphides [6] led to the conclusion that, depending on the conditions, in the conjugation with neighbouring multiple carbon–carbon bonds the sulphur atom can (1) exhibit electron-donating properties—in the attack on the substrate by electrophilic reagents or in its interaction with electron-accepting groups, (2) can behave as an electron acceptor owing to the involvement of the d-orbitals, which occurs in certain systems where there is attack by powerful electron-donating reagents, and (3) can stabilise the free-radical state of the system when the latter is attacked by free radicals or subjected to excitation by light owing to the overlapping of the p_C-d_S or p_C-p_S orbitals formally imitating the C=C group.

However, it has been established [6] that, in contrast to alkylthioacetylenes, the sulphur atom does not behave as an electron acceptor in alkylthio-olefins, for example in their reaction with amines.

In accordance with the foregoing considerations, there are literature data only for cationic and free-radical polymerisation of both substituted and unsubstituted alkyl vinyl and aryl vinyl sulphides.

a. Cationic polymerisation and copolymerisation of vinyl sulphides. The polymerisation of αβ-unsaturated sulphides was described for the first time by Reppe [7-10], who employed BF_3, SO_2, and I_2 as catalysts. Later it was noted that in the presence of $AlCl_3$ or other Friedel–Crafts catalysts vinyl sulphides undergo copolymerisation with alkenes, forming rubber-like materials [11,12] suitable as additives to lubricating oils [13].

The polymerisation of vinyl sulphides under cationic conditions was investigated in greater depth by Soviet workers [14-18]. It was found that cationic catalysts such as $FeCl_3.6H_2O$ and $SnCl_2$, in the presence of which alkyl vinyl ethers [19] polymerise in high yields, are completely inert with respect to alkyl vinyl sulphides. In the presence of $BF_3.OEt_2$ or $SnCl_4$, alkyl vinyl sulphides form low-molecular-weight oligomers [15] ($M \simeq 1000-2000$). The nature of the reaction differs significantly from the polymerisation of vinyl ethers where negligible traces of $BF_3.OEt_2$ give rise to an explosive reaction. A considerable amount of the catalyst and prolonged heating are necessary for the polymerisation of vinyl sulphides.

The low reactivity of vinyl sulphides in relation to cationic catalysts can be explained on the one hand by the lower nucleophilicity of their double bond compared with vinyl ethers and on the other by the possibility of the formation via the sulphur atom of comparatively stable complexes of the donor–acceptor type [16,17].

It is believed[20] that the reason for the weaker mesomeric effect of the sulphur atom compared with the oxygen atom is its greater covalent radius (r) compared with the atomic radius (R). This gives rise to steric hindrance to the overlapping of the $p_C - p_X$ orbitals (a measure of the tendency towards such overlapping is provided by the ratio R/r, which amounts to 1.90 for oxygen and 1.54 for sulphur). However, the order of the reactivities of the sulphur-containing monomers in polymerisation,

$$CH_2{=}CHSPh > CH_2{=}CHOCH_2CH_2SCH{=}CH_2 > CH_2{=}CHSCMe_3 > CH_2{=}CHSEt > CH_2{=}CHSCH_2CH_2OBu > CH_2{=}CHOCH_2CH_2SEt > CH_2{=}CHSCH_2CH_2SEt$$

cannot be accounted for solely by the differences between the nucleophilic properties of the double bond. The observed phenomenon is related to changes in the basicity of the sulphur atom, which constitutes the second reaction centre in the molecule or, in other words, to the capacity of the catalyst for complex formation via this atom. The decrease of the effective concentration of the catalyst must constitute an additional factor reducing the rate of cationic polymerisation. Thus phenyl vinyl sulphide shows the highest reactivity in ionic polymerisation and yields a polymer in the presence of iron(III) chloride which is inert with respect to all other monomers of this series, while 2-ethylthioethyl vinyl sulphide does not polymerise even on very prolonged heating with $BF_3.OEt_2$. All attempts[21] at the polymerisation of the optically active (+)-s-butyl *o*-vinylbenzyl sulphide under the influence of cationic catalysts ($SnCl_4$, BF_3, $TiCl_4$, $FeCl_3$, $ZnCl_2$, and ZnI_2) at temperatures ranging from $-78°$ to 115°C did not lead to the desired results either. Moreover, the above compound not only does not polymerise under these conditions but actively inhibits the polymerisation of styrene. The fairly marked tendency of t-butyl vinyl sulphide towards ionic polymerisation[16] is consistent with its enhanced tendency towards hydrolysis in an acid medium and may be accounted for by the greater nucleophilicity of the double bonds and the steric hindrance to the formation of a complex with the catalyst.

Cationic copolymerisation data[17] are in full agreement with the results obtained in homopolymerisation. Thus phenyl vinyl sulphide forms copolymers with styrene in the presence of $SnCl_4$ and with butyl vinyl ether in the presence of both $SnCl_4$ and $FeCl_3.6H_2O$. On the other hand, ethyl vinyl sulphide forms on initiation by $SnCl_4$ only an insignificant amount of a copolymer with butyl vinyl ether. Styrene, which usually polymerises very readily under the influence of $SnCl_4$, not only does not enter into copolymerisation with ethyl vinyl sulphide but is itself not polymerised in its presence.

The polymers and copolymers obtained on the basis of vinyl sulphides have many valuable properties: they can be used as ion exchangers[22] and dielectrics[23,24], and some are fire resistant[25]. In the copolymerisation[26] of α-alkenes with compounds having the general formula $ArS(CH_2)_nCH = CH_2$ (where X = Ar or Alk; $n = 1-12$) under the influence of $TiCl_4$, Et_3Al, Et_2AlCl, and $Et_3Al_2Cl_3$, polymers were obtained which did not lose their elasticity at 140°C in the course of 360 h, whereas polypropylene becomes brittle after only 12 h.

In conclusion one must note that the cationic polymerisation of sulphur-containing monomers is determined to a smaller extent by the properties of the double bond and to a greater extent by the nature of the sulphur atom, since the latter behaves as a second reaction centre binding the catalyst and lowering thereby its effective concentration. In other reactions such as hydrolysis or the addition of an alcohol, occurring under the influence of hydrogen chloride which does not show a tendency to form thionium complexes, vinyl sulphide and particularly sulphur-containing vinyl ethers can exhibit a fairly high nucleophilic reactivity of the double bond.

b. Polymerisation and copolymerisation of vinyl sulphides under the influence of radical initiators. In contrast to cationic polymerisation, free-radical polymerisation of vinyl sulphides is faster than the polymerisation of their oxygen analogues. Thus under the influence of azobisisobutyronitrile (AIBN) vinyl sulphide polymerises readily[18,27,28] giving a high yield of comparatively high-molecular-weight products, while vinyl ethers form only low-molecular-weight compounds after prolonged heating[29]. Benzoyl peroxide (BP) cannot be employed as the initiator, since it adds to vinyl sulphides via the mechanism[30]

$$(PhCOO)_2 + CH_2{=}CHSEt \rightarrow PhC(O)OCH_2\overset{\displaystyle SEt}{\underset{\displaystyle O(O)CPh}{CH}}.$$

The enhanced reactivity of vinyl sulphides compared with vinyl ethers is difficult to explain without resorting to the hypothesis of the expansion of the valence shell of sulphur with employment of its d orbitals. The considerable contribution of the d-orbital interaction is indicated also by the higher value of the stabilisation factor for vinyl sulphides[31] ($Q = 0.3-0.5$) compared with vinyl ethers[32] ($Q = 0.015$).

The possibility of the stabilisation of the intermediate free radical by the involvement of the d orbitals of the sulphur atom was indicated for the first time by Price[33-36].

An analogous state but of a biradical type arises when unsaturated sulphide molecules are excited by light, which explains the bathochromic shifts in their ultraviolet spectra[36].

The breakdown of coplanarity is of course found to entail a decrease of the resonance stabilisation of the radical[36]. Thus, in the copolymerisation of pentachlorophenyl vinyl sulphide initiated by AIBN, Holly[37,38] obtained $Q = 0.23$, whilst for phenyl vinyl sulphide[35] $Q = 0.32$. The decrease of Q for pentachlorophenyl vinyl sulphide is due to the *ortho*-effect of the chlorine atoms, resulting in a breakdown of coplanarity. The high value of the factor Q (0.6 ± 0.1) for divinyl sulphide[33] can be explained by the possibility of the additional resonance stabilisation of the intermediate radical:

$$\sim CH_2{-}\dot{C}H \leftrightarrow \sim CH_2{-}\underset{\displaystyle :S:}{\underset{|}{CH}}{-}\dot{C}H_2 \leftrightarrow \sim CH_2{-}\underset{\displaystyle :S}{\underset{\|}{C}}{-}\dot{C}H_2$$
$$\quad\quad\quad

A study of the polymerisation of *para*-substituted phenyl vinyl sulphides[40] established that the reactivity of the monomers in relation to the polymeric radical is directly related to the σ constants of the substituents. A similar tendency was observed also in the copolymerisation of such monomers with one another. It was found that their reactivity depends markedly only on the polar effect of the substituent, while in the polymerisation of substituted styrenes[41] the polar and resonance effects play equally important roles. The fairly high values of Q (Table 1) yet again indicate the possibility of the 3*d* orbital interaction of the sulphur atom with an adjacent radical centre.

Table 1. Copolymerisation of *p*-substituted phenyl vinyl sulphides (M_2) with styrene (M_1) and methyl methacrylate (M_1) at 60°C.

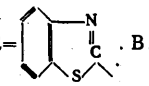
M_1	*p*-Substituent in M_2	r_1	r_2	Q	e
Styrene	MeO	3.98	0.18	0.35	−1.40
	Me	3.65	0.25	0.35	−1.10
	H	3.88	0.36	—	—
	Cl	3.57	0.32	—	—
	Br	3.42	0.31	—	—
Methyl methacrylate	MeO	0.77	0.04	0.46	−1.47
	Me	0.81	0.07	0.47	−1.29
	H	0.85	0.08	0.45	−1.26
	Cl	0.89	0.08	0.45	−1.24
	Br	0.85	0.20	—	—

Vinyl sulphides not only readily polymerise under free-radical conditions but they also copolymerise vigorously with other monomers[39,42–49]. The reactivities of the radicals derived from various monomers in relation to vinyl sulphides decrease in the sequence vinylcaprolactam[50] > methyl acrylate > methyl methacrylate > styrene, which is consistent with the reactivities of these radicals in relation to other monomers described in the literature[51].

It has been noted that any mixtures of ethyl vinyl sulphide with butyl vinyl ether in the presence of AIBN yield copolymers greatly enriched in ethyl vinyl sulphide units. Data for the compositions of the copolymers obtained from these monomers and methyl methacrylate show that in this case the sulphide monomers are more reactive than their oxygen analogues. Whereas the copolymers of vinyl ethers with the majority of monomers (for any composition of the initial mixture) contain as a rule not more than 50 mole % of vinyl units, vinyl sulphides can yield copolymers with a very high content of sulphide units. For example, in the copolymerisation of bis-(4-vinylphenyl)-sulphide (M_2) with styrene (M_1) the following monomer reaction factors were obtained[52]: $r_1 = 0.60$; $r_2 = 1.50$.

The reactivities of alkyl vinyl sulphides $AlkSCH{=}CH_2$ (M_2), where Alk = Me, Et, i-Pr, n-Bu, i-Bu, t-Bu, $PhCH_2$, and Ph, and of ethyl vinyl ether (M_3) in relation to various polymeric radicals M_1 (styrene, methyl methacrylate, and acrylonitrile) have been compared[31]. The authors obtained the empirical relation $\lg(k_{1,2}/k_{1,3}) = -0.188e_1 + 1.14$, which is in good agreement with the rearranged Alfrey-Price equations $\lg(k_{1,2}/k_{1,3}) = \lg(Q_2/Q_3) - (e_2 - e_3)e_1$. The differences between the polar and resonance factors for alkyl vinyl sulphides and ethyl vinyl ether were determined from the latter expression:

$$e_2 - e_3 = 0.43; \quad Q_2/Q_3 = 13.8.$$

The nature of the second substituent in vinyl sulphides does not influence significantly either their polymerisation or the degree of their involvement in copolymerisation[31,43]. However, it has been noted that, in the copolymerisation with styrene, phenyl vinyl sulphide is somewhat more reactive than alkyl vinyl sulphides and in homopolymerisation the rate of reaction decreases for $R = CH_2CH_2OH$ and particularly for R=  . B. On the other hand it has been stated[53] that vinylthiobenzothiazole polymerises readily in the presence of boron trialkyls or AIBN.

The rate of copolymerisation of vinyl sulphides with other monomers and their capacity for the formation of alternating copolymers increases in the sequence[31] styrene < methyl methacrylate < acrylonitrile, which parallels the sequence of the electron-accepting capacities of the monomers.

Although a spectrophotometric study of the synthesis of alternating copolymers of alkyl vinyl sulphides with acrylonitrile failed to reveal charge-transfer complexes[31] (CTC), the finding that isobutyl vinyl sulphide can copolymerise with acrylonitrile also in the absence of a radical initiator shows that charge-transfer complexes of the contact type can be formed and can be involved at least in the initiation of such copolymerisation.

At the same time the formation of such a complex has been confirmed spectrophotometrically[54] for the copolymerisation of vinyl sulphides with maleic anhydride. The equilibrium constant for its formation has been determined as 0.035 ± 0.007, while the analogous constant for vinyl ethers is 0.027 ± 0.002. This is related to the difference between the ionisation potentials of vinyl sulphides and vinyl ethers.

The copolymerisation of benzyl vinyl sulphide with SO_2 also proceeds with formation of charge-transfer complexes[55]. Copolymers with equal numbers of units were obtained from methyl vinyl sulphide and vinylene carbonate[56]. Attempts to copolymerise vinyl sulphides with phenylacetylene were unsuccessful[57].

Unfortunately the kinetics of the polymerisation of vinyl sulphides have so far been investigated very inadequately. One can mention the study of Tsuda et al.[58], who carried out the homopolymerisation of phenyl vinyl sulphide and calculated the apparent rate constant, the activation energy, and the entropy of reaction. In the course of a study of the copolymerisation of methyl vinyl sulphide with styrene, the propagation rate constant was determined[59] as 240 litre $mole^{-1}$ min^{-1}. Finally Koton and coworkers[60] determined the activation energy for the polymerisation of phenyl *p*-vinylphenyl sulphide, which proved to be 15.5 ± 1.2 kcal $mole^{-1}$.

In the majority of cases the information concerning the polymerisation of vinyl sulphides is descriptive. Thus it has been reported that the optically active (+)-s-butyl *o*-vinylbenzyl sulphide polymerises spontaneously[21]. When the process is carried out in the presence of AIBN, the product is a polymer with a high optical activity, which completely disappears when the polymer is acted upon by Raney nickel.

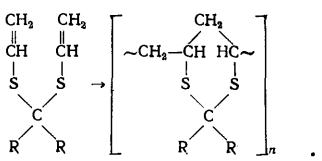
Graft-polymers from amine-containing vinyl sulphides and poly(alkyl acrylates) were obtained by radiation-induced polymerisation[61].

According to patent data, alkoxyalkyl vinyl sulphides readily polymerise and copolymerise with vinyl-containing compounds [62-66], such as derivatives of acrylic acid, vinyl chloride, vinylidene chloride, vinyl, allyl, and methylallyl ethers, and styrene and its derivatives. The polymers and copolymers are capable of being cross-linked [63,66] on heating as a result of transesterification or, in oxidation under mild conditions, as a result of the formation of a disulphide linkage. More vigorous oxidation (aqueous solution of hydrogen peroxide in an acid medium) leads to the formation of sulpho-groups and cation-exchange resins [63,64] which are superior in their ion-exchange properties to the cation exchangers based on polystyrenesulphonic acid [64].

Many patents describe the properties of the polymers and copolymers of vinyl sulphides [22,23,67-69]. It has been stated that thermoplastic polymers [70] with rubberlike properties [71-74], which are suitable for the formation of films and auxiliary materials in the textile industry, can be obtained on the basis of vinyl sulphides. Elastomers [75] with exceptional stability at high temperatures are formed in the copolymerisation of alkyl vinyl sulphides with ethylene in the presence of a small amount of allyl acrylate employed as the vulcaniser. Rubberlike copolymers have been obtained from butadiene and divinyl sulphide by copolymerisation in an emulsion [73]. The same sulphides are recommended as additives to styrene in order to improve the dielectric properties of polystyrene in relation to high-frequency currents [76].

It has been noted [77] that poly(alkyl vinyl sulphides) have higher glass points than the corresponding poly(alkyl vinyl ethers), which is due to the greater density of cohesion energy in the former.

More complex derivatives of the vinyl sulphide series (divinylmercaptals and divinylmercaptols), obtained by the dehydrochlorination of the corresponding bis-(β-chloroethyl)mercaptals and bis-(β-chloroethyl)mercaptoles, polymerise with formation of rubberlike polymers [78]. The polymerisation of the above monomers is carried out in the presence of AIBN (0.1–2 mole%) at 60–80°C both in bulk and in solution. The study of the properties of these polymers showed that the polymerisation proceeds mainly via an intermolecular–intramolecular mechanism with formation of rings in the chain, as in the radical polymerisation of divinylacetals [79]:



Depending on the conditions, linear or cross-linked polymers are obtained [80]. Polymerisation in solution and a low degree of conversion favour the formation of a linear polydivinylmercaptal containing cyclic units in the main chain and soluble in chloroform, benzene, and tetrahydrofuran (THF). Divinylthioacetal, divinylthiobutyral, and the divinylthioketal of acetone cyclopolymerise under the influence of AIBN, [81] forming soluble rubberlike polymers with $[\eta] = 0.1-0.2$. Under analogous conditions, divinylthioformal gives rise to a cross-linked polymer.

The polymerisation of a series of formaldehyde *S*-vinyl mercaptals under the influence of various initiators was investigated by Ringsdorf and coworkers [82]. In contrast to benzoyl peroxide, AIBN leads to polymers with $M = 27\,000$. In the presence of cationic catalysts, only small amounts of oligomers are obtained (owing to the formation of sulphonium ions).

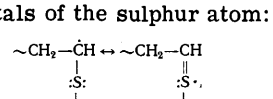
2. Polymerisation of Vinyl Thioacylates

The polymers synthesised on the basis of vinyl thioacylates have aroused considerable interest primarily because they can be used to prepare high-molecular-weight products containing mercapto-groups. The combination of the mercapto-group with a macromolecular structure leads to substances which are important in practice. Such polymers have been suggested as specific ion exchangers and protective agents against radiation [83,84] and also as model compounds for the elucidation of the role of the mercapto-group in certain enzymes [85]. The synthesis of the above polymers by the direct polymerisation of vinylmercaptans presents considerable difficulties owing to the low availability of the latter. Nevertheless, hydrolysis of polymers of vinyl thioacetate, preferably with a 10% NaOH solution in methanol, leads to the formation of polymers containing free mercapto-groups [86]. Polymeric protecting agents against radiation have been obtained by treating with hydrazine hydrate copolymers of vinyl thioacetate with *N*-vinylsuccinimide and *N*-vinylphthalimide [87]. However, these copolymers proved to be very unstable and were readily oxidised on standing in air, yielding insoluble strongly swelling products. The study of the kinetics of the oxidation of polyvinylmercaptan and its model low-molecular-weight analogues with molecular oxygen in various aprotic solvents in the presence of iron sulphate showed [88,89] that the rate of the reaction involving polyvinylmercaptan is more than ten times faster than that involving pentane-1,5-dithiol. For this reason, polythiols are used as cross-linking agents [86]. In most cases the oxidation of polythiols leads to the synthesis of insoluble polymers as a result of the formation of intermolecular disulphide bridges, but, depending on the oxidant, other derivatives can also be obtained. Thus, when stronger oxidising agents (for example HNO_3) were employed, polysulphonic acids were isolated [90].

Water-soluble copolymers containing mercapto-groups have been synthesised from *p*-vinylphenyl thioacetate [91,92]. The polymerisation and copolymerisation have been carried out under the influence of radical initiators. The solubility of the polymers decreased markedly on acidification.

The polymerisation of vinyl thioacetate has been investigated in greater detail [87,93]. It was established that the monomer polymerises fairly readily in the presence of AIBN and copolymerises under these conditions with *N*-vinylsuccinimide, *N*-vinylphthalimide, and *N*-vinylcarbazole. The polymerisation kinetics are characterised by a constant for chain transfer to the vinyl thioacetate molecule $C_M = 0.056$ at 60°C. For comparison Table 2 presents the constants for chain transfer by the monomer for certain vinyl esters.

The authors explained the observed phenomenon by the stabilisation of the radical centre as a result of the involvement of the *d* orbitals of the sulphur atom:



This is in full agreement with spectroscopic data and the chemical behaviour of vinyl thioacetate in free-radical addition reactions [98].

When the reactivities of vinyl acetate ($Q = 0.028$; $e = -0.30$) and vinyl thioacetate ($Q = 1.67$; $e = -1.34$) in

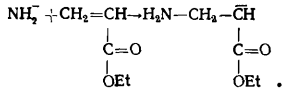
copolymerisation with *N*-vinylsuccinimde were compared, it was found that the replacement of oxygen by sulphur greatly enhances the reactivity of the monomer in copolymerisation.

Table 2. Constants for chain transfer by the monomer (C_M) for certain vinyl esters.

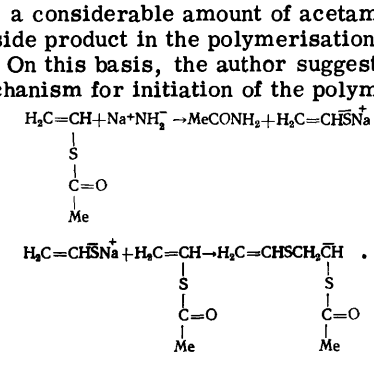
Monomer	Temp., °C	$10^3 C_M$	References
Vinyl acetate	60	0.15	94
Vinyl pelargonate	60	1.5	94
Vinyl stearate	60	2.3	94
Vinyl benzoate	79.6	0.7	95
Vinyl salicylate	70	8.0	96
Allyl acetate	70	0.723	97

Vinyl thioacetate copolymerises with methyl methacrylate [99], vinylene carbonate [100], diethyl maleate [101], maleic anhydride, and diethyl and dimethyl fumarates [102]. The products of the hydrolysis of the copolymers of vinyl thioloacetate and diethyl maleate can be used as cation-exchange resins and bases for coatings. After treatment with concentrated KOH solution in methanol, the copolymers of vinyl thioacetate and ethylene are converted into elastic materials which do not burn even at 250°C. [103,104]

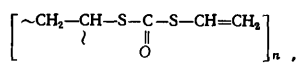
Liquid polymers of vinyl thioacetate have been obtained by its polymerisation with sodium in liquid ammonia [105]. According to elemental analysis and infrared spectra, under these conditions the polymers underwent ammonolysis and contained disulphide rings. The polymers have been used as protective agents against radiation. The polymerisation of vinyl thioacetate was investigated in greater detail by Leonard et al. [106] who showed that, in the polymerisation of vinyl thioacetate under the influence of sodium in liquid ammonia, polymers containing intramolecular and intermolecular disulphide bridges and mercapto-groups are formed, while thioacetate groups are completely absent (as a result of ammonolysis). It was established by elemental analysis that the polymers formed contain less than one amide group per polymer chain, which distinguished them from methacrylonitrile, methyl acrylate, ethyl acrylate, and n-propyl acrylate polymers for which initiation under these conditions takes place with participation of the amide anion [107,108]:



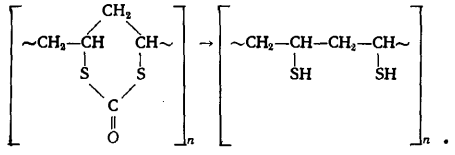
Moreover, a considerable amount of acetamide is formed as a side product in the polymerisation of vinyl thioacetate. On this basis, the author suggested the following mechanism for initiation of the polymerisation [106]:



Depending on the conditions, the *SS'*-divinyl ester of dithiocarbonic acid $(H_2C{=}CH{-}S{-})_2C{=}O$ forms a mixture of soluble and insoluble polymers [109], the soluble part consisting mainly of a polymer with *S*-vinyl thiocarbonate side chains:



If the polymerisation proceeds via an intramolecular-intermolecular mechanism, a soluble polymer containing trimethylene dithiocarbonate rings linked by methylene bridges is formed. These polymers can be converted into polyethylenethiols by subsequent alkaline hydrolysis:



III. POLYMERISATION AND COPOLYMERISATION OF VINYL MONOMERS CONTAINING OXIDISED SULPHUR

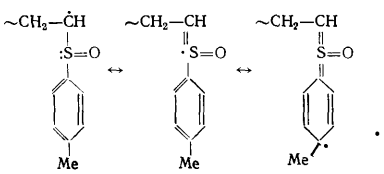
In contrast to α-vinyl sulphides, the double bond in α-vinyl sulphones and sulphoxides is highly activated in relation to nucleophilic reagents [6]. On the other hand, free-radical addition reactions are not very characteristic of such compounds. For example, thiols hardly react with vinyl sulphones on prolonged standing in air; in the presence of AIBN and on heating, a very slow reaction is observed [110]. The lower tendency of αβ-unsaturated sulphones to undergo homolytic addition reactions is explained by the fact that the sulphonyl group is incapable of stabilising adequately the free-radical state [34].

Numerous studies have been made on the structures of the sulphoxide and sulphone groups, the majority of which have been analysed in reviews [111-113]. Despite some conflict among the data obtained using different physical and chemical methods, one can regard it as proved that in the sulphone and sulphoxide groups there are linkages between sulphur and oxygen approaching in their properties a double bond. The *d* orbitals of the sulphur atom play a significant role in these linkages; the linkages are not of the "pure" semipolar type as has been suggested [36,114,115]. There is of course no complete analogy between these multiple bonds and the C=O bond of the keto-group. Firstly the S=O bonds are formed by atoms with much greater electronegativity differences than those between C and O, which enhances their polarity. Secondly these are $p_\pi - d_\pi$ bonds, in contrast to the $p_\pi - p_\pi$ double bonds. Therefore the problem of the conjugation of these bonds with unsaturated systems is also more complex. Nevertheless, the majority of investigators believe that conjugation with a sulphonyl group does not involve the S=O bonds but is limited to the involvement of the *d* shell of the sulphur atom. Examination of the polymerisation of these compounds leads to the same conclusion.

1. Synthesis of Polymers Containing Sulphoxide Groups

Polymers containing sulphoxide groups should in principle possess a set of interesting properties characteristic of their low-molecular-weight analogues, which serve as extracting agents for metals [116] and flotation

agents [117], and behave as physiologically active substances [118]. However, until recently these polymers were not obtained by the direct polymerisation of vinyl sulphoxides. It was believed [3] that the sulphoxide group inhibits both radical and ionic polymerisation. Indeed it was noted that methyl vinyl sulphoxide does not undergo homopolymerisation in the presence of radical initiators [119]. However it does copolymerise with styrene and methyl methacrylate giving low yields of copolymers with a low content of sulphoxide groups. Nevertheless, this was sufficient to determine the copolymerisation parameters and to calculate $Q = 0.10$ and $e = 0.9$. The low value of the resonance stabilisation factor compared with, for example, methyl vinyl sulphide [34] ($Q = 0.35$), led to the conclusion that there is no conjugation between the vinyl and sulphoxide groups or such conjugation is very weak. On the other hand, in the copolymerisation of the optically active *p*-tolyl vinyl sulphoxide (M_1) with styrene (M_2) a higher value of r_1 ($r_1 = 0.1 \pm 0.07$; $r_2 = 5.77 \pm 0.10$) was found [120] than for methyl vinyl sulphoxide (M_1) in its copolymerisation with the same monomer ($r_1 = 0.01$; $r_2 = 4.2$). This is probably related to the additional possibility of the delocalisation of the unpaired electron:



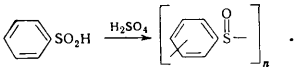
Polymers containing sulphoxide groups have been obtained by an indirect method†: by the polycondensation of sulphoxide-containing bifunctional compounds and by the oxidation of polythioethers or the products of the reaction of mercaptans with rubbers. Thus a sulphoxide-containing polycarbonate with a melting point of 230–250°C was obtained [121] by the reaction of phosgene with bis-(4-hydroxyphenyl) sulphoxide. The polycarbonate [122] based on bis-(4-hydroxy-3-methylphenyl) sulphoxide melts at 190°C.

Poly(phenylene sulphoxides) suitable for the formation of fibres, films, and high-temperature adhesives have been obtained [123] by the oxidation of the sulphide bridges in poly(phenylene sulphide) with nitric acid. The polymers are stable above 600°C. Other poly(phenylene sulphoxides) were obtained similarly [124] and were used to prepare, after heat treatment at 350–700°C in argon, thermostable non-combustible polymers [125].

The oxidation of polythietanes with one equivalent of hydrogen peroxide leads to the corresponding sulphoxides [126].

Polymers containing the sulphoxide group in the side chain have been obtained by the oxidation with hydrogen peroxide of the products of the addition of mercaptans to polybutadiene [127]. The authors noted that in all such cases sulphone as well as sulphoxide groups are formed and explained this observation by the different solubilities of the polymer in the course of the oxidation process. However, we showed [128,129] that, even when the medium remains homogeneous in the course of the oxidation of polymeric thioethers, selective oxidation cannot be achieved. The polymer contains sulphone as well as non-oxidised sulphide groups in addition to the sulphoxide groups. Moreover, the non-selectivity of the oxidation is also observed when acetic anhydride is used as a solvent, although it was established previously that monomeric sulphides are oxidised selectively in this medium to the sulphoxides [130,131]. The unusual behaviour in the oxidation of the sulphur atoms in the polymer is probably associated with the conformation of the polymer chain which hinders the approach of the oxidant to certain sulphide groups.

A polymer of the sulphonium type was obtained by the reaction of poly(methyl *p*-vinylphenyl sulphide) with dimethyl sulphate; this can be converted in turn into a sulphoxide polymer by treatment with a mixture of dimethyl sulphoxide and benzaldehyde in the presence of potassium t-butoxide [132]. Finally arenesulphinic acids form polymeric sulphoxides on dissolution in concentrated sulphuric acid [133]. Thus benzenesulphinic acid gives a 50% yield of a solid product which swells in alcohol and was shown subsequently to have the following structure [134]:



Direct polymerisation of vinyl sulphoxides was achieved for the first time by ourselves [129,135]. It was found that, contrary to the existing hypothesis concerning the inhibition of the polymerisation by the sulphoxide group, vinyl sulphoxides undergo homopolymerisation when acted upon by anionic catalysts. Naphthylsodium and the sodium–naphthalene complex were used as such catalysts. The process is fairly rapid and leads to the formation of oligomers ($M \simeq 2000$).

We may note that the rate of polymerisation of ethyl vinyl sulphoxide is somewhat lower than that of the corresponding sulphone, which may be related both to the lower nucleophilicity of the double bond in vinyl sulphoxides [6] and to the reduction of the efficiency of the catalyst in consequence of complex formation involving the sulphoxide group [136].

All attempts to polymerise vinyl sulphoxides under free-radical conditions failed despite the wide variety of initiators and conditions employed [129]. Nevertheless an inhibiting effect of sulphoxide groups is unlikely in this instance. It is sufficient to recall that dimethyl sulphoxide is quite widely used as a solvent in radical polymerisation processes and does not cause the destruction of the radical centres.

2. Polymerisation and Copolymerisation of Vinyl Sulphones

The polymerisation of $\alpha\beta$-unsaturated sulphones has been little investigated hitherto and is largely described in patents. According to these data, the polymers obtained from vinyl sulphones have valuable technical properties [137–141]. Thus the introduction of the sulphone group into the polymer increases its thermal stability and resistance to benzene [142,143]. The copolymers of dialkenyl sulphones [144] are recommended as additives to lubricating oils to improve their viscosity index. Vinyl sulphones are copolymerised with acrylonitrile and vinyl ethers in dimethylformamide [145] in order to obtain very strong thermostable and readily dyed fibres. Copolymers based on isopropenyl sulphones $RSO_2(CH_3)C{=}CH_2$ (R = alkyl, aryl, or alkylaryl) and vinyl acetate, methyl acrylate,

† Although these methods have no direct bearing on the polymerisation of vinyl sulphoxides, nevertheless it is thought necessary to examine them in this review since, as stated above, until recently polymers containing sulphoxide groups were not obtained by direct polymerisation.

styrene, acrylonitrile, and vinyl chloride are recommended for the synthesis of strong sheets, films, and compositions susceptible to mechanical treatment (moulding, extruding)[146]. Materials suitable for the formation of films and protective coatings and distinguished by a satisfactory capacity for being dyed are obtained by the copolymerisation of aromatic vinyl sulphones having the general formula $XC_6H_4(CH_2)_nY(CH_2)_2SO_2CH=CH_2$, where $X = SO_3H$, or SO_2CH_3 and $Y = O$, NH, or NC_2H_5, with acrylonitrile and vinyl chloride[147].

The study of the polymerisation of vinyl sulphones established that, despite their low tendency to undergo free-radical addition reactions, radical polymerisation of ethyl vinyl sulphone is fairly rapid and leads to a quantitative yield of the polymer[129,148]. Moreover, the rate of polymerisation of ethyl vinyl sulphone is higher than that of the corresponding sulphide[128], which may be explained by the absence of conjugation between the sulphenyl and vinyl groups in ethyl vinyl sulphone. This hypothesis had been proved earlier by Price[34,35], who obtained a very low reactivity factor ($Q = 0.07-0.11$) in a study of the copolymerisation of methyl vinyl and phenyl vinyl sulphones with styrene and vinyl acetate, in contrast to the corresponding sulphides ($Q = 0.35$).

At the same time one should note that, although the rate of homopolymerisation of ethyl vinyl sulphone is fairly high, it is possible to obtain only polymers with a low molecular weight. It was established subsequently[129] that the chain transfer constant for ethyl vinyl sulphone ($C_M = 0.087$) is very high, approaching the value of C_M for allyl acetate[97] and allyl chloride[149].

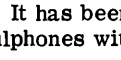
It might have been supposed that this is due to the presence of the mobile α-hydrogen atom, as happens in the polymerisation of various *S*-vinylmethylene disulphones[150,151]. The latter are known to form only oligomers under both free-radical and ionic conditions. This is due to the chain transfer by the active methylene group, the degree of polymerisation falling with increase of the acidity of the CH_2 group.

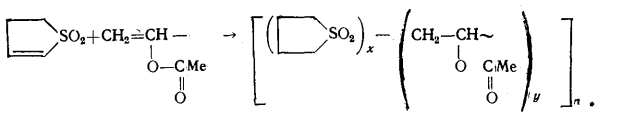
However, a study[129] of the kinetics of the polymerisation of ethyl vinyl sulphone under the influence of benzoyl peroxide showed that not only a high constant for chain transfer to the monomer and independence of the molecular weight of the polymer of initiator concentration but also an approach to unity of the reaction order with respect to the initiator is observed. Moreover, the activation energy for the process proved to be 23.8 kcal mole^{-1}, which is also somewhat high. All these findings indicate the formation of stable radicals in the process.

Stable radicals are probably formed as a result of the involvement of the SO_2 group in the chain transfer reaction. This is demonstrated also by the decrease of the rate of polymerisation in the presence of diethyl and dimethyl sulphones[129].

As expected, the anionic polymerisation of vinyl sulphones proceeds at a high rate, but, as in radical polymerisation, it leads to the formation of only low-molecular-weight products[129]. The low efficiency of the catalysts employed is also striking. In this case intense chain transfer is probably accompanied by the deactivation of the catalyst both as a result of metallation[152] and the formation of a complex via the oxygen atom of the sulphonyl group[153]. The unsuccessful attempts at the polymerisation of ethyl vinyl sulphone under the influence of Ziegler catalysts and boron alkyls[129] can also be evidently explained by the possibility of complex formation.

In the anionic copolymerisation of butyl vinyl sulphone with acrylonitrile a tendency was noted towards the formation of alternating polymers, which the authors attributed to steric effects[154]. $\alpha\beta$-Unsaturated sulphones copolymerise fairly readily with other monomers[155,156].

It has been noted that the copolymerisation of allyl sulphones with vinyl monomers leads to high-molecular-weight products[157]. 3-Sulpholene  does not polymerise at a "moderate" temperature (about 60°C); at an elevated temperature (80–140°C) a copolymer with alternating butadiene and SO_2 units is formed[158,159]. Although 2-sulpholene does not form homopolymers it does copolymerise with vinyl acetate[160]:



The highest sulpholene content in the copolymer does not exceed 50%, and an appreciable decrease of the viscosity of the copolymer is observed with increase of the sulpholene content in the monomer mixture.

Numerous data have been published in patents on the copolymerisation of vinyl sulphones[142-147,161-167]. Thus an interesting method for the preparation of cross-linked sulphone polymers includes the synthesis of oligomers capable of further polymerisation or copolymerisation with vinyl monomers[162]. The oligomers were obtained by the reaction with glycols or primary amines of monosulphones having the general formula $SO_2(CR=CR'R'')_2$ or polysulphones of the type $R'''(SO_2CR=CR'R'')_n$, where R''' is an organic substituent without functional groups whose valency is 2–6, R, R', and R'' = H, alkyl, or aryl. The oligomers are synthesised in the presence of an excess of the monosulphone (divinyl, propenyl vinyl, and ethyl vinyl sulphones) or polysulphone [1,4-bis(vinylsulphonyl)butane, 4,4-bis(vinylsulphonyl)biphenyl, etc.]. The polymerisation and copolymerisation of the oligomers are carried out under the influence of peroxide initiators such as H_2O_2, benzoyl peroxide, etc. Polymers of aminoaryl vinyl sulphones are recommended for the manufacture of polymeric dyes in view of the presence of a fairly large number of amino-groups susceptible to diazotisation[163,164]. Organometallic compounds and alkali metal hydrides or amides are employed as catalysts. Homopolymerisation and copolymerisation are carried out in bulk, in solution, or in a dispersion. The copolymers are suitable for the formation of fibres and also as stabiliser and auxiliary materials in the textile industry[165,166].

Polymeric dyes have also been obtained by the anionic polymerisation and copolymerisation of vinyl sulphones having the general formula $H_2C=CHSO_2ArN=NRNH_2$, where Ar is an aryl radical which can contain ring substituents[167].

It is noteworthy that, under free-radical conditions, vinyl sulphones copolymerise vigorously with inactive monomers, for example with vinyl acetate[34]. At the same time in the copolymerisation of methyl vinyl sulphone (M_1) with styrene (M_2) the percentage of its involvement is very slight ($r_1 = 0.01$; $r_2 = 2.0$).[34] Ethyl vinyl sulphone does not copolymerise with butadiene and behaves under these conditions merely as a diluent i.e. with increase of its concentration in the initial mixture the rate of homopolymerisation of butadiene falls[129].

In conclusion of this section one should note that the polymerisation of vinyl sulphones is fairly rapid both under

free-radical and ionic conditions. At the same time, owing to the specific features of the sulphone group, this entails the formation of only low-molecular-weight products, because of the intense chain transfer to the monomer. The polymerisation process is also complicated by side reactions leading to a decrease of the efficiency of the catalysts: interaction of the radical centre with the SO_2 group and metallation or complex formation involving the sulphone group in polymerisation under the influence of anionic catalysts.

The data presented above show that, despite the large number of studies on the polymerisation of unsaturated sulphur-containing compounds, there have been only a limited number of kinetic investigations. This hinders appreciably the interpretation of the results. Much still remains to be done in the field of the polymerisation of this interesting class of compounds.

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Light Fastness of Coloured Polymeric Materials

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The paper examines the photochemical phenomena underlying the photodegradation of dyes in coloured polymeric materials and determining the rate and degree of fading of the dyeings. Methods are described for assessing quantitatively the light fastness of coloured materials, and the principles of a scientifically based standardisation of methods for testing the light fastness of dyeings are discussed. The effects of the conditions of exposure and the physicochemical properties of the dye and the polymer matrix on the light fastness of the dyeing are also considered. A list of 106 references is included

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I. INTRODUCTION

Investigations of the action of light on coloured polymeric materials (films and fibres) are continually increasing every year. More than five hundred original papers have been published on this problem merely during the past five years. Such a wealth of publications is due to the increased ranges of dyes and polymer materials and the enhanced demands made on their light resistance.

The qualitative concept of the light fastness of a material is fairly definite. It implies the ability of the material to retain its initial properties under the influence of electromagnetic radiation in both visible and ultraviolet regions of the spectrum. In coloured materials both the dye and the polymer substrate undergo degradative processes under the influence of light.

In a coloured polymeric material both the polymer itself and the dye on it should have adequate resistance to light. If they differ markedly, the material will cease to function before its potential light fastness is exhausted. From this point of view an ideal material will be one in which polymer and colorant will have closely similar and high degrees of resistance to light.

The most obvious results of photodegradation are a change in the colour of the material and impairment of its mechanical properties. The changes in these properties during a given time of exposure are naturally most often chosen as criteria of resistance to light[1-4]. Despite the apparent obviousness and simplicity of such criteria, their practical use encounters very considerable and fundamental difficulties. A quantitative assessment of the colour of a material is already difficult because it must depend on subjective assessments by different observers. Certainly, the elaboration of formal systems of trichromatic coordinates, making possible the widespread use of instrumental estimates, shows promise. We must acknowledge the great importance of work[3,5-12] aimed at estimating objectively and instrumentally (photometrically) the change in colour undergone by coloured fibres during illumination.

No difficulty is presented by the quantitative evaluation of the mechanical properties of polymeric materials, since appropriate experimental methods have been well developed. However, the mechanical characteristics of a material are in general non-linear functions of time of exposure, so that results obtained for short exposures cannot form a reliable basis for prognostication[13]. Furthermore, little study has been made of the relation between chemical changes in the structure of a polymeric material and changes in its mechanical properties. It is therefore difficult to predict quantitatively the change in mechanical properties from the extent of chemical change, which causes the variation in the properties of the material[14].

The above comments make clear why the past years have seen an increase in the number of quantitative studies of photochemical processes occurring in coloured materials. Special mention may be made here of Refs. 15-22.

Information on the mechanism and the kinetics of the photodegradation of coloured polymer materials, revealing the factors determining their resistance to light, is of great interest for various fields of technology in which these materials (primarily films and fibres) are employed. The Soviet literature contains no reviews on the photostability of coloured polymer materials; among foreign publications the surveys by Giles[23] and by Brunnschweiler[2] may be noted. The present Review pays close attention to the main factors governing the resistance of coloured polymer materials to light, and summarises information on methods for its quantitative evaluation.

II. MONOCHROMATIC ILLUMINATION

1. Determination of Photostability from Quantum Efficiency of Photochemical Conversion

The change in properties of a coloured material under the influence of light is due to photochemical reactions occurring in the material. At least in principle, therefore, the light resistance with respect to any parameter can be related with a quantitative characteristic of the photochemical changes. The most rigorous of such characteristics is the quantum yield γ of a photochemical reaction, which is the reciprocal of the number of quanta of radiation absorbed in decomposing one reactant molecule or forming one product molecule. The quantum efficiency can obviously serve as a measure of the photostability. It is therefore useful to examine in greater detail the quantitative relation between quantum efficiency and the photochemical processes occurring in coloured polymers.

Wity monochromatic illumination the quantum yield[24] is calculated by definition from the relation

$$W = \gamma\Phi \qquad (1)$$

where W is the rate of the given chemical change and Φ the

rate of absorption of light, i.e. the number of quanta absorbed by the specimen in unit time. Formula (1) shows that the quantum yield γ is a coefficient of proportionality linking these two quantities.

If we denote by m the quantity of material undergoing conversion, we have

$$W = dm/dt . \qquad (2)$$

Here m is the integral of the concentration x throughout the volume v of the specimen:

$$m = \int_{(v)} x\, dv . \qquad (3)$$

If the concentration is the same throughout ($x = c$), then

$$m = cv \qquad (4)$$

and, as is usual with homogeneous dark and also liquid-phase photochemical reactions with stirring, the rate W is proportional to the change in concentration in unit time:

$$W = v\, dc/dt . \qquad (5)$$

When coloured polymer materials are illuminated, the concentration of absorbing centres varies non-uniformly through the thickness of the specimen, and the more general expression (2) must be used.

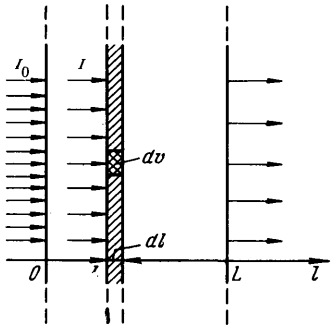

Figure 1. Diagram of plane-parallel specimen undergoing illumination.

The quantity of light absorbed by a specimen or one of its components can in principle be calculated by means of the Bouguer–Lambert–Beer law for a specimen of any shape and with any concentration distribution of absorbing centres. However, avoiding further complications and also with no loss of generality in the conclusions, we shall henceforward consider a specimen in the form of a plane-parallel layer of thickness L (a film) exposed on one side to a parallel beam of light perpendicular to the surface (Fig. 1). Here I_0 (in einsteins dm^{-2}) is the intensity of the light flux incident on the specimen, and I the intensity of the light flux reaching a layer at an arbitrary depth l.

In a multicomponent system every component is able to absorb light and undergo changes or cause changes in other components (stabilisation and sensitisation effects), which complicates Eqn. (1). For a binary polymer–colorant system, for example, the rate of photoconversion of the colorant is

$$W_c = \gamma_c \Phi_c + \gamma_c^p \Phi_p \qquad (6)$$

where Φ_c and Φ_p are the rates of absorption of light by colorant and by polymer respectively, and γ_c and γ_c^p are the quantum efficiencies of conversion of the colorant resulting from the action of light absorbed solely by the colorant (Φ_c) and solely by the polymer (Φ_p). The corresponding formula for the rate of breakdown of the polymer is

$$W_p = \gamma_p \Phi_p + \gamma_p^c \Phi_c .$$

This last formula is used in studying the photodegradation of polymers sensitised by colorants[25–28].

Although in the present paper attention is paid mainly to revealing the kinetic mechanism of the breakdown of a colorant on a fibre, not of the fibre-forming polymer itself, the arguments and mathematical expressions given below can be successfully applied to quantitative evaluation of the photodegradation of the polymer[29].

If the absorbing centres of colorant and polymer are mutually independent, the Bouguer–Lambert–Beer law gives

$$\Phi_c = I_0 S \varepsilon_c' \int_0^L x_c(l) \exp\left[-\int_0^l (\varepsilon_c' x_c(l) + \varepsilon_p' x_p(l))\, dl\right] dl , \qquad (7)$$

$$\Phi_p = I_0 S \varepsilon_p' \int_0^L x_p(l) \exp\left[-\int_0^l (\varepsilon_c' x_c(l) + \varepsilon_p' x_p(l))\, dl\right] dl , \qquad (7a)$$

in which S is the surface area of the specimen, ϵ_c' and ϵ_p' (in $M^{-1}\ dm^{-1}$) are the natural molar extinction coefficients of colorant and polymer, and $x_c(l)$ and $x_p(l)$ are the concentrations of colorant and polymer absorbing centres at depth l. Equations (7) and (7a) cannot be integrated in the general case of arbitrary concentration distributions, which leads to great complications in kinetic investigations of photoreactions in solid polymers.

In the simplest case, if $x_c = c_c$ and $x_p = c_p$, we obtain

$$\Phi_c = I_0 S \frac{\varepsilon_c' x_c}{\varepsilon_c' x_c + \varepsilon_p' x_p}\left[1 - e^{-(\varepsilon_c' x_c + \varepsilon_p' x_p)L}\right] , \qquad (8)$$

$$\Phi_p = I_0 S \frac{\varepsilon_p' x_p}{\varepsilon_c' x_c + \varepsilon_p' x_p}\left[1 - e^{-(\varepsilon_c' x_c + \varepsilon_p' x_p)L}\right] . \qquad (8a)$$

The parameters

$$f_c = \frac{\varepsilon_c' x_c}{\varepsilon_c' x_c + \varepsilon_p' x_p} = \frac{D_c}{D_c + D_p} = \frac{D_c}{D} \qquad (9)$$

$$f_p = \frac{\varepsilon_p' x_p}{\varepsilon_c' x_c + \varepsilon_p' x_p} = \frac{D_p}{D_c + D_p} = \frac{D_p}{D} \qquad (9a)$$

(where D_c, D_p, and D are the optical densities (decadic or natural) of colorant, polymer, and specimen as a whole) define the fraction, absorbed by the given component, of the total quantity of light $\Phi = \Phi_c + \Phi_p = I_0 S(1-10^{-D})$ (on passing to decadic optical densities): i.e.

$$f_c = \Phi_c/\Phi , \qquad (10)$$

$$f_p = \Phi_p/\Phi . \qquad (10a)$$

The parameters f_c and f_p are often termed[30] "shielding coefficients", since they allow for the internal filtering effect of the second component.

When relations (10) and (10a) are incorporated, Eqn. (6) is written

$$W_c = (\gamma_c f_c + \gamma_c^p f_p)\Phi . \qquad (6a)$$

When one of the components is photochemically inactive, e.g. if the polymer does not sensitise photodecomposition of the colorant ($\gamma_c^p = 0$), formula (6) becomes

$$W_c = \gamma_c f_c \Phi = \gamma_c \Phi_c \qquad (6b)$$

which is convenient for assessing quantitatively the factors

influencing the light fastness of a colorant. If the colorant does not sensitise photodegradation of the polymer (i.e. $\gamma_p^c = 0$), the rate of breakdown of the latter is

$$W_p = \gamma_p f_p \Phi = \gamma_p \Phi_p . \quad (11)$$

It follows from (6a) that the light fastness of a colorant increases with decrease in W_c. Light fastness is therefore more conveniently characterised by the reciprocal of the rate of photoconversion

$$\tau_c = 1/W_c . \quad (12)$$

The parameters γ_c and γ_c^p represent in general the most important objective factors determining the light fastness of a colorant on a fibre, and enable a quantitative comparison to be made of the light fastness of different dyes on different kinds of fibres. However, τ_c will be a more rigorous characteristic of light fastness, taking into account not only quantum efficiency but also the rate of absorption of light by the sample.

When comparing the light fastness of different colorants by means of τ_c, we must pay special attention to the dependence of this parameter on the concentrations both of the colorant in the polymer and of the absorbing centres of the polymer. The concentration dependence of Φ_c and Φ_p is determined by the relations (7), (7a), (8), and (8a). The parameters γ_c and γ_c^p may also depend on concentration, as will be shown below. However, even without detailed analysis it is obvious that, for example, τ_c will be longer at a low colorant concentration than at a higher concentration of the same colorant (provided that no aggregation of the dye occurs, which would affect the rate of the photochemical processes), since in the former case values of Φ_c and hence of W_c will be smaller. With this definition of τ_c the light fastness of a given colorant will vary. Hence it is necessary to standardise the concentrations at which a comparison is made of the light fastness of different dyes, and this in turn requires knowledge of the specific dependence of rate of photoconversion on the concentration of colorant on the fibre.

2. Dependence of Rate of Photochemical Reactions on Concentration of Absorbing Centres

For photochemical reactions, in contrast to dark reactions, the concept of reaction order is usually devoid of meaning. According to Eqn. (1) the rate of a photochemical reaction is indeed determined by the product of the two quantities γ and Φ, each of which may be a complicated function of reactant concentrations. Only in the simplest cases, over comparatively short intervals of time, can the product approximate to a parabolic relation of the type

$$\gamma \Phi = kc^p \quad (13)$$

where k no longer has the significance of a rate constant, but is a proportionality coefficient depending in general on the reactant concentration.

If the action of monochromatic radiation on a sufficiently virogously stirred solution produces photoconversion of a dye or related compound, formula (1) leads to an equation of the type (provided that quantum efficiency is independent of reactant concentration) [31]

$$dc/dt = -\frac{\gamma I_0}{L}\frac{D_c}{D}(1-10^{-D}) \quad (14)$$

where c is the molar concentration of the dye, I_0 (in einsteins $dm^{-2}\ s^{-1}$) the intensity of the incident light flux, L (dm) the thickness of the layer of illuminated solution, $D_c = \epsilon_c c L$ the optical density of the dye, $D = D_c + D_{solv}$ the optical density of the solution, in which D_{solv} is the optical density of the solvent, and ϵ_c is the decadic molar extinction coefficient of the dye. At low optical densities $D < 0.1$ we have $(1-10^{-D})/D \simeq 2.3$ to within 10%, and the expression (14) then has the form of a first-order kinetic equation

$$dc/dt = -2.3\gamma I_0 \epsilon_c c = -k_1 c \quad (15)$$

with the rate constant $k_1 = 2.3\gamma I_0 \epsilon_c$. At high optical densities $D > 1$, we have $(1-10^{-D})/D = 1/D$ to within 10%, and the dependence of dc/dt on c is described by a hyperbolic function.

At optical densities in the range 0.01–2 different functional relations, easily approximated by power series, are obtained between W and c.[24,32] An important condition for a simple power form is that the photochemical reactant should be uniformly distributed through the thickness of the specimen. Only then is the concentration x constant through this thickness and proportional to the total quantity of substance m, while the rate of photoconversion is proportional to the change of concentration in unit time dx/dt. Conducting the photochemical reaction in a sufficiently vigorously stirred solution will guarantee the above condition.

In a coloured polymeric material—whether film or fibre—the condition of uniform distribution of absorbing centres (the optical densities of coloured materials are usually around unity) already breaks down at the start of exposure, owing to more intense fading of the dye in the surface layers. As a result, the dye concentration varies from point to point, and it is not possible to integrate Eqn. (14) for the general case. This feature of solid-phase photochemical processes has been ignored in certain publications [24,31,33]. The optical density ceases to be a linear function of thickness, and is given by the integral

$$D = \varepsilon \int_0^l x(l)\,dl,$$

where $x(l)$ is the local concentration, depending on the depth of that layer l. Yet it was concluded [31] that, if the local rate of photoconversion is proportional to the quantity of light absorbed (order of reaction with respect to absorbed light intensity $n = 1$), the local rate dx/dt and the observed total rate dm/vdt should coincide. It can easily be shown that this conclusion is in general incorrect.

On the assumption that there is no diffusion of photodecomposition products, we suppose that illumination of a film produces a colorant distribution represented by the equation

$$x_c = \sigma_c/a_c - b_c l \quad (16)$$

where σ_c, a_c, and b_c are empirical coefficients enabling us to describe the monotonic increase in colorant concentration with distance from the exposed surface. Assuming for simplicity that the polymer is non-absorbing, i.e. that $\epsilon_p' = 0$, we then find from Eqns. (6) and (7) that the mean observed rate per unit volume is

$$W_c/v = \frac{\gamma_c' I_0 \epsilon_c'}{L}\int_0^L \frac{\sigma_c}{a_c - b_c l}\exp\left[-\int_0^l \frac{\epsilon_c' \sigma_c}{a_c - b_c l}\right] dl \quad (17)$$

or, after integration,

$$W_c/v = \frac{\gamma_c' I_0}{L}\cdot\frac{\sigma_c \epsilon_c'}{a_c^\beta b_c \beta}[a_c^\beta - (a_c - b_c L)^\beta] \quad (18)$$

where $\beta = \epsilon_c' \sigma_c / b_c$. At the same time the local rate at

depth l is

$$W_c(l) = dx_c/dt = \gamma_c \epsilon_c' x_c I_0 e^{-\epsilon_c' \int_0^l x_c dl} = \gamma_c I_0 \frac{\epsilon_c' \sigma_c}{a_c^\beta}(a_c - b_c l)^{\beta-1}. \quad (19)$$

The ratio of rates (18) and (19)

$$\frac{W_c}{vW_c(l)} = \frac{[a_c^\beta - (a_c - b_c l)^\beta]}{Lb_c\beta\,(a_c - b_c l)^{\beta-1}} \quad (20)$$

obviously not only differs from unity but also depends on the depth l, which should in general be the case. It follows from the above discussion that experimental investigation of the dependence of the rate of photoprocesses (in particular fading) on the reactant concentration encounters considerable difficulties.

The most comprehensive investigations of the effect of colorant concentration on rate of fading in polymer films have been made by Giles and his coworkers [23,34-38]. Giles adopts as the main criterion of the light fastness of a dye its characteristic fading time t_f, which is the time required for the initial colorant concentration c_0 to decrease by a certain amount, e.g. by 10% or 50% ($t_{0.1}$ or $t_{0.5}$). Despite the simplicity and the convenience of the experimental determination of this criterion, its theoretical interpretation is in several cases difficult. The very definition of fading time already contains an ambiguity. The concentration of colorant in the test material becomes non-uniform as fading progresses, even if it had been uniform during coloration, and the concept of concentration for the specimen as a whole loses its meaning for optical densities exceeding 0.1. In most of Giles's experiments, therefore, t_f characterises not the time of decay of the initial colorant concentration (by a certain amount) but that of the optical density of the specimen or the mean colorant concentration.

The concept of total concentration is valid for low optical densities, and from (15) we then have

$$t_{0.5} = \ln 2/2.3\gamma I_0 \varepsilon_c = 0.3/\gamma I_0 \varepsilon_c \; . \quad (21)$$

This indicates that t_f is independent of c_0 for colorant concentrations corresponding to optical densities $D \leq 0.1$, and the graph of $\lg t_{0.5}$ against $\lg c_0$ should be a straight line parallel to the $\lg c_0$ axis, making an intercept of $-0.52 - \lg(\gamma I_0 \epsilon_c)$ on the $\lg t_{0.5}$ axis. Such a relationship was observed for small initial concentrations of colorant homogeneously distributed in a film [38]. If the light is monochromatic, such graphs can be used to determine γ for known I_0 and ϵ_c by extrapolation to $c_0 = 0$. However, Giles used polychromatic radiation in most of his experiments.

At optical densities exceeding unity we can no longer use Eqn. (14), obtained for stirred solutions, where the colorant concentration is constant throughout the thickness of the layer: instead, we must apply the equation

$$\frac{d}{dt}\int_0^L c\,dl = -\gamma I_0 \; . \quad (22)$$

Introducing the mean concentration

$$\bar{c} = \int_0^L c\,dl/L \quad (23)$$

we obtain

$$d\bar{c}/dt = -\gamma I_0/L \quad (24)$$

which in effect is used by Giles for high optical densities. Here $d\bar{c}/dt$ is the observed total rate of photoconversion, which is related in extremely complicated fashion to the local rate (see above), so that the true order of the photochemical reaction cannot be assessed from this relation, as it is determined by the local rate.

The characteristic time can be defined in terms of the mean concentration, and in the present case

$$t_{0.5} = 0.5c_0 L/\gamma I_0 \; . \quad (25)$$

The plot of $\lg t_{0.5}$ against $\lg c_0$ will then be a straight line of unit slope making an intercept $\lg(0.5L/\gamma I_0)$ on the ordinate axis. Giles obtained relations of this type in several cases for large initial concentrations [23,34-38]. With monochromatic illumination we can also determine γ from this relation. With polychromatic illumination a quantity equivalent to the product γI_0 should be the same, if γ is independent of colorant concentration, for low initial concentrations, when γI_0 occurs in the experimentally determined quantity $-0.52 - \lg(\gamma I_0 \epsilon)$, and for high initial concentrations, when γI_0 can be calculated from the experimental value of $\lg(0.5L/\gamma I_0)$.

It is in general impossible to calculate the fading time theoretically and relate it to the characteristics of coloured material and light source for the practically important range of optical densities $D = 0.1-1.0$, since this would require knowledge of the specific time variation of the distribution of absorbing centres through the thickness of the specimen. In the simplest case, when breakdown of the absorbing centres can be represented as the single reaction

$$A_1 + h\nu \rightarrow A_2$$

the distribution of the concentration of the reactant A_1 through the thickness at any instant can in principle be found by solving the set of non-linear equations in first-order partial derivatives (when A_2 does not absorb)

$$\begin{aligned} \partial x_1/\partial t &= -\gamma \varepsilon_1 I x_1 \\ \partial I/\partial l &= -\varepsilon_1 I x_1 \end{aligned} \quad (26)$$

in which x_1 is the concentration of A_1 at depth l, where the light intensity is I, and ϵ_1 is the molar extinction coefficient of A_1. The distribution $x_1 = f(l)$ would be obtained by solving Eqns. (26), but it is not yet possible to obtain a solution.

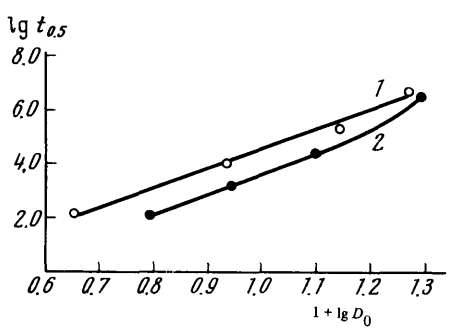

Figure 2. Dependence of characteristic fading time of the reactive dye Propionic Bright Red NZV exposed to PRK-2 lamp on initial concentration in cellulose film [25,26]: 1) covalently bound; 2) adsorbed.

With most coloured films and fibres the plots of $\lg t_f$ against $\lg c_0$ obtained by Giles [23,34-38] are only qualitatively consistent with the theoretical relation following from Eqns. (21) and (25). The slope of the linear portions of the curves at high initial concentrations usually differs from unity.

Giles explains such departure from the theoretically predicted behaviour by a purely geometrical factor—aggregation of the dye—which leads to a change in quantum efficiency with increase of concentration. It appears to the Reviewers that aggregation is only one of the possible causes.

Reactive dyes[39], which combine chemically (covalently) with certain functional groups in the fibre, are incapable of aggregation in the polymer substrate. Therefore the observed[25] increase in the light fastness of such dyes with increase in their concentration in the fibre cannot be explained by aggregation. Figs. 2 and 3 illustrate logarithmic plots of the characteristic fading time of reactive dyes against their concentration on cellulosic and polyamide films[25-27]. The appearance of a concentration effect with reactive dyes may be attributed to concentration-dependent self-quenching.

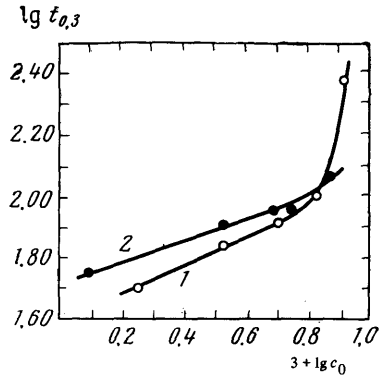

Figure 3. Dependence of characteristic fading time of the reactive dye Propionic Bright Red NZV exposed to BUV-30 lamp on initial concentration in a polyamide film[28]: 1) covalently bound; 2) adsorbed.

Analysis of the results obtained by Giles et al.[23,34-38] indicates that, although the characteristic time t_f is a convenient parameter for assessing the light fastness of a colorant, it is usually difficult to relate theoretically to photochemical parameters for the purpose of predicting light fastness.

A far more rigorous approach is to assess light fastness by means of the quantity $\tau_c = 1/W_c$ determined from the initial rates of fading at various colorant concentrations[17,26,27]. An advantage of this method is that the determination of quantum efficiency is independent of the concentration distribution of absorbing centres established during exposure. It is important merely that their concentration should be constant initially and not vary too rapidly with time. Furthermore, the quantum efficiency determined from the initial rate is independent of the accumulation of reaction products and is characteristic of the initially prepared system[28]. However, certain difficulties are encountered in determining light fastness from initial rates of fading.

1. In some cases the kinetics of fading determined for the initial period may change markedly with time. If two dyes have the same initial rate of fading and markedly different subsequent rates, for example, assessment of their light fastness from $\tau_c = 1/W_{c,0}$ will be incorrect. In this case the quantity τ_c determined from the initial rate cannot represent the real light fastness of the colorant.

2. Choosing the duration of the initial portion of the kinetic curve, along which the rate is calculated, is a very complicated matter. It is important that this section should correspond to a visually perceptible and practically important degree of fading of the dyeing. Fading is a superficial phenomenon in the sense that almost complete fading of a dyeing may be perceived, whereas the total quantity of colorant in the substrate has changed by at most 20–30%. It appears to the Reviewers that the most suitable characteristic time is $t_{0.1}$, and the initial rate in this method[17,26] should correspond to a diminution of the initial dye content by at most 10%.

III. POLYCHROMATIC ILLUMINATION

1. Calculation of Rate of Photodegradation of Coloured Materials

The large majority of investigations on photochemical changes in coloured materials have been made with polychromatic sources of ultraviolet radiation and visible light having various types of distribution of intensity with wavelength. This situation is primarily due to the practical requirement of forecasting light fastness in polychromatic sunlight and also to the simpler technique of polychromatic exposure.

Considering the principal quantitative relations determining light fastness under polychromatic illumination, we first assume that the effects of light of different wavelengths is additive and that sensitisation is absent. The total rate of photochemical conversion will then be the sum of the rates W_λ due to different portions of the incident spectrum. If this spectrum is discrete, consisting of several lines of wavelengths $\lambda_1, \lambda_2, \ldots, \lambda_n$, we have

$$W = \sum_{i=1}^{n} W_i = \sum_{i=1}^{n} \gamma_i \Phi_i \qquad (27)$$

where W_i, γ_i, and Φ_i are respectively the rate of conversion, the quantum efficiency, and the rate of absorption of light at wavelength λ_i. If, however, the radiant spectrum is continuous, extending from λ_0 to λ_m, we find that

$$W = \int_{\lambda} \omega_\lambda \, d\lambda = \int_{\lambda} \gamma_\lambda \, d\Phi_\lambda \, . \qquad (27a)$$

The quantities W_i and Φ_i correspond to Eqns. (1) and (7), while

$$\omega_\lambda = \lim_{\Delta\lambda \to 0} \frac{\Delta W}{\Delta \lambda} \qquad (28)$$

is the limit of the ratio in which ΔW is the rate of photoconversion due to the width $\Delta\lambda$ of the radiated spectrum at wavelength λ.

The quantity $d\Phi_\lambda$ is given by a formula analogous to (7):

$$d\Phi_\lambda = I_{0\lambda} S \varepsilon'_{c\lambda} \int_0^L x_c \exp\left[-\int_0^l (\varepsilon'_{c\lambda} x_c - \varepsilon'_{p\lambda} x_p) \, dl \right] dl \, d\lambda \qquad (7b)$$

where $\epsilon'_{c\lambda}$ and $\epsilon'_{p\lambda}$ are the molar extinction coefficients of colorant and polymer at wavelength λ, and $I_{0\lambda}$ is the spectral density of the radiation at the same wavelength. For

concentrations $x_c(l)$ and $x_p(l)$ constant through the thickness of the specimen Eqn. (7b) simplifies to

$$d\Phi_\lambda = \frac{D_{c\lambda}}{D_\lambda} I_0 (1 - 10^{-D_\lambda}) d\lambda \qquad (8b)$$

where $D_{c\lambda}$ and D_λ are the optical densities of the colorant and of the specimen as a whole at wavelength λ.

Since the change from summation to integration is clear from a comparison of corresponding formulae, we shall henceforward suppose for simplicity that the radiated spectrum comprises two lines at λ_1 and λ_2 (the extension to a larger number of lines is self-evident). The rate of photoconversion of the absorbing centres, when sensitisation or initiation occurs by the absorption of light by other centres, will then be (for the colorant)

$$W_c = \gamma_{c_1}\Phi_{c_1} + \gamma_{c_2}\Phi_{c_2} + \gamma^p_{i_1}\Phi_{p_1} + \gamma^p_{i_2}\Phi_{p_2}. \qquad (6c)$$

The initial rate of fading with a uniform distribution of the colorant is given by the expanded equation

$$W_{c_0} = I_{1_0} D^{-1}_{1_0} (1 - 10^{-D_{1_0}})[\gamma_{c_1} D_{c_{1,0}} + \gamma^p_{i_1} D_{p_1}] + I_{2_0} D^{-1}_{2_0} (1 - 10^{-D_{2_0}}) \times \qquad (29)$$

$$\times (\gamma_{c_2} D_{c_{2,0}} + \gamma^p_{c_2} D_{2_0})$$

in which the subscripts 1 and 2 relate to wavelengths λ_1 and λ_2, and the subscript 0 to the initial state.

Direct extrapolation of fading data obtained with a source having one spectral distribution (e.g. monochromatic) to a source having a different spectral distribution (e.g. polychromatic) is in general inadmissible, and would lead to especially marked distortions when colorants having different spectral characteristics are compared. Nevertheless, if the quantum efficiencies are known for different portions of the radiant spectrum, formula (27) or (27a) can be used to calculate the rate of photochemical conversion for any source and thus the conditions under which fastness ratings are determined can be standardised. When sensitisation occurs, Eqn. (27) for the simplest case of a binary system can be expanded to

$$W_c = \sum_{i=1}^{n} (\gamma_{ic}\Phi_{ic} + \gamma^p_{ic}\Phi_{ip}). \qquad (27b)$$

The fastness rating is then determined from the equation

$$\tau_c = 1/\sum_{i=1}^{n} (\gamma_{ic}\Phi_{ic} + \gamma^p_{ic}\Phi_{ip}) . \qquad (12a)$$

2. Standardisation of Methods of Fastness Testing

Formula (12a) contains all the parameters required to standardise the conditions for the determination of light fastness. As mentioned earlier, standardisation must be effected with respect to the initial rates of fading of the dyeing. The initial rate W_{c0} depends explicitly [Eqn. (29)] on the radiation intensities at the different wavelengths $I_{1,0}$ and $I_{2,0}$ and on the optical densities $D_{0,i}$ at these wavelengths.

Thus the main factor to be standardised is the spectral distribution of intensity of the light source. This condition is essentially satisfied automatically in all experiments on natural fading, since the same light source is used. If different sources are employed, the same values $I^{st}_{0,i}$ adopted as standard must be substituted, for all the test colorants, in an expression of type (29). Determination of light fastness from the initial rate $W_{c,0}$ will then be standardised with respect to the radiant flux.

Standardisation of the optical densities occurring in Eqn. (29) is a more complicated matter. Firstly, it is impossible to arrange that the optical densities for different substances should coincide at all wavelengths. Furthermore, the quantum efficiencies γ_i may depend on the optical density implicitly (through the colorant concentration). Therefore, although the change of optical density is most often used as a criterion of light fastness, comparison of different colorants with respect to light fastness is most correctly made at the same initial concentrations in the polymer. If the light fastness has been determined at different concentrations, values of D_{st} corresponding to the concentration adopted as standard with a specimen of standard thickness L_{st} must be substituted in a formula of type (29) in order to obtain comparable results:

$$D^{st}_i = \epsilon_i c_{st} I_{st} .$$

Dimensionally the light-fastness rating τ_c is the time required for unit molar change in concentration of the colorant in the coloured material under standard conditions. Thus it is in some measure a generalisation to rigorous conditions of the characteristic time concept widely used by Giles et al.[23,34-38].

IV. PHYSICOCHEMICAL PARAMETERS OF COLOURED MATERIAL DETERMINING ITS LIGHT FASTNESS

For the simple case of a binary system and an incident spectrum comprising two lines the light-fastness rating is related to the physicochemical parameters of the coloured material by the equation [see Eqns. (12) and (29)]

$$\tau_c = 1/(I_{1_0}\theta_1 + I_{2_0}\theta_2) \qquad (12b)$$

where the I_{0i} are the spectral characteristics of the source, and the

$$\theta_i = D_i^{-1}(1 - 10^{-D_i})(\gamma_{ic} D^p_{ic} + \gamma^p_{ic} D_{pi}) \qquad (30)$$

depend only on the spectral (D_i, D_{ic}, and D^p_{ic}) and other properties (γ_{ic}, γ^p_{ic}) of the absorbing medium at the given wavelength λ_i.

1. Spectra of Colorants and Polymers

According to Eqn. (12b) a decrease in any term $I_{oi}\theta_i$ produces an increase in light fastness. The problem of improving the light fastness of coloured fibres must therefore be attacked by analysing how these terms can be reduced. Since $I_{1,0}$ and $I_{2,0}$ are external parameters independent of the material (e.g. the time-averaged spectrum of sunlight or the spectrum of some standard source), τ_c can be lengthened only by diminishing the θ_i.

The absorption spectra of most dyes consist of an intense band in the visible, which determines the colour, and one or two bands in the ultraviolet[40] (Fig. 4). Dyes are usually most sensitive ($\lambda_{c,i}$ large) to the ultraviolet region of the solar spectrum. Hence, of two dyes possessing the same absorption bands in the visible, the one whose ultraviolet band is further displaced to wavelengths below 300 nm, i.e. to a region where the intensity of sunlight is low†, is the more stable, for the product $I_{oi}\theta_i$ is small. Thus the light fastness of a colorant can be enhanced by introducing substituents that shift the ultraviolet absorption band to a region where the source has low intensity.

† Solar rays having $\lambda > 290$ nm reach the surface of the Earth.

A theory of colour, relating the chemical structure of a colorant molecule with its spectrum, could be of great help in this respect. However, the development of such a theory, based on the quantum chemistry of the ground and excited states of polyatomic molecules[41-45], is far from complete. The controlled preparation of compounds having a specified spectrum can therefore be based only on intuition and semi-empirical rules.

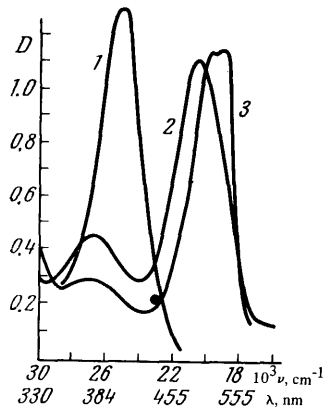

Figure 4. Absorption spectra of some reactive dyes in water[27]: 1) Reactive Yellow 2KT; 2) Reactive Scarlet 2ST; 3) Propionic Bright Red NZV.

An interesting phenomenological classification of the electronic spectra of various organic compounds has been worked out by Shigorin and his coworkers[45]. For an examination of a considerable quantity of data on absorption and luminescence spectra they formulated a rule governing the nature of the lowest energy levels responsible for long-wavelength absorption or emission: the nature of the lowest excited states (of $n\pi^*$ or $\pi\pi^*$ type) of complex molecules containing several interacting chromophoric systems is determined mainly by groups producing the smallest energy difference

$$h\nu = E_{S^*,T} - E_{S_0} \qquad (31)$$

between the lowest excited (S^*, T) and ground (S_0) electronic states. It follows that complex molecules containing different kinds of chromophoric groups should have different relative arrangements of singlet and triplet levels of $n\pi$ and nl types. On the other hand, the relative arrangement of electronic states is itself determined by the structure of the whole molecule. Hence, in order to explain the observed spectral luminescent properties of complex molecules containing $n\pi$ or nl electrons, it is necessary to know the relative arrangement of the five lowest electronic states —S_0, $S_{\pi\pi^*}$, $T_{\pi\pi^*}$, $S_{n\pi^*}$, and $T_{n\pi^*}$.

The spectrum of the polymer may have a significant effect on the light fastness of a colorant because of a shielding effect. Formula (12b) shows clearly that, if the polymer has no sensitising action ($\gamma_c^p = 0$), increase in the optical density of the polymer D_{pi} in the region of the ultraviolet absorption band of the colorant leads to an increase in the total optical density D_i, and hence a decrease in θ_i and an increase in τ_c. Absorption bands in the spectra of fibre-forming polymers (Fig. 5, curves *a* and *b*) usually lie in the far ultraviolet[13,46], so that their shielding effect is small under terrestrial conditions of exposure to sunlight ($\lambda > 300$ nm). In several cases, therefore, the shielding effect is strengthened by introducing into the polymer an ultraviolet absorber—a colourless additive having a strong absorption band in the region of the ultraviolet band of the colorant[23,46-50]—which produces an increase in D_i and hence also in τ_c.

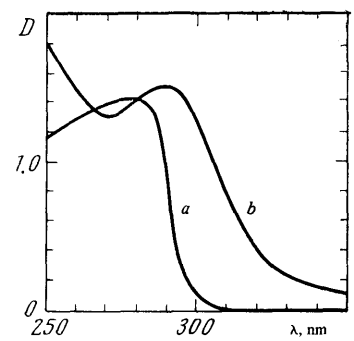

Figure 5. Absorption spectra of fibre-forming polymers[13,45]: *a*) poly(ethylene terephthalate); *b*) polyamide.

2. Factors Influencing the Quantum Efficiency of Photodecomposition of the Colorant

An obvious method for improving the light fastness of a colorant is to diminish either of the quantum efficiencies γ_c and γ_c^p. Quantum efficiency depends on several factors, whose significance can be most simply understood by using as a specific example data[15-17] showing that the photoreduction of azo-dyes can be represented by the scheme

0) $HX + h\nu \rightarrow HX^*$, $Q + h\nu \rightarrow Q^*$ } absorption of light
1) $HX^* \rightarrow HX$ (k_1)
1a) $Q^* \rightarrow Q$
2) $HX^* \rightarrow HX'$ (k_2)
3) $Q^* \rightarrow$ decomposition (k_3)
4) $HX' \rightarrow HX$ (k_4)
5) $HX' + Q \rightarrow QH + X^{\cdot}$ (k_5)

where HX is a reducing agent (e.g. phenylglycollic acid) simulating the polymer medium, Q is the colorant, HX* and Q* are excited states of reductant and colorant molecules, and HX′ is the active state of the reductant molecule initiating reaction (5), which produces fading of the colorant Q. Reaction (3) does not take place ($\gamma_c = 0$) under anaerobic conditions. With $D > 2$ the steady-state rate of fading is

$$W_c = -\frac{dQ}{dt} = I_0 S \frac{D_{HX}}{D_{HX} + D_Q} \cdot \frac{k_2}{k_1 + k_2} \cdot \frac{k_5[Q]}{k_4 + k_5[Q]} \qquad (34)$$

where D_{HX} and D_Q are the optical densities of reductant and colorant respectively, and [Q] is the concentration of the latter. Comparison of (34) with formulae (6), (7) and

(9) shows that

$$I_0 S \frac{D_{HX}}{D_{HX} + D_Q} = \Phi_p \ , \qquad (34a)$$

$$\frac{k_2}{k_1 + k_2} \cdot \frac{k_5[Q]}{k_4 + k_5[Q]} = \gamma_c^p \ . \qquad (34b)$$

Equation (34), obtained theoretically from a kinetic reaction scheme, agrees well with experimental results.

Formula (34b) gives the explicit dependence of γ_c^p on several factors, and is convenient for analysing their effects. According to this equation γ_c^p can be written as the product $\gamma_1\gamma_2$, where $\gamma_1 = k_2/(k_1 + k_2)$ characterises the ratio of the rates of processes involved in the conversion of the excited state HX* of the reductant, and

$$\gamma_2 = k_5[Q]/(k_4 + k_5[Q])$$

is the corresponding relation for the active state HX′. The transition of HX* and HX′ to the ground state (processes 1 and 4) may either be radiationless or involve radiation (luminescence). The larger the corresponding rate constants k_1 and k_4, the smaller obviously will be γ_c^p, which at the limit, when $k_1 \gg k_2$ and $k_4 \gg k_5$, will tend to

$$\gamma_{c\,(line)}^p = \frac{k_2 k_5[Q]}{k_1 k_4} \ .$$

Here γ_c^p will be proportional to the colorant concentration, which will obviously lead to considerable simplification of the concentration dependence of W_c (on $c = [Q]$—see formula (13)). The relation between the parameters k_1, k_2, and k_4 is determined by competition among processes (1), (2), and (4), and depends on the structure of the excited states HX* and HX′. The quantity k_5 characterises the chemical reactivity of the state HX′.

If an acceptor A of electronic excitation energy (such as a diene) is introduced into the system, the excited state may be deactivated[46] by induced energy transfer:

$$6)\ HX^* + A \rightarrow HX + A^* \ (k_6)$$
$$A^* \rightarrow A \ .$$

The constant k_1 is then written

$$k_1 = k_1' + k_6\ [A]$$

where k_1' characterises as before all the processes yielding the ground state, both radiationless and involving quenching. At high values of the transfer constant k_6 the quantity γ_c^p will be small, which should enhance the light fastness of the colorant.

In several cases[46] additives (e.g. benzophenone, arylates with fused rings, etc.) may transfer energy efficiently to another molecule, i.e. they may be energy donors D:

$$7)\ HX + D^* \rightarrow HX' + D \ (k_7) .$$

The constant k_2 can then be written

$$k_2 = k_2' + k_7\ [D]$$

where k_2' as before characterises process (2). In this case γ_c^p will obviously undergo a greater increase the larger is the constant k_7.

In practice the polymer in which the colorant is distributed may itself be donor or acceptor of energy. It is interesting that the same additive may be either donor or acceptor depending on the chemical structure of the colorant. Introduction of an appropriate additive can obviously improve the light fastness of a colorant to a certain extent.

The direction of the energy transfer accompanying the interaction of two molecular species one of which is excited can be determined by the application of Vavilov's rule[51] to the electronic absorption and emission (luminescence) spectra. This states that energy is transferred efficiently to a molecule having an absorption band coinciding in position with the luminescence band of the excited molecule. The physical meaning is that the luminescence level of the donor D should lie roughly at the same height as the "absorption" level of the acceptor A (quantum-mechanical resonance).

Interesting semi-empirical rules have been established[52-56] between the spectral characteristics and the photochemical reactivity of a phosphor–matrix (organic additive–polymer) system. The photochemical reactivity and the mechanism of the primary step are determined by the nature and the relative positions of the excited electronic levels of the interacting species, as well as by structural features and their capacity for complex formation. The above workers were able to make a classification permitting qualitative prediction of the character of photochemical processes.

As has been stated above, the light fastness of coloured materials is determined, according to Eqn. (12a), by the quantum efficiencies of photodecomposition of colorant and polymer at various wavelengths and by the rates of absorption of light at the same wavelengths. The quantum efficiency of photodecomposition of a colorant, and hence its light fastness in a polymer matrix, depend most strongly on the following factors—(*a*) the state of the colorant in the polymer matrix, (*b*) the reactivity of the colorant under the conditions of exposure, (*c*) the chemical nature of the polymer matrix, (*d*) the nature of the colorant–polymer bond, (*e*) the humidity and the temperature of the surrounding medium and the material, and (*f*) the composition of the ambient atmosphere.

(*a*) State of Colorant in Polymer Matrix

A colorant can be distributed in a polymeric material either as single molecules or as aggregates of various sizes[23,34-39]. The light fastness of the dyeing is substantially affected by the state of the colorant in the polymer matrix, which depends on the chemical nature of the colorant, the physical nature of the matrix, and the dyeing conditions[23,34-39].

The electron microscopy of ultrathin regenerated cellulose films coloured with direct dyes has shown[35,37,57-59] that the dyes are present in the substrate as aggregates of various sizes, and that improved light fastness is obtained with dyes that form aggregates in the film. Unfortunately, no quantitative data have been published relating the size of the aggregates and the degree of aggregation of a colorant in a substrate to its light fastness. In general, however, aggregation of a dye in a polymeric material tends to enhance its light fastness, for the reasons indicated below.

1. Aggregation of a dye is accompanied by a decrease in the ratio of the surface area to the mass. Since light acts at the interface between the dye and the surrounding medium, the rate of fading W is proportional to this ratio S/m, and will diminish as the ratio becomes smaller.
2. In an aggregate the dye molecules are in more intimate contact with one another than is the case with a molecular distribution, and transfer of excitation energy will be more probable between the molecules in an aggregate than between the individual molecules.
3. The effect of self-shielding will be more strongly

developed when the dye is aggregated, although it is present even with a molecular distribution. Such a strong effect may lead to complete absorption of light in the upper layers of aggregates and hence abnormally slow photodecomposition of the dye.

It is known from the practical dyeing of textile materials that light fastness is enhanced by all factors promoting the formation of dye aggregates in the fibre. This applies in particular to the transition from fibres of more compact structure (cotton) to fibres of less dense structure (viscose rayon)[23], for the degree of aggregation of dyes increases with increase in the proportion of amorphous regions, where such aggregates are formed. Loosening the dense structure of cotton by mercerisation also improves the light fastness of a dyeing[23,39].

The effect of dye aggregation on light fastness has been somewhat overstated by Giles[23,34-38] in his attempt to reduce the behaviour of diverse and complicated systems on exposure to the breakdown or preservation of dye aggregates, on which basis he classifies all types of fading rate curves. Such a one-sided approach is completely unjustified, since, as the Reviewers have shown earlier, the dependence of the kinetics of the photodecomposition of dyes on their concentration and on their distribution in the matrix is extremely complicated. The non-universality of Giles's "aggregate" theory is especially clearly demonstrated by reactive dyes[25,26,39], which form covalent bonds with local active centres in fibres: i.e. they are incapable of aggregating in the substrate. Nevertheless, these dyes on cellulosic and polyamide substrates give fading curves[35,60] which correspond to aggregation of the dye according to Giles's classification.

(*b*) Reactivity of Colorant

Whereas the quantity of energy absorbed by a colorant molecule is determined by the spectral properties of colorants and polymer combined with the characteristics of the incident spectrum, the effect of this energy on the colorant, i.e. the direction and the depth of photochemical changes in the colorant, depends on its reactivity. Dyes of completely different chemical structure may have closely similar spectral characteristics. For example, yellow vat, azo, and nitro dyes, while having similar absorption spectra, will differ markedly in reactivity and hence in light fastness.

The chemistry of the photochemical breakdown of various classes and groups of dyes is the least studied aspect of the problem of light fastness. A few schemes have been suggested for the photodecomposition of azo[3,17,61], nitro[62-64], cationic[65-67], vat[18-22], and other classes of dyes. Most of them, however, are hypothetical, and their experimental demonstration was usually made under conditions remote from the conditions of use of coloured materials (the colorant was usually exposed in solution). The photodecomposition of a dye begins at the most reactive group in the molecule. For example, an azo-dye undergoes degradation at the azo-group, a nitro-dye at the nitro-group, a triphenylmethane dye at the central carbon atom, and a vat dye at a carbonyl group.

The light fastness of colorants depends not only on their reactivity under the conditons of exposure but also on the reversibility and irreversibility of the photoprocesses. Thus azo-dyes undergo irreversible breakdown at the azo-group; oxidation–reduction of vat dyes under the influence of light, on the other hand, is a reversible change, so that vat dyes have exceptionally high light fastness.

Despite the specific character of the mechanism of the photodecomposition of different classes and groups of dyes, in all cases the reactions involve either oxidation or reduction[32,40]. As oxidative mechanism of photodegradation is assumed and confirmed for the vast majority of dyes, a reductive mechanism being involved only in the fading of dyes on substrates of protein character[23].

Evidence that photodecomposition takes place by an oxidative or a reductive mechanism has been found in an analogy[23,68-71] between the behaviour of dyes under illumination and in dark redox reactions: the rates of the dark redox reaction and of photodecolorisation of the dye show the same correlation dependence on the Hammett σ constant. However, the attempt to relate the rate of photochemical reactions with the Hammett σ constant by analogy with dark reactions cannot be regarded as soundly based, since the colorant molecules involved in dark reactions are in the S_0 ground state, whereas those involved in photoreactions are in the completely different quantum-mechanical states S^* and T^*.

In the Reviewers' opinion an oxidative mechanism is most plausible for the photodecomposition of dyes in a polymer matrix (fibre or film), since all the conditions of exposure promote the formation of oxidising agents from substances present in the surrounding atmosphere or in the material itself. Among such oxidants may be oxygen in its various forms, peroxy-compounds formed by photodegradation of the fibre polymers, and other oxidising agents contained in the atmosphere of industrial towns. One source of peroxide compounds is water contained in the material itself and in the surrounding atmosphere.

(*c*) Chemical Nature of Polymer Matrix

Since light acts both on the colorant and on the polymer matrix in which the latter is distributed, the chemical and physical nature of this matrix cannot fail to affect the rate of photodecomposition of the dye. Different photochemical reactions yielding different products, which are involved in breaking down the colorant, occur in the matrix under the influence of light depending on the chemical structure. Thus the ultraviolet irradiation of coloured cellulosic and polyamide fibres gives rise to peroxy-compounds capable of decolourising dyes[9]. Models of polyamides of low molecular weight, e.g. *N*-pentylhexanoamide, on exposure to ultraviolet radiation form[72] an amide hydroperoxide having the structure $-CH_2.CO.NH.CH(OOH).CH_2-$.

Protein substrates, on the other hand, exhibit reducing properties on exposure, these being due to such amino-acids as tryptophan and histidine[23,70]. The explanation is that dyes fade by different mechanisms on protein and on non-protein substrates. The rate of fading of the same colorants (e.g. azo-dyes) is considerably lower on a protein fibre than on cellulosic fibres. It appears to the Reviewers that protein substrates, several of whose amino-acids develop reducing properties, retard the photo-oxidative degradation of dyes, probably by reacting with oxidants.

(*d*) Nature of Colorant–Polymer Bond

Different types of bond—hydrogen, van der Walls, coordinate, ionic, and covalent—may be formed between the colorant and the macromolecules of the polymer matrix. The type of bond, which depends on the chemical nature of colorant and polymer, will influence the light fastness of the system to the extent that the bond can promote the

transfer of excitation energy from the colorant molecules to the polymer macromolecule (improvement of light fastness) or from the macromolecule to the colorant molecules (impairment of light fastness). Energy transfer between two components in direct contact is theoretically possible, since even in the absence of contact between molecules (removal to 100 Å) the effect of concentration-dependent self-quenching operates[31,32,67].

Transfer of excitation energy between dye and polymer could occur most simply if they were linked by a chain of conjugated double bonds, i.e. if a single chromophoric system were formed between dye and polymer. However, such coloured polymers have not yet been prepared. Even reactive dyes, which form a more stable covalent bond with the polymer than do other classes, do not yield a single chromophoric system with the substrate.

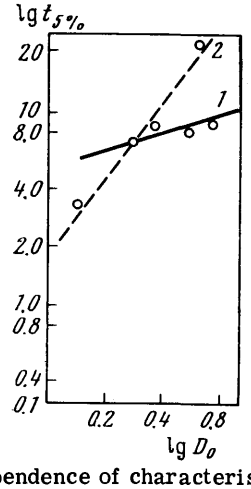

Figure 6. Dependence of characteristic fading time of Pararosaniline on initial optical density of films[23]: 1) regenerated cellulose; 2) polyacrylonitrile.

The effect of the nature of the bond is evident with cationic dyes: dyeings produced on cellulosic fibres by means of a third component (a mordant) have poor light fastness, whereas the same dyes exhibit considerably better light fastness on polyacrylonitrile fibres (ionic bond)[23] (Fig. 6).

With reactive dyes the covalent bond formed with a cellulosic fibre has a favourable influence on the light fastness, but only at low concentrations[27]. The light fastness of reactive dyeings on polyamide fibres is less affected by the covalent bond[25]. Fig. 7 illustrates the concentration dependence of the light fastness $t_{0.1}$ for the reactive dye Propionic Bright Red NZV in two forms (covalently fixed and adsorbed) on cotton cloth[27]. Only in the adsorbed form does the dye undergo aggregation with increase in its concentration in the fibre, and this aggregation effect begins to prevail over the favourable effect of the covalent bond.

(*e*) Effect of Humidity and Temperature of Atmosphere and of Textile Material

Under practical conditions of the exposure of coloured textile materials variations of the temperature and humidity of the surrounding atmosphere and of the material are interrelated, so that they can be studied separately only under laboratory conditions.

Effect of temperature. Hedges[73] investigated the effect of temperature on the fading of dyes on cotton and wool in atmospheres differing in relative humidity, and found that the activation energy of decomposition of the dye is 2 kcal mole^{-1}. Since the primary steps of photoexcitation have an activation energy close to zero[40], subsequent secondary photoreactions of decomposition must depend on the ambient temperature.

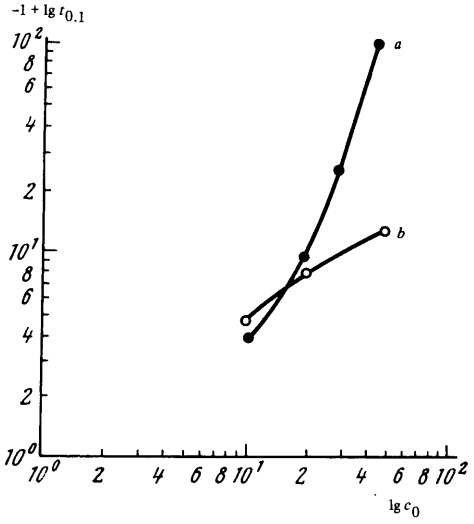

Figure 7. Dependence of characteristic fading time of the reactive dye Propionic Bright Red NZV on its initial concentration on cotton cloth[27]: *a*) hydrolysed form of dye; *b*) covalently bound form of dye.

Raising the temperature usually affects the results of light-fastness testing indirectly, the rate of fading being somewhat lower because of the diminished moisture content of the specimen. This effect is apparent with hydrophilic fibres[23]. The opposite effect is sometimes observed on hydrophobic fibres: i.e. raising the temperature causes a sharp acceleration of fading.

Investigations by the Standards Committee of the American Association of Textile Chemists and Colorists revealed[74,75] that the rates of fading of many dyes on synthetic fibres, when exposed in a Fade-Ometer and in sunlight, increase sharply with rise in temperature of the black panel (the surface temperature of a black specimen on exposure). Similar results were obtained by Friele and Selling[76].

It was suggested[23] that, in the absence of moisture on a hydrophobic fibre, (i) dye aggregates break down under the influence of atmospheric oxygen, and (ii) polar groups of the dye molecules become more accessible to attack by atmospheric oxygen, hydrogen bonds being absent between dye and water. However, these hypotheses are not supported by the experimental results. It is especially difficult to accept the last suggestion, since traces of moisture are retained as monolayers in fibrous material even at a very high temperature (up to 200°C)[77].

(*f*) Effect of Moisture in the Atmosphere and in the Specimen

The effect of moisture on the rate of fading of dyes is well known, and affects the reproducibility of light-fastness testing under natural conditions, when the intensity of irradiation varies and hence the atmospheric humidity and the moisture content of the specimen [78,79]. Increase in humidity usually accelerates degradation of the dye by light. In several cases a linear relation is observed between the light fastness and the moisture content of the specimen. The formula

$$F = K\sqrt{T}(w + c)$$

was suggested [73] to link the rate of fading of a dye, expressed as percentage decomposition F, with the temperature T °K and the moisture content w% of the specimen, K and c being constants. Lead showed [80] that the fading of dyes on wool is sharply accelerated at relative humidities of 45–80% in the surrounding air.

Despite the large number of results establishing that the light fastness of fibre dyeings is extremely sensitive both to the ambient humidity and to the moisture content of the fibrous material itself, from which quantitative relations have been elicited between them [81], the reasons for such sensitivity have not yet been finally clarified. The above mechanism of the deterioration of coloured polymers under the influence of light suggests that the role of water as a supplier (source) of species (oxygen, hydrogen, peroxide, etc.) that actively decompose the dye is extremely important and specific to various colorants and fibres. In general, however, water will be involved, either directly or indirectly, in photodecomposition of the colorant and of the fibre itself.

Assuming a photo-oxidative mechanism of breakdown for most colorants under actual conditions of use (atmospheric humidity and oxygen), we can suppose that the main function of water is to produce peroxy-compounds. Photochemical formation of a peroxide in the presence of colorants, oxygen, and water has been demonstrated with basic and vat dyes, which have a sensitising effect [73-78,80,81,83-87]. The formation of hydrogen peroxide has been shown also with dyes having no sensitising activity, but the quantity of peroxide isolated is considerably smaller in this case. The suggested [61-65] mechanism of formation of hydrogen peroxide can be reduced to the scheme

$$Q^S + h\nu \rightarrow Q^{S*} \rightarrow Q^T$$
$$Q^T + O_2^T \rightarrow Q^+ + O_2^-$$
$$O_2^- + H^+ \rightarrow HO_2$$
$$2HO_2 \rightarrow H_2O_2 + O_2^T,$$

where S and T denote singlet and triplet states, and the asterisk indicates an excited state of the colorant molecule **Q**. The resulting peroxide is able to break down not only the colorant but also the fibre itself [78,79].

Nevertheless, even when the moisture content of the fibre is very low (~5%) and the colorant content is 0.3–2%, each molecule of the latter is associated with 50–300 molecules of water: i.e. the excess of water present relative to the dye is such that further increase in the water content of the fibre should have no effect on the photochemical reactions. The actual situation, however, is quite different. Although calculations show [23] that the rate of fading should become constant at a very low moisture content (< 0.1%), in practice the rate has not become constant even at a content of 40%.

This can be explained by the fact that the relative humidity of the air in direct contact with the specimen is a very important factor influencing the light fastness of a dyeing. The humidity in this boundary zone is usually considerably lower than that of the total volume of surrounding air. McLaren [81] made a comprehensive investigation of the relation between the humidity of the surrounding air, that of the air in the boundary layer, the moisture content of the fibre, and the light fastness of the dyeings. He introduced the special concept of effective humidity, corresponding to that of the air in the boundary layer, and established a link between the effective humidity and the duration and intensity of irradiation of the specimen.

The effective humidity should be one of the exposure parameters to be standardised.

(*g*) Effect of Composition of Atmosphere

The deterioration of coloured fibres under the influence of light must be regarded as involving photochemical processes occurring in a system comprising fibre, the colorant, and the surrounding medium. Therefore the composition of this atmosphere should and does play an extremely important part in fading. Since oxidation, reduction, and hydrolysis lead to breakdown of colorants on the fibre, any pollutant of the atmosphere must be regarded as being possibly involved in these fading processes. The composition of the atmosphere is of paramount importance in the functioning of coloured materials in the open air and in light-fastness testing under natural conditions, i.e. in tests of fastness to light and weathering. However, it will be shown below that the composition of the atmosphere may also have an effect in accelerated tests under fading lamps.

Among pollutants of interest in connection with their effect on the action of light on coloured fibres are oxides of nitrogen, sulphur dioxide, carbon dioxide, ozone, and aldehydes. All these chemically active substances are present in the atmosphere, in which their contents may vary within wide limits depending on the type of locality (urban or rural), its geographical position, the season of the year, and the time of day. The Table lists the concentrations of the above substances in the atmosphere at three sites in the USA [88].

Pollutant concentrations in atmosphere of rural and urban localities of the USA.

Pollutant	Concentration, ppm by vol.		
	rural	Los Angeles	Chicago
Oxides of nitrogen	0.01	0.26	0.22
Sulphur dioxide	0.03	0.05	0.25
Carbon dioxide	—	23.00	16.00
Ozone	0.06—0.11	0.21	0.005
Aldehydes	—	0.3	—

The first to observe the effect of atmospheric composition on the rate of fading of dyes was Lazerev [88,89], who found an exponential relation between rate of deterioration and the oxygen content of the atmosphere.

The Table shows that the atmosphere of industrial towns has a well defined acidic character, which may promote the photodecomposition of dyes. These pollutants may break

down dyes even in the absence of light, i.e. by dark reactions, but illumination promotes their degrading action.

Sulphur dioxide enters the atmosphere of industrial towns from the combustion of coal containing up to 4% of sulphur. A considerable quantity accumulates from the use of coal as fuel (e.g. in Chicago), and the atmosphere is reducing in character, since sulphur dioxide is a strong reductant. When petroleum is used as fuel, oxidising products accumulate in the atmosphere. The main source of oxides of nitrogen is the exhaust from cars [90]. Ozone is present in the atmosphere of towns and of rural localities; its content varies with height above the Earth's surface [90].

Sulphur dioxide, nitrogen dioxide, and aldehydes absorb ultraviolet radiation of wavelengths 280–300 nm, and the excited molecules are involved in a series of successive reactions entailing formation of ozone. In contrast to sulphur dioxide, activated nitrogen dioxide reacts reversibly with oxygen, which may lead to the accumulation of ozone in the atmosphere even at low concentrations of N_2O_4.[91]

The products of the combustion of petroleum in diesel engines contain aldehydes, which in turn, in the presence of ozone and under the influence of light, form peroxides [92].

As already noted, sulphur dioxide is able to reduce dyes on the fibre. Azo-dyes are especially sensitive to the action of this gas, which breaks down the azo-group. Therefore azo-dyes are most fugitive to light and least durable on wool, since this fibre has enhanced affinity for sulphur dioxide, and absorbs it from the atmosphere [93-95].

Aminoanthraquinone blues, violets, and reds, as well as certain disperse azo-dyes, are very sensitive to the action of oxides of nitrogen [97]. Rowe and Chamberlain [98] established that the decomposition of aminoanthraquinone colorants under these conditions results from diazotisation of primary amino-groups and nitrosation of secondary amino-groups, together with oxidation, the direction of which depends on the nature of the colorant. The fastness of disperse dyes to light in an atmosphere of oxides of nitrogen is inversely proportional to their ability to form salts [99]. Under these conditions disperse dyes are most sensitive to illumination on cellulose acetate, polyester, and to a less extent polyamide and polyacrylonitrile fibres [100]. The effect of the nature of the fibre probably depends on its ability to adsorb oxides of nitrogen.

Ozone also activel accelerates the photochemical decomposition of disperse and other classes of dyes [101-103]. Breakdown of the former is attributed [103] to electrophilic attack by ozone on aromatic amino-groups, so that the rate of fading should depend on the nucleophilic strength of the nitrogen atom in arylamine dyes. In fact changes in the structure of the dye, tending to diminish the electron density on the nitrogen, make the latter less susceptible to attack by an electrophilic reagent, whether ozone or oxides of nitrogen, and improve the light fastness [104-106].

The rate of breakdown of a dye on illumination in an atmosphere containing ozone depends on the distribution of the dye through the fibre, and decreases with increase in the depth of penetration into the fibre [103]. This is probably due to the role of diffusion in the effect of ozone: the accessibility of the dye to all attacking reagents, including ozone, decreases with distance from the fibre surface. Heat-treatment of a coloured cellulose triacetate fibre, like its surface hydrolysis, increases the light fastness in an atmosphere containing ozone [88], which also is probably due to diminished accessibility of the dye.

Since ozone is formed in ample quantities when xenon lamps are used, measures must be taken to remove it from the atmosphere in which the specimen is exposed.

* * *

Several fundamental conclusions can be drawn from an analysis of the literature surveyed.

1. Measurement of the initial rate of photodegradation of polymer and dye should form the basis for the quantitative assessment of the light fastness of coloured polymeric materials.
2. Interaction of polymer and colorant (both stabilising and sensitising) must be taken into account in assessing the light fastness of coloured polymers.
3. The main factors influencing the light fastness of a coloured polymer depend on the quantum efficiencies of photoreactions of polymer and colorant and on their rate of absorption of light.
4. Coloured polymer materials can be protected from the action of light by lowering the quantum efficiencies of the photoreactions of colorant and polymer and by diminishing their rates of absorption of light.

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Complex Fertilizers Based on the Nitric Acid Decomposition of Phosphates

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The conditions governing the equilibrium in the reaction of fluoroapatite and mineral admixtures in natural phosphate raw materials with nitric acid and also certain problems of the kinetics of the decomposition of phosphate minerals are considered in the review. The principles of several technological schemes in the manufacture of Nitrophoska are described. The most important trends in new studies designed to obtain complex fertilizers by the decomposition of phosphates with nitric acid are also indicated. It is concluded that a promising method for the manufacture of Nitrophoska involves a procedure with cooling, retaining the main, fruitful idea of employing for the decomposition of phosphates nitric acid without the addition of other acids or their salts.
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I. INTRODUCTION

The method of processing natural phosphates with nitric acid proposed in 1908 by Pryanishnikov and Britske[1,2] for the manufacture of a phosphate fertilizer [$CaHPO_4$ (precipitate) and a nitrate fertilizer (calcium nitrate)] could not find wide application before the end of the First World War, since at that time there was no synthesis of ammonia and its oxidation to nitric acid on an industrial scale.

In recent years, with the rapid and powerful growth of the manufacture of synthetic ammonia developing along progressive and economical lines, there has been a greater possibility of obtaining cheap nitric acid and its employment not only for the above two single fertilizers but also, and mainly for combined (complex) fertilizers — nitrophosphates (Nitrophos and Nitrophoska) containing nitrogen, phosphorus, potassium, and other nutrient elements.

The growing importance of the manufacture of fertilizers based on the nitric acid decomposition of phosphates together with their processing by sulphuric acid, which has been developing most rapidly, arises because nitric acid is employed in two ways in the decomposition of phosphates: as a source of active hydrogen ions and as a carrier of nitrogen — a useful component of fertilizers.

In the most rational process unpleasant waste is not formed, as happens in the sulphuric acid decomposition of phosphates, accompanied by the formation of phosphogypsum, which has so far not found a useful application.

The employment of nitric acid permits a more complete extraction of fluorine and lanthanides from apatite An advantage of nitric acid is also the possibility of using as a starting material low-grade phosphorites containing considerable amounts of iron and aluminium compounds.

The method of nitric acid processing of phosphate raw materials has undergone extensive development since the initial studies carried out at the Fertilizers, Insecticides, and Fungicides Research Institute (NIUIF) from 1925[3-5]. Some of the versions of the manufacture of simple and complex fertilizers from nitric acid - phosphoric acid solutions investigated in the Soviet Union and elsewhere have not found large-scale applications, while others have been improved and have assumed a dominant position under modern conditions.

Technological nitric acid processing of phosphates includes the following main stages: (1) intrinsic decomposition of the phosphate raw material with nitric acid; (2) isolation of calcium from the nitric acid - phosphoric acid solution obtained after the decomposition of the phosphate; (3) neutralisation of the solution with ammonia (ammoniation) or lime; (4) conversion of the neutralised solution into a fertilizer †. In certain versions the processing of phosphates includes additional operations such as the separation from solution of the insoluble residue, the decomposition of sodium or potassium fluorosilicate, and precipitation of lanthanide phosphates.

The above stages in the manufacture of nitrophosphates are involved in a close interrelation, the nature of which is described below for individual specific procedures.

II. PHOSPHATE DECOMPOSITION PROCESSES

In a general form the decomposition of fluoroapatite with nitric acid can be represented by the equation:

$$Ca_5(PO_4)_3F + 10\,HNO_3 = 3H_3PO_4 + 5Ca(NO_3)_2 + HF + 290\ \text{kJ mole}^{-1}. \quad (1)$$

Under the industrial conditions of the interaction with nitric acid at a concentration of 50-55%, the reaction temperature is maintained at 50-60°C mainly as a result of the heat of reaction (1)[6,7].

The conditions governing the equilibrium in this process have been established with some approximation by means of a graphical analysis of the $CaO-P_2O_5-N_2O_5-H_2O$ system, which was investigated at 0°, 5°, 25°, 50°, 75°, and 100°C. The metastable state of the system at 50°C was also investigated[11].

In the acid regions of the diagram of the system the following solid phases in equilibrium with saturated solutions at the above temperatures were discovered: $Ca(NO_3)_2$ (tetrahydrate, trihydrate, dihydrate, and the anhydrous

† The present review is restricted to the analysis of the manufacture of solid fertilizers only and does not deal with the specific problems of the synthesis of liquid and suspension fertilizers based on the decomposition of phosphates with nitric acid.

salt), $Ca(H_2PO_4)_2.H_2O$, and $CaHPO_4$. More basic phosphates, including hydroxy-apatite, are found only in a narrow region of highly dilute solutions.

The main conclusion from the analysis of the system is that in the interaction of fluoroapatite with a stoichiometric amount [according to Eqn. (1)] of nitric acid (at a concentration of 47% and above) the phosphate should be completely decomposed following the attainment of equilibrium. Indeed, experimental conditions have been found ensuring in practice a high (98–99%) degree of decomposition of natural phosphates at 45–60°C [12-17].

The study of the 50° isotherm (in the equilibrium and metastable states) by the method of "secondary projections" of the system showed[18,19] that, within the limits of the nitric acid concentrations employed under technological conditions (47–60%) in amounts relative to stoichiometry corresponding to 100–140%, the composition point *C* of the resulting solutions is in the crystallisation region of $Ca(H_2PO_4)_2.H_2O$ (Table and Fig. 1). These data show that the decomposition of fluoroapatite by nitric acid at 50°C proceeds in accordance with the following equation:

$$Ca_5(PO_4)_3F + 10HNO_3 = (3-n)H_3PO_4 + 0.5n\,Ca(H_2PO_4)_2 + (5-0.5n)Ca(NO_3)_2 + n\,HNO_3 + HF \quad (2)$$

Thus both theory and industrial practice permit variation of the conditions governing the decomposition of phosphates within wide limits. This applies not only to the concentration and the specified amount of nitric acid but also to the process temperature. This situation favours the optimisation of the technological conditions in subsequent stages of the nitric acid process.

Conditions for the formation of $Ca(H_2PO_4)_2.H_2O$ in the nitric acid–phosphoric acid solution at 50°C.

Conditions	Stable equilibrium	Metastable equilibrium
Concn. of HNO_3, %	71.0—38.5	77.5—37.5
Amount of HNO_3 relative to stoichiometry, %	116.5—93.6	158.0—109.0

Under the conditions of the decomposition of fluoroapatite at 50°C presented in Table 1, $Ca(H_2PO_4)_2$ and calcium nitrate are present in solution. Analysis of the equilibrium in the $CaO-P_2O_5-N_2O_5-H_2O$ system showed that calcium nitrate may be isolated from solution in the form of the anhydrous salt directly in the course of the decomposition of the phosphate at the same temperature, provided that nitric acid at a concentration in excess of 71% is employed in an amount exceeding 116.5% relative to stoichiometry. Therefore an experimental study was made of the decomposition of the apatite concentrate under the given conditions[18].

The study of the $CaO-P_2O_5-N_2O_5-CaSiF_6-H_2O$ five-component system at 60°C [20] showed that in the presence of potassium fluorosilicate and fluoride, formed on acid treatment of phosphates, the crystallisation regions of $CaHPO_4$ and calcium nitrate expand, while that of $Ca(H_2PO_4)$ contracts. Under certain conditions (low HNO_3 and H_3PO_4 concentrations in solution), this leads to the decomposition of $Ca(H_2PO_4)_2$ with deposition of $CaHPO_4$ in the solid phase:

$$Ca(H_2PO_4)_2 \rightleftarrows CaHPO_4 + H_3PO_4.$$

Calcium fluorosilicate can in turn decompose with formation of CaF_2 and SiO_2. The observed secondary phenomena can inhibit the decomposition of the phosphate raw material as a result of the formation of a crystalline crust on the phosphate grains and can also impede the separation of an insoluble precipitate. The complex processes associated with the presence of fluorine compounds in the system require further investigation.

The study quoted above[20] also revealed the favourable effect of free H_2SiF_6 in the phosphoric acid solution, which can partly or completely prevent the decomposition of $CaSiF_6$. In this connection it was of interest to determine the fluorine balance in the course of the nitric acid decomposition of natural phosphates.

In the processing of the apatite concentrate (process temperature 50°C) it was found that, when 55% nitric acid is employed, the bulk of fluorine (77%) passes to the liquid phase[21]. In the presence of 80% nitric acid, the evolution of fluorine into the gas phase (SiF_4) increases sharply—only about 18% of fluorine remains in the liquid phase[19]. The use of Karatau phosphorites also entails an increase in the evolution of fluorine into the gas phase—the degree of extraction of fluorine into the liquid phase in the presence of 55% nitric acid is about 58%.[21] The amount of fluorine in the insoluble residue is only about 1–3% of its content in the starting material.

The appreciable content of fluorine (H_2SiF_6) in the liquid phase necessitates its isolation: conditions have been developed[6,7,14,22] for the precipitation of Na_2SiF_6 from nitric acid – phosphoric acid solutions with the aid of a sodium nitrate (or sodium carbonate) solution. The gaseous fluorine compounds evolved are absorbed. The characteristic features of the absorption of HF and SiF_4 were investigated[23,24].

The direct requirement for sodium (or potassium) fluorosilicates is limited compared with the possible volume of their manufacture in fertilizer factories where phosphate raw materials are processed. For this reason, intense studies are being made at present on various versions of the manufacture from fluorosilicate – containing waste of products such as cryolite, aluminium, sodium, and ammonium fluorides, hydrofluoric acid, and others, the requirement for which increases from year to year[25-28].

The apatite concentrate contains about 0.9% of cerium-group lanthanides the bulk of which (98–99%) passes to the nitric acid – phosphoric acid solution. A process has been developed for the isolation from solution of lanthanide phosphates at 60–80°C and for 50% neutralisation of the first hydrogen ion dissociated from H_3PO_4 by lime, ammonia, or sodium carbonate to give a pH of 2–2.5.[29] The degree of precipitation of the lanthanides reaches 75–80%. The precipitate is separated from the solution by decantation. It is useful to treat the solutions by successive procedures – initially for the isolation of sodium fluorosilicate and then for the isolation of lanthanide phosphates. A number of other methods for their isolation have also been developed.

The kinetics of the decomposition of phosphate materials have not as yet been completely elucidated. Mainly experimental studies[6,7,14,16] were undertaken to investigate the influence of individual factors on the rate of reaction with nitric acid of the apatite concentrate and phosphorite from Krolevets, Izyum, Polpinsk, Zozh, Egor'evsk, Vyatsk, and Karatau deposits. These studies established

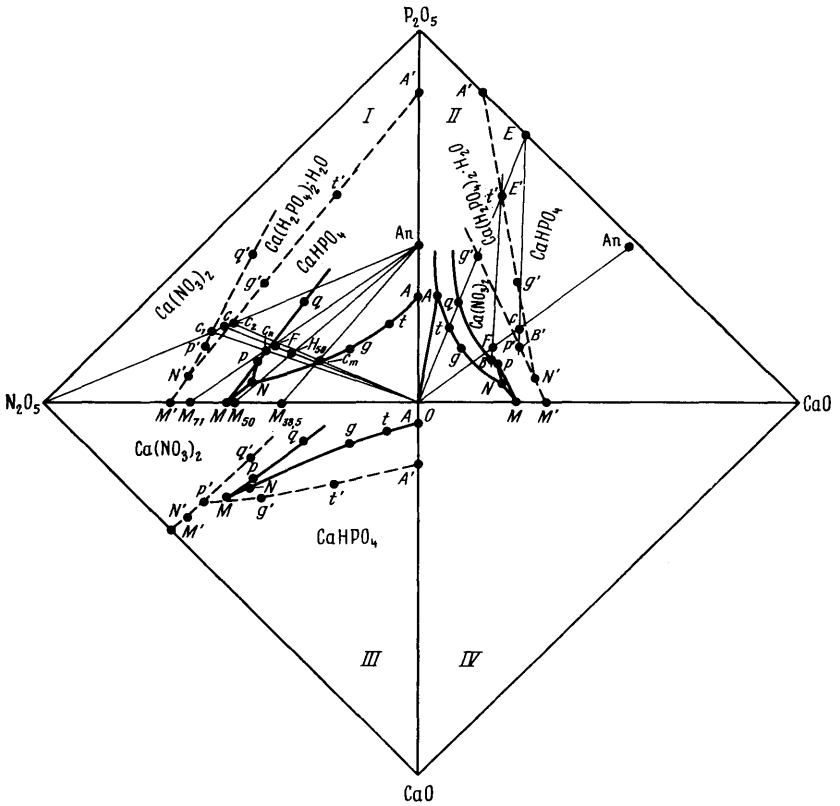

Figure 1. Graphical analysis of the $CaO-P_2O_5-N_2O_5-H_2O$ system at 50°C (decomposition of fluoroapatite with nitric acid)[18].

the principal relations: for example, the decomposition of phosphorites proceeds at a relatively high rate and the degree of extraction of P_2O_5 into the solution can reach 98–99% in the first 15–30 min. Apatite is decomposed by nitric acid more slowly — the reaction virtually reaches completion in the course of 60–90 min. The reason is that apatite is less reactive: its overall (external and internal) specific surface is smaller by a factor of 5–30 than that of phosphorites for the same degree of comminution[30].

The decomposition of natural phosphates accelerates with increase of temperature in the range 30–60°C. The temperature coefficient for each 10 deg C is about 1.3. With increase of the relative amount of nitric acid per unit amount of phosphate, the degree of neutralisation of the mixture of nitric and phosphoric acid falls, and therefore the rate of reaction increases.

The influence of the initial nitric acid concentration in the range 47–55% is small. It has been found[19] that, with increase of the HNO_3 concentration to 80%, a high degree of extraction of P_2O_5 into the solution is reached in about 3.5 h, mainly due to the precipitation under these conditions of $Ca(NO_3)_2$ crystals, which passivate the surface of phosphate grains.

The kinetics of the acid decomposition of phosphates have been investigated,[31-33] and it has been established that the interaction of apatite with inorganic acids under certain conditions (temperature and concentration) takes place entirely under diffusion-dependent conditions. The rate of reaction for 50% nitric acid is determined by the diffusion of ions from a temperature as low as 30°C. A study of the rate of decomposition of apatite by phosphoric acid[31] led to the conclusion that the driving force of the dissolution of apatite is the concentration gradient of calcium ions at the surface and in the bulk of the solution. In a study[32,33] of the kinetics of the interaction of apatite with acid, it was found that the rate of the process depends on the rate of diffusion of hydrogen ions to the interface, on the activity of hydrogen ions, on the solubility of the reaction products, and on the passivation of the surface by crystalline deposits (in this instance, of calcium nitrate), and also on the viscosity of the liquid phase and other physicochemical factors. The diffusion of H^+ and Ca^{2+} ions is accompanied by ion exchange (with NO_3^- and $H_2PO_4^-$ ions in the nitric acid decomposition), which accelerates the diffusion of the ion pair.

It has also been established experimentally[32,33] that under identical conditions the highest rate of reaction is obtained in the decomposition of apatites by hydrochloric and nitric acids: it is higher by a power of ten than in the reaction with phosphoric acid.

The behaviour of iron-containing impurities in the initial material is very important for the assessment of the nitric acid methods for the processing of phosphates. In a study of the kinetics of the decomposition by acids of the silicate mineral glauconite, which is present in phosphorites, it was established[31] that, despite the high degree of dissociation of nitric acid, it decomposes glauconite comparatively slowly. This is due to the formation of a dense SiO_2 envelope around the mineral grains, which inhibits

diffusion (passivation occurs). However, in the joint decomposition of such minerals together with phosphate, the resulting phosphoric acid accelerates the process. In practice, under continuous process conditions, the degree of extraction of $Fe_2O_3 + Al_2O_3$ into the solution amounts to about 70%. Iron and aluminium oxides react with phosphoric acid and form sparingly soluble phosphates, which leads to a loss of P_2O_5.

The presence of lower oxides of iron and also of organic substances in phosphorites leads to increased losses of nitric acid. On decomposition with nitric acid, low-grade phosphorites form considerable amounts of finely dispersed precipitates (mainly SiO_2), the separation of which by decantation or filtration is difficult.

One of the methods[6,7,12] for the decrease of the harmful influence of impurities in phosphorites in the course of nitric acid processing, which has been investigated, is heat treatment of the phosphorites. Optimal oxidative roasting conditions, which diminish the dissolution of iron and aluminium oxides, eliminate the losses of nitric acid, and improves the properties of the precipitates facilitating their decomposition, have been established for various phosphorites (from the Egor'evsk, Vyatsk, Polpinsk, Sozh, and other deposits). Thus heat treatment of phosphorites converts them into a starting material suitable for conversion by nitric acid into complex fertilizers without secondary enrichment.

The study of the problem of the separation of the insoluble residue formed in a finely dispersed state in the decomposition of the Karatau phosphorite is very important. The formation of the precipitate has been investigated[34,35] and methods and apparatus for the accelerated filtration of the sludge have been recommended.

III. ISOLATION OF CALCIUM FROM NITRIC ACID-PHOSPHORIC ACID SOLUTIONS AND ITS NEUTRALISATION

In the conversion of nitric acid–phosphoric acid solutions into fertilizers free phosphoric and nitric acids are neutralised. Technological processes based on the neutralisation of the solutions with lime or limestone, with precipitation and isolation of $CaHPO_4$ and formation of calcium nitrate as a second product were developed initially[14,36-40]:

$$3H_3PO_4 + 5Ca(NO_3)_2 + 3CaCO_3 \rightarrow 3CaHPO_4 + 5Ca(NO_3)_2 + 3CO_2 + 3H_2O. \quad (3)$$

A version of the synthesis of ammonium nitrate from calcium nitrate by treatment with ammonium carbonate solution was investigated:

$$Ca(NO_3)_2 + (NH_4)_2CO_3 \rightarrow 2NH_4NO_3 + CaCO_3. \quad (4)$$

This method for the preparation of the citrate-soluble $CaHPO_4$ and of the low-percentage (15% N) hygroscopic calcium nitrate has been applied on a limited scale[41,42].

The possibility of obtaining from nitric acid–phosphoric acid solutions of the water-soluble $CaHPO_4$ (instead of the citrate buffer-soluble $CaHPO_4$), discovered in a graphical analysis of the $CaO-P_2O_5-N_2O_5-H_2O$ equilibrium system[3], should be noted. This version merits technical development.

The common procedures for the preparation of complex nitrogen-phosphorus fertilizers include the neutralisation of phosphoric and nitric acids with ammonia. Ammonia, which is the primary product of the fixation of atmospheric nitrogen, is now the most readily available, the most concentrated, and the cheapest nitrogen carrier, which accounts for the attempts to introduce nitrogen into complex fertilizers in the form of ammonia to the maximum possible extent

The phosphoric acid obtained by the sulphuric acid decomposition of phosphate is neutralised with ammonia, which results in the formation of fertilizers (Ammophos or Diammophos), which contain between 5.2 and 2.6 P_2O_5 units per unit weight of nitrogen. Depending on the initial phosphate material, Ammophos contains different amounts of P_2O_5 in a water-soluble form: for example 95% in the processing of the apatite concentrate and 75–80% in the processing of the Karatau phosphorite.

Numerous agrochemical studies led to the discovery that the majority of soils can assimilate almost equally readily both water-soluble and citrate-soluble forms of phosphate fertilizers. In the USSR the Government Standard GOST 11365-65 specifies that in Nitrophoska not less than 55% of the P_2O_5 assimilated must be in a water-soluble form.

Mention should be made of the current trend in world practice to increase as far as possible the content of water-soluble P_2O_5 in fertilizers, which may be accounted for by the greater universality of the use of water-soluble P_2O_5 under various natural conditions.

In accordance with the requirements of agriculture, agrochemical science has established for various types of soil and agricultural crops specific and most widely used weight ratios of nutrient elements ($N-P_2O_5-K_2O$) in complex fertilizers. Fertilizers meeting these requirements have been conventionally termed balanced. A considerable proportion of the balanced fertilizers should have the ratios $N : P_2O_5 : K_2O = 1 : 1 : 1$.

Owing to its relatively low nitrogen content, in most cases Ammophos is not a balanced product. Therefore, it is either mixed with nitrogen fertilizers (ammonium nitrate, carbamide) or a mixture of ammonium phosphate and nitrate (Nitroammophoska) the composition of which is defined by the formula 17 : 17 : 17 (95% of P_2O_5 is in a water-soluble form), is produced.

Nitroammophoska is a complex fertilizer obtained by the sulphuric acid processing of natural phosphates. It was therefore of considerable interest to compare the nitric acid method with the manufacture of Nitroammophoska.

The solutions obtained under the usual conditions (Table 1) of the nitric acid decomposition of phosphates contain virtually the entire P_2O_5 and CaO from the starting material. In the processing of the Khibinsk apatite concentrate, the $CaO : P_2O_5$ weight ratio in the solutions is 1.3 and in the decomposition of the Karatau phosphorite it is about 1.6.

Complex fertilizers from nitric acid–phosphoric acid solutions (Nitrophos and Nitrophoska) are also obtained by their neutralisation with ammonia. Depending on the amount of ammonia introduced and on the calcium content in solution, the phosphate in the fertilizer can be present in water-soluble and citrate-soluble forms[43]. According to Eqn. (1), the nitric acid–phosphoric acid solution has the composition of $3H_3PO_4 + 5Ca(NO_3)_2$.

The theoretical compositions of the liquid and solid phase formed in the ammoniation of the nitric acid-phosphoric acid solutions could be determined beforehand by analysing the equilibrium five-component system $CaO-P_2O_5-N_2O_5-NH_3-H_2O$, which has been investigated in detail at 25°C and partly at 50°C.[44] This analysis has not been published but the experimental data are available,[7,43]. In order to obtain the bulk of P_2O_5 in a water-soluble form, only the first hydrogen ion of phosphoric acid should be

neutralised in the initial solution:

$$3H_3PO_4 + 5Ca(NO_3)_2 + 3NH_3 = 1.5Ca(H_2PO_4)_2 + 3NH_4NO_3 + 3.5Ca(NO_3)_2. \quad (5)$$

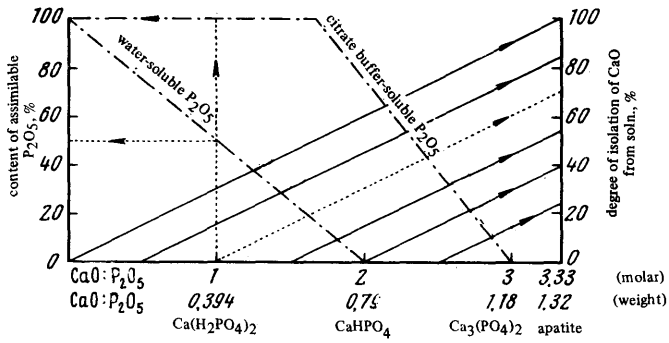

Figure 2. Dependence of the assimilable and water-soluble P_2O_5 content in Nitrophoska on the CaO : P_2O_5 ratio in the nitric acid–phosphoric acid solution from the apatite concentrate[47]; dashed line — example quoted for the Ca : P_2O_5 = 0.394 ratio.

Under these conditions, an appreciable amount of calcium nitrate remains in the reaction mixture, its presence impairing the physical properties (high hygroscopicity) of the fertilizer and reducing the concentration of nutrient materials in it. With increase of the degree of ammoniation, an increasing amount of P_2O_5 is converted into the citrate-soluble $CaHPO_4$:

$$3H_3PO_4 + 5Ca(NO_3)_2 + 6NH_3 = 3CaHPO_4 + 6NH_4NO_3 + 2Ca(NO_3)_2. \quad (6)$$

The preparation of $CaHPO_4$ for animal feed from nitric acid–phosphoric acid solution which had been freed from fluorine in a preliminary treatment is based on this reaction. The formation of $CaHPO_4$ for animal feed by the nitric acid decomposition of the apatite concentrate[45] and Karatau phosphorite[46] has been investigated.

In order to obtain Nitrophoska containing P_2O_5 partly or completely in a water-soluble form, the excess calcium must be removed from the nitric acid–phosphoric acid solution as far as possible (see the nomogram in Fig. 2).

The wide variety of methods for the binding of the excess calcium largely determine the nature of the nitrophosphate manufacturing processes. The characteristics of these processes are to a considerable extent reflected in their economic efficiency.

Two groups of methods for reducing the relative CaO content, which can be conventionally termed chemical and physicochemical, are known and widely employed. In recent years procedures of both these types have been considerably improved in the manufacture of nitrophosphates[48-60].

Among chemical methods, the nitric acid–carbonate method[49], characteristically requiring a preliminary complete ammoniation of the solution associated with the precipitation of the citrate-soluble $CaHPO_4$ [see Eqn. (6)], has found limited application. Only after neutralisation of the solution to pH 4 is it treated with NH_3 and CO_2 in order to form calcium carbonate at pH 7–8:

$$Ca(NO_3)_2 + 2NH_3 + CO_2 + H_2O = CaCO_3 + 2NH_4NO_3. \quad (7)$$

The $CaHPO_4$ and $CaCO_3$ precipitates are not separated in the nitric acid–carbonate method and remain in the fertilizer. Therefore, Nitrophoska obtained by this procedure from the apatite concentrate contains only 35–37% of nutrient substances and has the unfavourable ratios N : P_2O_5 : K_2O = 1 : 0.7 : 1.

Nitrophos from Karatau phosphorite contains up to 28.5% of nutrient substances and has the ratio N : P_2O_5 = 1 : 0.6. The entire P_2O_5 in the fertilizer is in the citrate-soluble formed. The comparatively low grade of the fertilizer and the inadequately balanced ratio of nutrient substances explain why this method has not become very common, despite its relatively favourable technical and economic characteristics.

Several procedures for the binding of calcium oxide by sulphate ions [sic] forming the sparingly soluble calcium sulphate, also belong to the class of chemical methods. Sulphate ions are introduced with sulphuric acid (the nitric acid–sulphuric acid method) with ammonium or potassium sulphate (the nitric acid–sulphate methods), and sometimes simultaneously with sulphates and with sulphuric acid.

In the preparation of Nitrophoska with 50% of P_2O_5 in a water-soluble form by the nitric–sulphuric acid method, theoretically only 30% of fluoroapatite is decomposed by nitric acid, the remainder reacting with sulphuric acid:

$$Ca_5(PO_4)_3F + 3HNO_3 + 3.5H_2SO_4 + 7H_2O = 3H_3PO_4 + 1.5Ca(NO_3)_2 + 3.5CaSO_4 \cdot 2H_2O + HF. \quad (8)$$

The neutralisation of the solution to pH 3.2 (at 80–100°C) proceeds according to equation

$$3H_3PO_4 + 1.5Ca(NO_3)_2 + 4.5NH_3 = 1.5CaHPO_4 + 1.5NH_4H_2PO_4 + 3NH_4NO_3. \quad (9)$$

It follows from Eqn. (9) that the amount of the water-soluble and citrate-soluble P_2O_5 in the product is 50% each. Under industrial conditions Nitrophoska is obtained with P_2O_5 which is assimilable (in the water- and citrate-soluble forms) to the extent of about 90%, of which up to 50% is in a water-soluble form.

According to Eqn. (9), the N : P_2O_5 ratio in the neutralised solution is 1 : 2 and therefore, in order to obtain a balanced fertilizer of the 1 : 1 grade, one introduces more than twice the amount of nitric acid required according to Eqn. (8). In practice the consumption of nitric acid per unit of nutrient substances does not differ from that in processes without the use of sulphuric acid, i.e. in fact sulphuric acid is consumed in the method described only in the binding of part of CaO and increases the cost of the raw material component.

Another important feature of the sulphuric acid method is that the calcium sulphate precipitate is not separated from the solution owing to its fairly unfavourable crystal structure and remains in the product. Consequently the concentration of Nitrophoska does not exceed 34–35% of the sum of nutrient substances. This procedure has been applied on an industrial scale in the USSR.

The above disadvantages have so far hindered a wide-scale application of the nitric acid–sulphuric acid method in world industry. In recent years the sulphuric acid method has been greatly improved[61,62] — it has been found that comparatively large readily filtered gypsum crystals are formed when part of the final solution returning to the process in order to dilute the reaction mass is circulated. This procedure makes it possible to include in the manufacturing scheme for sulphuric acid Nitrophoska the filtration and washing of the gypsum, as a result of which its concentration of nutrient substances can be increased to 50–51% for a fertilizer of the N : P_2P_5 : K_2O = 1 : 1 : 1 grade.

A version of the above scheme with replacement of

part of the sulphuric acid by ammonium sulphate was also investigated. The circulation scheme has been proved on an experimental industrial apparatus. The increased cost of the raw material, compared with other methods, persists in the circulation scheme but the improvements can enhance the efficiency of the present apparatus operating in accordance with the nitric acid–sulphuric acid procedure.

The nitric acid–sulphate method, in which a 40% solution of ammonium sulphate is used to bind the excess calcium (see Fig. 3), has found a relatively wider application in world industry[63,64]:

$$3H_3PO_4 + 5Ca(NO_3)_2 + 5(NH_4)_2SO_4 + 3NH_3 + 10H_2O = 3NH_4H_2PO_4 + 10NH_4NO_3 + 5CaSO_4 \cdot 2H_2O. \quad (10)$$

In this method the precipitated calcium sulphate is filtered off and converted by treatment with ammonium carbonate solution:

$$CaSO_4 + 2NH_3 + CO_2 + H_2O = (NH_4)_2SO_4 + CaCO_3. \quad (11)$$

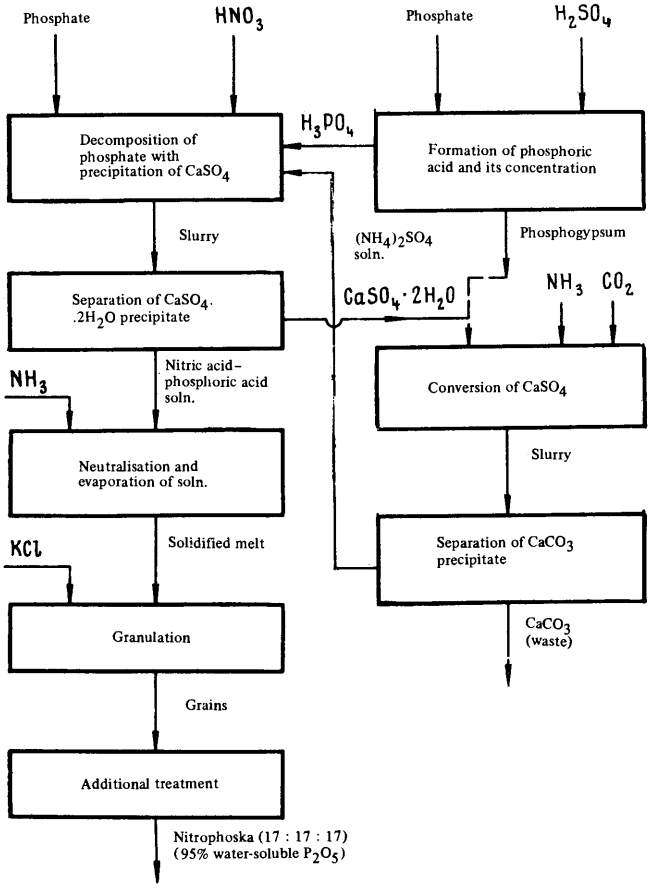

Figure 3. Fundamental scheme of the nitric acid–sulphate method for the manufacture of Nitrophoska.

The calcium carbonate precipitate is a side product and the ammonium sulphate solution formed is returned to the process The advantages of this method include the preparation of concentrated Nitrophoska in which the content of the total nutrient substances for the 1 : 1 : 1 grade is up to 51% and about 95% of P_2O_5 is in a water-soluble form.

The precipitation of calcium oxide requires the introduction of an amount of ammonium sulphate for which the $N : P_2O_5$ ratio decreases to 1 : 0.66. Thus, in order to obtain a more balanced product with the $N : P_2O_5 = 1 : 1$ ratio, it is necessary to introduce additional phosphoric acid, i.e. in this case sulphuric acid is also indirectly involved in the manufacture of Nitrophoska via the preparation of phosphoric acid by extraction.

A version has been developed, which provides for the additional introduction of sulphuric acid (together with nitric acid and ammonium sulphate solution) to decompose the phosphate, in an amount necessary to form phosphoric acid which balances the large amount of nitrogen introduced with ammonium sulphate[65].

The indirect or direct introduction of sulphuric acid into the process lowers the economic efficiency of the nitric acid method of manufacture of complex fertilizers, effectively reducing the amount of the cheapest P_2O_5 introduced in the form of natural phosphates. This version can be applied using the ammonium sulphate solution obtained as a side product in the manufacture of caprolactam.

Among the chemical methods in the next group, mention should be made of the nitric acid – phosphoric acid process based on the decrease of the $CaO : P_2O_5$ ratio in the nitric acid–phosphoric acid solution by the addition of phosphoric acid[66,67]. The process essentially differs little from the nitric acid–sulphuric acid process, since in the latter case sulphuric acid is also indirectly involved in the reaction whereby phosphoric acid is produced by extraction with formation of gypsum as waste.

Complex ternary fertilizers are usually manufactured from the commonest and cheapest potassium raw material–potassium chloride. Studies have been made on the nitric acid processing of phosphates (mainly Karatau phosphorites) also using potassium sulphate[68].

The manufacture of chlorine-free Nitrophoska is of great importance for the cultivation of many agricultural crops, the quality of which is adversely affected by the presence of chloride ions in the fertilizer. A characteristic feature of chlorine-free Nitrophoska is an enhanced content of K_2O: a product with the approximate ratios of 1 : 1 : 1.5 is obtained: the relative amount of water-soluble P_2O_5 does not exceed 50%.

The usefulness of the industrial process with introduction of potassium sulphate depends on the scale of the manufacture of potassium sulphate salts and also on the requirement for a complex fertilizer with an enhanced K_2O content. However, until recently the use of K_2SO_4 was impeded by the small scale of the manufacture of this salt.

High-grade chlorine-free Nitrophoska can be obtained by introducing potassium in the form of the carbonate (with separation of calcium carbonate) or the hydroxide (studies on the technology of the manufacture of Nitrophoska using these reagents are desirable).

The group of physicochemical methods for the reduction of the CaO content in nitric acid–phosphoric acid solutions includes the polythermal crystallisation of calcium nitrate, i.e. by reducing its solubility in the $CaO–P_2O_5–N_2O_5–H_2O$ system on lowering the temperature. This system has been inadequately investigated at temperatures below 0°C, so that the so called "freezing out" of calcium nitrate has been investigated mainly empirically under the conditions of the technological process[7,48,69]. It was shown

that the degree of precipitation of calcium nitrate tetrahydrate and hence the content of water-soluble P_2O_5 in the fertilizer (for nitric acid concentrations in the range 47 to 55% and amounts of nitric acid up to 140% of stoichiometry) depend on temperature (in the range from -15° to +20°C). With increase of the concentration and amount of nitric acid and with decrease of solution temperature, the yield of calcium nitrate and the content of water-soluble P_2O_5 in the product increase (Fig. 4).

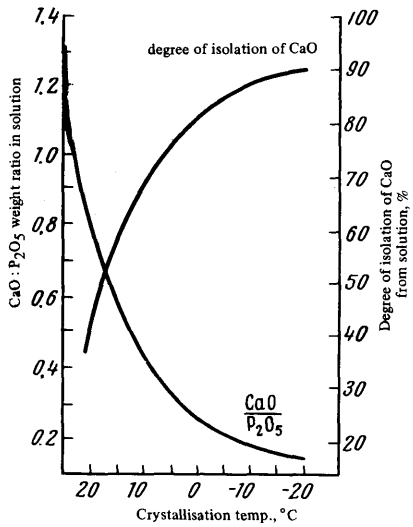

Figure 4. Temperature variation of the degree of isolation of CaO from the nitric acid–phosphoric acid solution (in the decomposition of the apatite concentrate with nitric acid at a concentration of 56–58%)[70].

In the application of the process on an industrial scale with separation of calcium nitrate by cooling, certain technical difficulties were encountered, which delayed the wide scale application of this method. The point is that calcium nitrate tetrahydrate can form an encrustation on the cooled surface of the crystalliser, gradually decreasing the heat transfer coefficient, i.e. increasing the energy expenditure on cooling.

The initial proposals[71,72] for the manufacture of Nitrophoska by the cooling method provided for the formation of the fertilizer with up to 40% of water-soluble P_2O_5 and the simultaneous manufacture of a second product – calcium nitrate (a nitrogen fertilizer containing 15.5% of nitrogen).

The manufacture of Nitrophoska with cooling of the solution to +10°C by the method of Vol'fkovich and Loginova[72] was tested in the USSR on an experimental industrial scale at a nitrogen fertilizer factory, where studies were also made on the nitric acid–carbonate and nitric acid–sulphate methods[39].

The method using polythermal crystallisation of calcium nitrate emphasises the principle of using nitric acid alone for the decomposition of phosphate with simultaneous introduction into the product of nitrogen as a nutrient element.

For the economics of the procedure, it is also important that the entire P_2O_5 enters the process only as the natural phosphate, i.e. in the cheapest form.

The potential economic efficiency of the method with cooling promoted the development of many improvements to the technological process. In recent years multistage cooling (to -5°C) of the slurry obtained in the decomposition of the phosphate raw material with nitric acid (58 to 60%) was used in several countries. The crystallisers are gradually filled and unloaded, so that a continuous flow of the cooled pulp is achieved. This ensured the formation of a coarsely crystalline calcium nitrate, which is readily separated from the mother liquor on filters and in centrifuges. After the additional treatment of the mother liquor, it is possible to obtain Nitrophoska of the 1 : 1 : 1 grade containing about 50% of the total nutrient substances. The amount of P_2O_5 assimilated in the product reaches 96%, including 80–85% of water-soluble P_2O_5.[73–77]

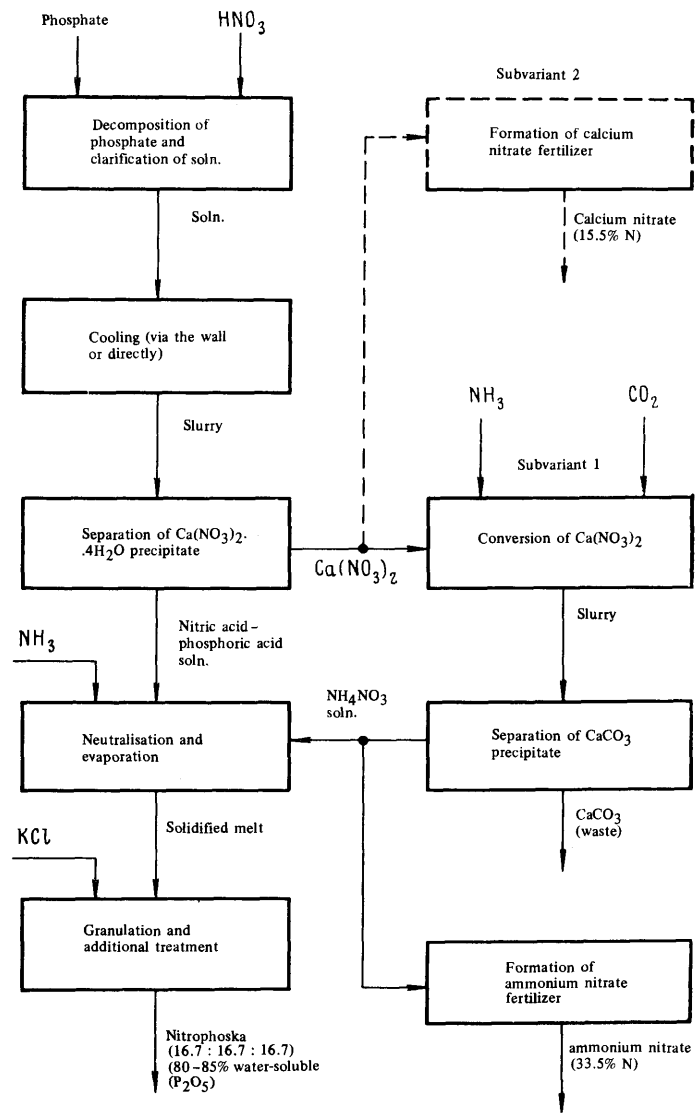

Figure 5. Fundamental scheme of the manufacture of Nitrophoska by the method with polythermal crystallisation of calcium nitrate.

The conversion of the ammoniated mother liquor into the solid fertilizer was also improved and the conversion of the calcium nitrate tetrahydrate isolated into ammonium nitrate [see Eqn. (4)] was introduced. The 95% ammonium nitrate solution can be added in different amounts to the mother liquor in order to maintain the specified $N:P_2O_5$ ratio in Nitrophoska. The remaining ammonium nitrate is issued as a second product — a nitrogen fertilizer with 34% of nitrogen (Fig. 5).

The conversion of calcium nitrate yields a side product (calcium carbonate), which can be used in agriculture for the impregnation of soils with lime and in many manufacturing processes: in the formation of $CaHPO_4$, $Ca(H_2PO_4)_2$, etc. The weight of calcium carbonate is about 75% of that of calcium sulphate (calculated for the anhydrous form) produced in the manufacture of phosphoric acid by extraction for the same amount of phosphate raw material.

The comparatively low cost of the raw material, the satisfactory quality of the product, the possibility of altering the $N:P_2O_5$ ratio in the fertilizer without much difficulty, and the more satisfactory situation as regards industrial waste explains why the manufacture of Nitrophoska by the cooling method has expanded in many countries. During recent years, the output capacity of the existing factories and factories under construction for the manufacture of Nitrophoska by this method in Norway, German Federal Republic, Denmark, France, USA, and Romania reached 6 000 000 tons per year[77].

A further improvement of the cooling method was developed in Czechoslovakia[70,78]. It consists in the replacement of heat exchange via the cooled surface by direct removal of heat by the cooling liquid (for example white spirit), which is immiscible with the slurry The process is continuous, eliminating the encrustation of the cooled surfaces by calcium nitrate crystals. The energy expenditure on the cooling of the slurry is reduced by approximately 10%. This process has been adopted on an industrial scale.

Fig. 6 shows the dependence of the $N:P_2O_5$ ratio and the content of the citrate-soluble or water-soluble P_2O_5 in Nitrophoska obtained by the above method for different amounts of nitric acid used for the decomposition of the apatite concentrate[47]. The possibility of precipitating part of the calcium nitrate as the anhydrous salt directly in the decomposition of natural phosphates with concentrated (80%) nitric acid at a temperature of the order of 60°C has been established experimentally[18,19]. The amount of calcium nitrate isolated makes it possible to obtain Nitrophoska containing up to 80% of P_2O_5 in the water-soluble form. The scheme of the technological process developed on the basis of these studies is close to the usual scheme for sulphuric acid extraction. The development of a modern technology for the concentration of nitric acid makes this process for the manufacture of Nitrophoska very promising. It is useful to continue this study of the process on an experimental industrial scale.

A new trend has arisen in the conversion of nitric acid–phosphoric acid solutions into fertilizers by extracting phosphoric and nitric acids with organic solvents[79]. One of these methods[80–83] consists of extraction with t-pentyl alcohol. The washed organic phase is neutralised with ammonia. On standing, the extract separates into the pure organic solvent and an aqueous slurry containing ammonium nitrate and phosphates. After evaporation and addition of potassium chloride, Nitrophoska of 18 : 18 : 18 grade is obtained.

For the complete isolation of calcium nitrate, the organic phase is washed with a solution of ammonium nitrate. The resulting aqueous phase together with the wash solution is treated with ammonium carbonate to convert calcium nitrate into ammonium nitrate [see Eqn. (4)]. The method has not yet found wide scale application in industry.

A further procedure of this kind has been developed, in which isobutyl alcohol is used as the organic solvent[84–86]. The final products are ammonium dihydrogen phosphate and ammonium nitrate and the waste is calcium carbonate. The method has been applied on an experimental industrial apparatus.

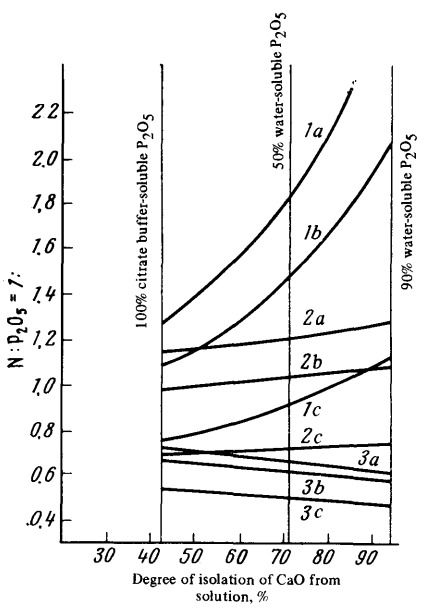

Figure 6. Variation of the $N:P_2O_5$ ratio with the degree of isolation of CaO from the nitric acid–phosphoric acid solution in the decomposition of the apatite concentrate with nitric acid[47]: *1*) method with cooling, no recycling ammonium nitrate; *2*) nitric acid–sulphuric acid method; *3*) nitric acid–sulphate method, without recycling of ammonium sulphate and method with cooling and with recycling of ammonium nitrate; percentage of nitric acid relative to the stoichiometric amount required to decompose the apatite; *a*) 100; *b*) 110; *c*) 140.

Another new trend in the nitric acid processing of phosphates is associated with the use of carbamide[87–90]. Its importance is that carbamide, which forms the readily soluble carbamide phosphate $CO(NH_2)_2.H_3PO_4$ and binds calcium nitrate in the complex $Ca(NO_3)_2.4CO(NH_2)_2$, makes it possible to obtain fertilizers with a high proportion of P_2O_5 in the water-soluble form with a smaller amount, than in other procedures, of calcium isolated from the nitric acid–phosphoric acid solution. It would be useful to investigate further the nitric acid processing of phosphates using carbamide in order to develop effective versions of the manufacturing process for concentrated and balanced water-soluble nitrophosphates.

The preparation of the nitric acid–phosphoric acid solutions for subsequent conversion into fertilizers is not exhausted by the procedures enumerated above. Other versions and methods have been proposed and investigated.

IV. CONVERSION OF AMMONIATED SOLUTIONS INTO SOLID FERTILIZERS

The concluding stages of the processing of the solutions include a number of operations such as the isolation of water (by evaporation or drying), granulation with addition of potassium salts, conditioning (cooling, screening, powdering, librication, encapsulation, pressing, and others). These operations depend to only a slight extent on the methods of preparation of the solutions and therefore different types of apparatus may be employed regardless of the methods used to decrease the relative amount of calcium and for the ammoniation process.

The ammoniated slurry is granulated under industrial conditions with recycling and simultaneous drying of the product in a drum drier ("spherodiser") or in a drum granulator-drier in the industrial application of the nitric acid–sulphuric acid, nitric acid–sulphate, and nitric acid–phosporic acid methods. Such apparatus for the isolation of water and granulation does not use the heat of neutralisation of the acid and therefore entails a high energy expenditure.

The nitric acid–phosphoric acid method is also employed with preliminary neutralisation of the ammoniating-granulating solution and drying of the product in a drum drier. In this version the heat of neutralisation is largely used for the removal of water.

Numerous varieties of industrial apparatus are used to evaporate the neutralised solutions until the formation of a solidified melt and to granulate the latter in spray towers without additional drying of the product. Abroad this process is termed "prilling". The advantage of this method consists in a minimal energy expenditure.

In other schemes neutralised solutions are also evaporated and then granulated in a blade granulator with recycling and subsequent drum drying of the product. Certain companies outside the Soviet Union employ also a different variety of apparatus for technological processes which are essentially of the same type.

V. COMPARATIVE ANALYSIS OF TECHNOLOGICAL PROCESSES IN THE MANUFACTURE OF COMPLEX FERTILIZERS

In the manufacture of complex fertilizers by modern methods 76–87% of the cost is represented by that of the raw materials. The consumption and quality of the raw material are therefore important factors, which reflect the economic efficiency of the methods of manufacture.

For all types of complex fertilizers of the same grade, the consumption of N, P_2O_5, and K_2O is virtually identical: for example, for fertilizers with the $N:P_2O_5:K_2O = 1:1:1$ ratios, it amounts to 0.33–0.35 tons per ton of each nutrient substance. However, the unit costs of nitrogen and P_2O_5 in different raw materials are not the same. The cheapest types of raw material are synthetic ammonia and natural phosphates (apatite and phosphorite concentrates). Therefore, the method of manufacture of a complex fertilizer which requires the cheapest raw materials containing nitrogen and phosphorus will be economically the most efficient ‡.

Comparison of the technological processes used to manufacture complex fertilizers shows[91] that the relative consumption of nitrogen introduced with ammonia (synthetic ammonia or ammonium sulphate) and nitric acid is virtually the same for all the methods considered here. The amount of ammonia nitrogen is in the range 57–62% and that of the nitrogen introduced with nitric acid is 43–38%.

All the methods for the manufacture of both Nitroammophoska and Nitrophoska involve the additional consumption of sulphuric acid (directly or in the manufacture of phosphoric acid). The only exception is the manufacture of Nitrophoska with isolation of calcium nitrate by cooling. The cooling method differs from all others for the synthesis of complex fertilizers also by the fact that the entire P_2O_5 is introduced in the cheapest form — as the natural phosphate. In other words the decomposition of the phosphate raw material in this method is achieved with nitric acid alone, without the additional consumption of sulphuric or phosphoric acid.

The above analysis leads to the conclusion that the cost of the manufacture of Nitroammophoska by treatment with phosphoric and nitric acids and also of Nitrophoska by the nitric acid–sulphuric acid and nitric acid–phosphoric acid methods is highest. The nitric acid–sulphate methods occupy an intermediate position and the manufacture of Nitrophoska by procedures involving the isolation of calcium nitrate by cooling should be least expensive. This conclusion is confirmed by the finding that in the last manufacturing process moderate cooling is employed: a temperature from +10° to -10°C, which can be achieved by combination with the synthesis of ammonia involving a relatively low energy expenditure.

The above data disprove the common view expressed by some investigators[92,93] that the manufacture of Nitrophoska can be useful only provided that the reserves of sulphur in the country are limited or when the sulphur-containing raw material is expensive. However, in fact the cooling method permits economically efficient processing of the phosphate raw material without any consumption of sulphur, using the same amount of nitric acid as in other methods for the manufacture of Nitrophoska — a complex fertilizer.

Approximate calculations of the intrinsic unit cost of the nutrient substances obtained by different methods confirm the above conclusions[52,53,58,91,94–96].

When calcium nitrate is manufactured as a commercial by-product, the manufacture of Nitrophoska by the cooling method takes place without waste. The conversion of calcium nitrate into ammonium nitrate makes it possible to obtain calcium carbonate as a by-product. Compared with the methods for the manufacture of complex fertilizers involving the formation of calcium sulphate as waste, the formation of calcium carbonate simplifies and reduces the cost of the employment of the calcium waste.

The determination of the capital costs is important for the assessment of the different methods of manufacturing complex fertilizers. In certain published studies[94,96] the specific capital investment with the associated cost of the manufacture of Nitrophoska by the cooling method is lower than in the manufacture of Nitroammophoska, while in the manufacture by other procedures[95] the costs are at approximately the same level.

Analysis of the present development of the technology of the nitric acid processing of natural phosphates shows that the method with polythermal crystallisation of calcium nitrate and conversion of the latter into ammonium nitrate or without conversion is promising.

The main advantages of the process with cooling are the lowest cost of the raw material in consequence of the

‡ Since regardless of the method of manufacture, potassium is in most cases introduced as the chloride, its cost does not affect the comparative assessment of the manufacture of complex fertilizers.

effective processing of the cheapest phosphate raw material without the consumption of sulphuric or phosphoric acid, the possibility of obtaining complex fertilizers of different grades on the same apparatus without significant changes in the technological process, and the formation of calcium carbonate as the by-product instead of calcium sulphate (when calcium nitrate is converted into ammonium nitrate).

Studies on new technological processes for the manufacture of complex fertilizers retaining the basic and fruitful idea of employing nitric acid for the decomposition of natural phosphates without the addition of other acids or their salts are useful and merit support.

It is clear from the foregoing that the processes involving the conversion of natural phosphates by nitric acid into complex fertilizers have greatly developed in recent years both in terms of scale and the wide variety of chemical-engineering manufacturing schemes and as regards their more detailed physicochemical investigation. These processes are of great interest and promise and they have been investigated both theoretically and technically to an extent sufficient for the selection of the optimal scheme for the manufacture of Nitrophoska with polythermal crystallisation of calcium nitrate, meeting the highest technical and economic requirements among all other known methods for the synthesis of complex fertilizers.

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Electrochemistry of Selenium and Tellurium

A.I.Alekperov

The review deals with the principal advances in the electrochemistry of selenium and tellurium. Problems concerning the kinetics and mechanisms of the cathodic reduction of selenium and tellurium to different valence states and their anodic oxidation in aqueous and non-aqueous solutions are discussed.
The practical applications of electrochemistry in the isolation, refining, and determination of small amounts of the two elements are described.
The bibliography includes 178 references.

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I. INTRODUCTION

Selenium and tellurium belong to the class of rare elements which are widely employed in various branches of modern engineering. These elements have many specific properties. As their purity improves, new properties are discovered and the scale and specific features of their applications are extended.

With expansion of the field of their applications, there arises the necessity for an intense investigation of the chemical and physicochemical properties and also of the technology of the preparation of pure and ultrapure selenium, tellurium, and their compounds.

The present state of the chemistry and technology of the preparation of pure and ultrapure selenium and tellurium have been described in monographs by Chizhikov and Schastlivyi[1,2], Kudryavtsev[3], Nazarenko and Ermakov[4], Bagnoll[5], and Yukhtanov[6] and in reviews[7,8].

The first study on the electrochemistry of tellurium was published at the beginning of the 19th century. Almost 100 years later the study of the electrochemical behaviour of selenium was begun. Subsequently, isolated papers, frequently containing contradictory data, appeared from time to time. Systematic study of the electrochemical properties of selenium and tellurium began in the 1950's–1960's in connection with their large-scale applications in modern engineering. Extensive data have now accumulated, a systematic account of which requires a separate review.

II. ELECTROCHEMICAL BEHAVIOUR OF SELENIUM AND TELLURIUM ELECTRODES IN ELECTROLYTES OF DIFFERENT COMPOSITIONS

1. OXIDATION-REDUCTION POTENTIALS OF SELENIUM AND TELLURIUM

Selenium

Apart from the metallic state, selenium can exist in the −2, +2, +4, and +6 states of oxidation. For the most stable states, the oxidation-reduction potentials can be represented schematically as follows[9]:

$$H_2Se \xrightarrow{-0.40} Se \xrightarrow{+0.74} H_2SeO_3 \xrightarrow{+1.15\text{в}} SeO_4^{2-}: \text{ acid solutions,}$$

$$Se^{2-} \xrightarrow{-0.92} Se \xrightarrow{-0.366} SeO_3^{2-} \xrightarrow{+0.05\text{в}} SeO_4^{2-}: \text{ alkaline solutions.}$$

The standard potential of the selenium–selenous acid system has been determined[10] by direct measurement of the equilibrium constant of the reaction

$$Se(\text{hexagonal}) + 2I_2(\text{cryst.}) + 3H_2O \rightleftarrows H_2SeO_3 + 4H^+ + 4I^-$$

and a value of +0.74 V† was adopted.

In view of the fact that a state of equilibrium is reached for the above system, it was concluded that the selenium–selenous acid system is reversible.

The steady-state potential of the selenium electrode in selenous acid solutions corresponds to the equilibrium potential of the selenium–selenous acid system[11]. The equilibrium state of the selenium–selenous acid system is also reached in solutions containing tin(II) chloride. The reduction of selenous acid by $SnCl_2$ permits the calculation of the equilibrium constant for the reaction[12]

$$H_2SeO_3 + 2SnCl_2 + 4HCl = 2SnCl_4 + Se + 3H_2O\ .$$

Titrations of selenous acid solutions with tin(II) chloride at different hydrochloric acid concentrations established[13] that in 2–8 M HCl the potential of the Se/SeO_3^{2-} system is +0.74 V. Hence it follows that in the above HCl concentration range selenium in solution in the SeO_2–HCl system exists preferentially as selenous acid.

Tellurium

It dissolves in alkalies and acids with oxidising properties. It forms compounds in both positive (Te^{2+}, Te^{4+}, and Te^{6+})‡ and negative (Te^{2-}, Te_2^{2-}) valence states. Tellurium(IV) compounds are the most stable. In the quadrivalent state tellurium forms numerous complexes[4]. In 2.5 M hydrochloric acid solution the tellurium complex has the composition H_2TeCl_6.[14] As stated by Iofa et al.,[15] in 3.5–7 M HCl there exist at least four different complex tellurium ions which are interconverted as the hydrochloric acid concentration is varied.

The potential of the tellurium electrode in hydrochloric acid solutions of tellurium(IV) was first measured by Reichinstein[16] and Kazarnovskii[17]. With increase of hydrochloric acid concentration from 0.05 to 4.5 M, the potential of the tellurium electrode also rises. It assumes the highest value (+0.567 V) in 2.5 M HCl. It was adopted[16,17] as the equilibrium standard potential of the Te/Te^{4+} system. This is not quite correct, since the authors made not altogether justified assumptions, namely that $TeCl_4$ is completely dissociated into Te^{4+} and Cl^- and that the activity coefficient is unity.

The introduction of a correction by Yakovleva and Andreev[18] in the calculation of the standard potential of the tellurium electrode in hydrochloric acid solutions cannot also be regarded as entirely justified. The authors state that, since there are no literature data for the activity coefficients of Te^{4+} ions and it is difficult to determine them, they can be assumed equal to the activity coefficients of $[Fe(CN)_6]^{4-}$ ions. The activity coefficient of an electrolyte is known to depend on the interaction between the ions with formation of ionic association complexes. Evidently the electrostatic and specific interactions between different ions must differ and hence one cannot assume the identity of the activity coefficients of different ions.

Thus +0.576 V should not be regarded as a standard potential but as an experimental or apparent potential observed in the Te/Te^{4+} system when the concentration ratio in the latter corresponds to the stoichiometry of the electrochemical reaction

$$Te^{4+} + 4e \rightleftarrows Te\ .$$

By measuring the equilibrium potential in the deposition of tellurium from hydrochloric acid solutions by tin(II) chloride, it was established[13] that at hydrochloric acid concentrations in the range 2–3 M the apparent reduction potential is almost independent of acid concentration and amounts to +0.584 V. With further increase of acid concentration, the reduction potential falls.

The surface of the tellurium electrode is rapidly oxidised, the oxide film having a significant influence on the electrode potential. The electrodes treated in an atmosphere of hydrogen at −200°C and then heated to 400°C in a high vacuum exhibit a potential in buffer solutions (free from O_2) which corresponds to the Te/TeO_2 system (in the pH range 2–12).[19]

Schuhmann[20] obtained the following data by direct measurements of the potential of the tellurium–tellurous acid system:

$$Te + 2H_2O = TeO_2(\text{solid}) + 4H^+ + 4e, \qquad \varphi = +0.529\ \text{V},$$

$$Te + 2H_2O = TeOOH^+ + 3H^+ + 4e, \qquad \varphi = +0.559\ \text{V}.$$

With increase of pH, the potential of the tellurium electrode shifts in alkaline solutions and assumes a negative value. The e.m.f. of the cell Te(solid) | TeO_2(solid) | buffer solution ‖ calomel electrode at 25°C and in the pH range 2.2–8 is described by the equation $\varphi = 0.349 - 0.058$ pH.[21] Under these conditions, the electrode can be used as an indicator electrode in acidimetric titrations.

In 1 M NaOH solution the potential of the Te/TeO_3^{2-} system is −0.395 V (s.c.e.)§.[18] The sharp change of the potential of the tellurium electrode in alkaline electrolytes is due to the reaction $3Te + 6NaOH = Na_2TeO_3 + 2Na_2Te + 3H_2O$.

As a result of this reaction, the composition of the electrolyte near the electrode probably changes, Te^{2-} ions appear and create completely different conditions at the tellurium electrode. Another cause of the fall of the electrode potential as the concentration of alkali is altered may be a change in the composition and structure of the tellurite ions.

† The standard potentials are quoted relative to the hydrogen electrode.

‡ The valence indices characterise the degree of oxidation and not the ionic structures.

§ s.c.e. = saturated calomel electrode.

The standard potential of the TeO_3^{2-}/TeO_4^{2-} system in alkaline solutions was obtained on the basis of the oxidation of tellurite with hypoiodate[9]:

$$Te_2O_3^{2-} + 2OH^- = TeO_4^{2-} + H_2O + 2e.$$

It was found that $\varphi = +0.4$ V.

Thus the potentials of tellurium systems can be represented schematically as follows:

$$H_2Te \xrightarrow{-0.72} Te \xrightarrow{+0.529} TeO_2(solid) \xrightarrow{+1.026} H_6TeO_6(solid) \text{ acid solutions,}$$

$$Te^{2-} \xrightarrow{-1.14} Te \xrightarrow{-0.57} TeO_3^{2-} \gtrless^{+0.46} TeO_4^{2-} \text{ alkaline solutions.}$$

More detailed information about the carefully adjusted potentials of tellurium systems and the variation of the potential of the tellurium electrode with pH is given by Pourbaix[22].

2. ELECTROLYTIC REACTIONS AT SELENIUM AND TELLURIUM ELECTRODES

Selenium

Comparison of the conductivities in the S, Se, Te series shows that the conductivity of sulphur is very low, tellurium resembles metals as regards its conductivity, and selenium exhibits semiconductor properties. Semiconductor properties and photosensitivity have a marked influence on the electrochemical behaviour of selenium.

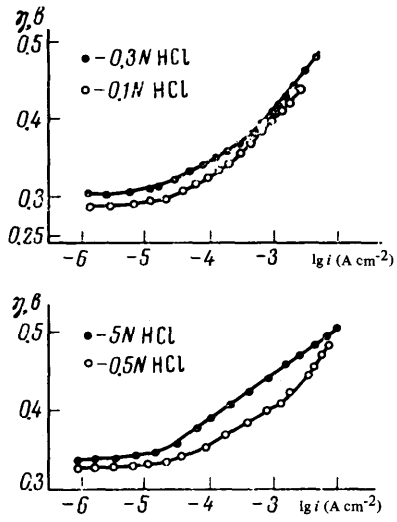

Figure 1. Polarisation curve obtained with the tellurium electrode in hydrochloric acid solutions[29].

In the polarisation of selenium with n- and p-type of conduction in 0.1 N sulphuric acid solution, Gobrecht et al.[23] noted that polarisation of n-type selenium hardly changes on illumination and is determined mainly by the ohmic resistance of the electrode. Illumination of p-type selenium lowers appreciably the cathodic polarisation. Anodic polarisation decreases much less on illumination. The different effects of illumination on the cathodic and anodic processes show that the decrease of the cathodic polarisation in the given case does not occur solely due to a decrease of the ohmic resistance of selenium under the influence of light. The high cathodic polarisation is evidently caused by the fact that in the cathodic reduction of hydrogen ions free electrons are involved, the concentration of which in p-type selenium may be very low.

A high cathodic polarisation in the dark and its decrease on illumination were noted in the electrolytic deposition of selenium at a selenium electrode from selenous acid solutions[24] and also from weakly and strongly acid solutions of selenium dioxide[25].

After the application of an external e.m.f. to the electrodes of the electrolytic cell consisting of two selenium electrodes immersed in 57% H_2SeO_3, the cathode acquires a high sensitivity to illumination, amounting approximately to 1000 ma lm^{-1}.

It is believed[26] that such high light sensitivity of a photoelectric cell of this kind is due to the formation on the surface of the selenium electrode of a blocking layer by adsorbed hydrogen atoms (a solid solution of hydrogen in selenium) generated by the reduction of H+ ions at the electrode.

The photoelectric effect at the selenium electrode (gold foil coated by red selenium) in aqueous hydrochloric acid solution has been investigated[27].

Tellurium

When a tellurium electrode is immersed in 0.1 N H_2SO_4 or 0.1 N NaOH solutions at low current densities (5×10^{-6}–1×10^{-5} A cm^{-2}), a sharp potential jump towards lower positive values associated with a fall of IR is observed in the initial stage of the cathodic polarisation. The subsequent slow variation of the potential (before attaining a steady value) is associated with the reduction of the oxide film, the formation of a double layer, the reduction of H^+ ions, and the formation of hydrogen molecules on the electrode surface.

In the anodic polarisation the rapid initial increase of the potential is associated with the ionisation of H_2 formed in the cathodic polarisation. The subsequent slow change of the potential is a consequence of the evolution of oxygen accompanied by the oxidation of the metal[28]. When the surface of the electrode is completely covered by oxides, the potential acquires a constant value and changes only with current density.

The $\eta - \lg i$ polarisation curves (the variation of the hydrogen overvoltage η with $\lg i$), measured with the aid of a tellurium electrode in 0.05–5 N H_2SO_4, in buffer solutions at pH 3–13, and in 0.1 N NaOH have two linear sections with slopes of about 0.04 V and about 0.12 V. On this basis, it has been suggested that[28] in the above media the evolution of hydrogen on tellurium takes place via an electrochemical mechanism.

In hydrochloric acid solutions the slope of the $\eta - \lg i$ curves varies with the acid concentration (Fig. 1). In solutions at hydrochloric acid concentrations below 0.3 N the $\eta - \lg i$ curves consist of two linear sections with slopes $\upsilon_1 \simeq 0.04$ V and $\upsilon_2 \simeq 0.12$ V. It was suggested[29] that in these solutions the evolution of hydrogen at tellurium proceeds via an electrochemical mechanism in which the formation of hydrogen molecules from H^+ and adsorbed hydrogen atoms is the rate-determining stage. In more concentrated hydrochloric acid solutions the $\eta - \lg i$ curve has a single linear section with a slope of 0.06 V.

In order to account for the change in slope in more concentrated hydrochloric acid solutions, it was suggested[29] that the evolution of hydrogen at tellurium proceeds via a "dual mechanism", i.e. there may be two rate-determining stages proceeding at very similar rates.

In the derivation of the kinetic equation for the possible stages in the cathodic evolution of hydrogen at tellurium, the authors calculated the slopes of the $\eta - \lg i$ curves for different mechanisms on the basis of the theoretical concept of Bockris and Potter[30]. The results showed that, in more concentrated hydrochloric acid solutions at low current densities, the evolution of hydrogen at tellurium can proceed via a dual electrochemical-catalytic mechanism with two different rate-determining stages having similar rates.

At low current densities ($1 \times 10^{-5} - 5 \times 10^{-4}$ A cm^{-2}) in hydrochloric acid solutions the evolution of hydrogen at a tellurium electrode proceeds via a slow discharge mechanism. On further increase of current density (to 1×10^{-2} A cm^{-2}), cathodic dissolution begins with formation of tellurium hydride[31].

As at mercury[33] and other electrodes[34,35], in the electrochemical reduction of $Fe(CN)_6^{3-}$ at the tellurium electrode[32] a decrease of the concentration of the indifferent electrolyte (KCl) near the zero-charge point [$\varphi = -0.30$ V (s.c.e.)] entails a decrease of the current on the $i - \varphi$ curves owing to the effect of the electrical double layer on the kinetics of the electrochemical reaction. An increase of the concentration of the indifferent electrolyte leads to a gradual removal of inhibition of the reaction and at a concentration of 0.1 N the inhibition is completely removed. Chloride and bromide ions do not have an appreciable influence on the kinetics of the electrochemical reduction of $K_3[Fe(CN)_6]$ at tellurium, while iodide ions sharply inhibit the reaction.

3. ANODIC AND CATHODIC DISSOLUTION OF SELENIUM AND TELLURIUM

Selenium

In the anodic polarisation of the selenium electrode in neutral and acid solutions vigorous anodic dissolution of selenium takes place. Depending on the electrolysis conditions and the composition of the electrolyte, the anodic reaction product can be selenous acid or a mixture of selenous and selenic acids. In selenous acid solutions the acid itself becomes concentrated, the anodic reactions occurring without appreciable inhibition with an apparent yield close to 100%.[25]

An important factor in the refining of selenium is the preparation of selenous acid, which is synthesised by the combustion of technical selenium in a stream of oxygen with subsequent dissolution of the resulting selenium dioxide in distilled water. The data obtained[25] suggest that the electrochemical method (anodic dissolution of selenium or interaction of electrically regenerated chlorine with powdered selenium in a single bath) may be promising for the synthesis of selenous acid.

The high resistance of selenium (10^5–10^{11} Ωcm) hinders the use of pure selenium as the material of anodes. For this reason, anodes consisting of a mixture of selenium and graphite have been employed. The most suitable ratio is Se : graphite = 3 : 1.

Measurements of polarisation curves with the aid of the selenium–graphite anode in different electrolytes have shown that at low current densities the anodic curves are the same to a first approximation as the curves obtained in the anodic dissolution of thin selenium films. At high currents (> 10 mA cm^{-2}) there is a linear relation between current density and polarisation.

The form of the polarisation curves shows that the principal reason for the high polarisation is the ohmic potential drop in the electrode itself, and in the electrolyte in the case of H_2SeO_3 solutions, which have a low conductivity.

Selenous acid is synthesised by the reaction of electrically regenerated chlorine with selenium without an inert current-conducting material. A mixture of HCl and NaCl solutions has been employed as the electrolyte with a current density at the anode (graphite) of 30–40 mA cm^{-2}; the cathode consists of a PVC fabric membrane impregnated with titanium. The resulting acid contains small amounts of H_2SeO_4.

In the anodic polarisation of the selenium electrode containing Br_2, HBr and $HBrO_3$ appear as impurities[36] in the solution in addition to H_2SeO_3.

By electrolysing selenous acid at the anode, it is possible to prepare selenic acid and its salts:

$$H_2SeO_3 + H_2O - 2e \rightarrow H_2SeO_4 + 2H^+.$$

The method of anodic oxidation of selenous acid was proposed for the synthesis of selenic acid and its salts free from admixtures of other elements[37–39].

A separate study on the cathodic distribution of selenium has apparently not been made. However, it has been noted[37] that in the electrolysis of KOH solutions with selenium as the cathode and platinum as the anode, polyselenide ions of the type Se_n^{2-} are formed, in which n may be 4.4.

Tellurium

In the electrolysis of alkaline solutions using tellurium electrodes tellurium dissolves both anodically and cathodically. The cathodic dissolution results in the formation of Te^{2-} and Te_2^{2-} ions.

The formation of Te_2^{2-} ions in the cathodic polarisation of tellurium in alkaline solutions was pointed out a long time ago by Le-blanc[40] and Müller and Nowakowsky[41], who observed that in the electrolysis of solutions of alkalies using the tellurium electrode a gas was not evolved at either electrode, both dissolving. In the electrolysis of KOH solution, the solution at the cathode becomes red (polytellurides are formed). The anode dissolves tellurium in an oxidation state close to four, the Te^{4+} ion passing into the solution; most of these ions react with OH^- ions, forming TeO_3^{2-}. Under the conditions where the solution contains simultaneously positive and negative tellurium ions, the equilibrium $3Te \rightleftharpoons 2Te^{2-} + Te^{4+}$ is established. In concentrated alkaline solutions with a measurable amount of products the equilibrium in this reaction is displaced to the right and on dilution of the solution the reaction proceeds in the opposite direction.

The main product in the cathodic dissolution of tellurium in solutions at pH < 9 are Te^{2-} ions, while at pH > 12 the product is Te_2^{2-} ions. In the pH range 9–12 a mixture of Te^{2-} and Te_2^{2-} is formed in the solution. According to the literature[42,43], the overall reaction in the dissolution of the tellurium cathode can be represented as follows:

$$Te + 2(n-1)H^+ + ne = (n-1)H_2Te + \frac{2-n}{2}Te_2^{2-}.$$

The number of electrons n per atom of dissolving tellurium is 2 in acid solutions and 1 in alkaline solutions.

It has been noted[44] that in alkaline solutions the steady-state potential φ_{st} of the tellurium electrode changes very slowly with time, reaching 0.15 V in 1 N KOH and 0.08 V in 0.1 N NaOH. After a preliminary cathodic polarisation of the electrode, φ_{st} is −0.75 V and gradually shifts towards less negative values. This shift takes place as a result of the spontaneous oxidation of Te_2^{2-} (formed from the tellurium electrode in the cathodic polarisation) to Te and TeO_3^{2-}.

The polarisation of the tellurium electrode in NaOH solutions[45] and $Ba(OH)_2$ and NH_4OH solutions[46] was investigated by Awad. In 0.005–0.01 N NaOH at current densities of 1×10^{-6}–1×10^{-3} A cm^{-2} the $\eta - \lg i$ curves have a single linear section with a slope of about 0.1 V. In more concentrated solutions (up to 5 N NaOH) there are two sections with the slopes $v_1 \simeq 0.04$ V and $v_2 \simeq 0.1$ V. It is suggested that at low NaOH concentrations the rate-limiting stage in the cathodic process is the discharge of Na^+ ions. At current densities of 1×10^{-4}–1×10^{-2} A cm^{-2} in 0.5–5 N NaOH solutions the $\eta - \lg i$ curves are to some extent located at potentials more positive than that of the normal hydrogen electrode. In the region near the cathode the solution becomes red, indicating the formation of polytellurides.

Comparison of the experimental slopes with the calculated value (0.06 V) obtained in accordance with the reaction $2Te + 2e \rightarrow Te_2^{2-}$ suggests that a direct formation of Te_2^{2-} by this reaction is impossible.

Therefore Awad[46] postulated that the cathodic dissolution of tellurium proceeds in stages with participation of the electrolyte cation according to the following mechanism:

$$Te + Na^+ + e \rightarrow NaTe ,$$
$$NaTe \rightarrow Te + Na^+ + e ,$$
$$NaTe + Te + e \rightarrow Te_2^{2-} + Na^+ .$$

Awad[46] believes that in $Ba(OH)_2$ and NH_4OH solutions the multistage process can be represented in the following manner on the assumption that tellurium is present as diatomic species:

$$M^+ + Te_2 + e \rightarrow MTe_2 , \quad (1)$$
$$MTe_2 + M^+ + e \rightarrow M_2Te_2 , \quad (2)$$
$$M_2Te_2 + Te_2 + e \rightarrow M_2Te_4^- , \quad (3)$$
$$M_2Te_4^- + e \rightarrow 2M^+ + 2Te_2^{2-} . \quad (4)$$

In 0.5 N NH_4OH and 0.005 and 0.01 N $Ba(OH)_2$ solutions the rate of dissolution is controlled by the discharge of the electrolyte cation, i.e. stage (2) is rate-determining. At high $Ba(OH)_2$ concentrations, the rate is determined by the electrochemical reaction, i.e. stage (4) is slow. However, Awad's experimental data do not confirm his ideas concerning the stoichiometric numbers of the above reactions. The order of the reaction with respect to sodium ions in the double layer is inconsistent with the experimental data. Therefore Komandenko and Rotinyan[47] believe that the formation of Te_2^{2-} probably proceeds without involvement of the alkali metal cation via the mechanism

$$Te + OH^- + e \rightarrow TeOH^{2-} ,$$
$$TeOH^{2-} + Te + e \rightarrow Te_2OH^{3-} \quad \text{slow stage},$$
$$Te_2OH^{3-} + Te + e \rightarrow Te_3OH^{4-} ,$$
$$Te_3OH^{4-} + Te + e \rightarrow 2Te_2^{2-} + OH^- .$$

One can also assume that the polytelluride is formed as the result of the reaction of the Te^{2-} ion with elemental tellurium on the surface of the electrode. However, polarisation data alone, which were used to establish the mechanism of cathodic dissolution of tellurium, are insufficient. It is also necessary to establish the nature of the intermediates and to determine the current yield of the most stable product which accumulates and is responsible for the slow stage. It is therefore difficult at present to give a definite preference for a particular mechanism.

The cathodic dissolution of tellurium is used in some cases for the preparation of hydrogen tellurides[37].

The anodic behaviour of tellurium has been investigated in acid[48–51] and in alkaline[40,52,53] solutions. On the basis of polarisation measurements, Fishman et al.[50] and Awad[51] suggest that the Te^{4+} ion is formed in anodic polarisation. However, the physicochemical properties of tellurium compounds and also experimental data[48] provide adequate grounds for the belief that in acid solutions the primary anodic product is Te^{2+}. Apart from its electrochemical reaction, Te^{2+} subsequently undergoes disproportionation, and, in weakly acid electrolytes, hydrolysis.

In 1.5–3 N NaOH solutions at a current density of 10–40 mA cm^{-2} the anodic dissolution of tellurium proceeds with a 100% current yield. At higher concentrations of alkali the current yield exceeds 100%.

When lower concentrations of alkali are employed, an insoluble form of tellurous acid is formed on the surface of the anode, which markedly increases the resistance.

The anodic process proceeds via the overall reaction $Te + 4OH^- - 4e \rightarrow H_2TeO_3 + H_2O$,[52] which consists of a series of consecutive stages:

$$Te + OH^- - e \rightarrow TeOH ,$$
$$TeOH + OH^- - e \rightarrow TeO + H_2O ,$$
$$TeO + OH^- - e \rightarrow TeOOH ,$$
$$TeOOH + OH^- - e \rightarrow H_2TeO_3 .$$

III. CATHODIC AND ANODIC DEPOSITION OF SELENIUM AND TELLURIUM

1. DEPOSITION FROM AQUEOUS SOLUTIONS

Selenium

Depending on the composition of the electrolyte and the electrolysis conditions, selenium may be deposited in the form of red amorphous and grey hexagonal modifications or their mixture. The electrolytic deposition of red amorphous selenium is carried out in acid and weakly alkaline selenous acid electrolytes[54–56]. The electrolysis is performed at 20–40°C and a current density of 10–20 mA cm^{-2}.

With the development of xerography towards the end of the 1950's, interest was aroused in methods for the preparation of films of amorphous selenium on a metallic base. In order to obtain fairly strong films of red amorphous selenium in the electrolysis of selenous acid and its salts, Graham et al.[57] investigated the effect of the pH of the medium wetting the reactants, the material of the electrode, temperature, and illumination on the structure and electrophysical properties of the deposits. The electrolysis was performed in two baths: (1) acid bath: 350 g of SeO_2 per litre of water, pH 0.8; (2) alkaline bath: 211 g of SeO_2 per litre of dilute NaOH solution, pH 8.

Citric acid was employed as the wetting agent. Selenium was deposited on platinum, bright nickel, black nickel, gold, copper, silver, chromium, and lead electrodes. The electrolysis was carried out in the temperature range 5–40°C and under illumination ranging from moderate to very intense from three 500 W lamps focussed on the surface of the electrode. The most satisfactory coatings were obtained on platinum and nickel. However, the resulting red amorphous selenium deposits proved to be unsuitable for xerography. According to the authors, this is due to the high impurity content in the electrolytic amorphous selenium.

The preparation of selenium coatings by electrolysis was also reported by Krusenstiern and Meier [58].

In acid solutions selenium is deposited on iron, nickel, and copper with and without external polarisation. In neutral solutions without external polarisation it is deposited only on iron. In alkaline solutions selenium is deposited on the above metals only when external polarisation is applied. In all cases the rate of deposition of selenium depends on the nature of the metal [59].

It has been noted [25] that in the electrolysis of 2 M H_2SeO_3 (temperature 20–40°, current density 0.03–0.06 mA cm^{-2}), 2 M $KHSeO_3$ (pH ~ 7), and 2 M H_2SeO_3 + 2 M KCl (current density 2.5 mA cm^{-2}) solutions grey hexagonal selenium is deposited on platinum and nickel cathodes.

In the temperature range 45–70°C at a current density of 10–30 mA cm^{-2} a mixture of grey hexagonal and red amorphous selenium is deposited on the cathode. At elevated temperatures (70–100°C) grey hexagonal selenium (the so called metallic selenium) is deposited on the cathode [60].

The addition of H_2SO_4 and HNO_3 to the electrolyte up to a concentration of 1.2 *N* lowers the potential in the bath from 3.5 to 2.5 V but does not have an appreciable influence on the nature of the electrolytic selenium [61]. In the electrolysis of selenium-containing solutions the acidity of the electrolyte has a marked influence on the cathodic process [25]. A grey, fairly loose deposit of elemental selenium, which is weakly attached to the metallic base, is formed on the cathode from 2 M H_2SeO_3 solutions. At low current densities the current yield of selenium is 45–50%.

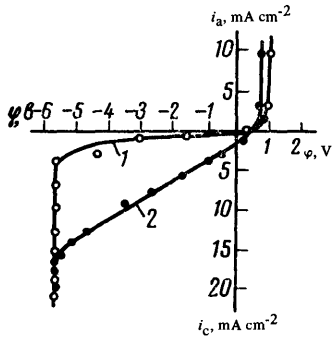

Figure 2. Cathodic–anodic polarisation curves for a 2 M H_2SeO_3 solution: 1) in the dark; 2) under illumination [25].

The cathodic process is accompanied by a high polarisation, which falls appreciably when the surface of the electrode is illuminated (Fig. 2). At high current densities the polarisation is affected by the semiconductor properties of the selenium deposited on the electrode. The high potential gradient in the surface layer of selenium leads to the electrical breakdown of the surface layer. Under the breakdown conditions, vigorous evolution of hydrogen takes place on the electrode. The current yield of selenium falls to 20–25%.

When the surface of the cathode is illuminated, the electrode potential shifts towards positive values and the electrical breakdown of the surface barrier does not occur, the discharge of H^+ diminishing sharply and the current yield of selenium coming close to the theoretical value [62].

Von Hippel and Bloom [63] deposited grey hexagonal selenium from a sulphuric acid electrolyte containing 840 g of SeO_2 per litre of 18 *N* H_2SO_4 and recommended that grey selenium be electrodeposited at 90°C, a temperature which promotes the maximum rate of formation of nuclei. Dense and homogeneous deposits of selenium firmly adhering to the metallic base were obtained on the cathode. Analogous results were achieved also when H_2SeO_4 was employed instead of H_2SO_4. Von Hippel and Bloom [63] recommend that highly acid electrolytes (18 *N* H_2SO_4 + 150 g $litre^{-1}$ SeO_2 at 55–120°C) be employed to coat various articles made of nickel, silver, antimony, and steel. The surface of the cathode was initially coated with the corresponding metal selenide.

A 9 : 1 selenium–graphite mixture was employed as the material of the anode. Under these conditions, the loss of selenous acid in the cathodic reaction is compensated by its formation by the anodic oxidation of selenium. The resulting grey hexagonal selenium coatings can be used in the manufacture of rectifiers and photocells. Selenium coatings obtained by electrolysis in highly acid electrolytes have a distinct texture [64].

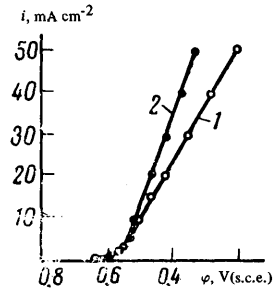

Figure 3. Cathodic polarisation curves for a solution of 840 g of SeO_2 in 1 litre of 18 *N* H_2SO_4; 1) in the dark; 2) under illumination [66].

The electrolytic deposition of the grey hexagonal modification of selenium on a platinum cathode at 95°C from concentrated sulphuric acid containing selenium dioxide has been reported [65].

The cathodic reduction of selenium in highly acid electrolytes (SeO_2 + 55–60% H_2SO_4 or H_2SeO_4) is accompanied by a relatively low polarisation.

At low current densities the polarisation of the selenium electrode hardly changes under illumination. The effect of illumination on the polarisation of the selenium electrode in concentrated sulphuric and selenic acid electrolytes begins to have an appreciable effect at current densities in excess of 10 mA cm^{-2}. The slight

decrease of cathodic polarisation (Fig. 3) under illumination is probably associated with a decrease of the ohmic resistance of selenium under the influence of light.

The $\eta - \lg i$ polarisation curves for the cathodic deposition and anodic dissolution of selenium, measured in concentrated sulphuric and selenic acid electrolytes at low current densities (1×10^{-4}–1×10^{-2} A cm^{-2}), have a single linear section with a slope of 0.7 V (Fig. 4). The exchange current found from the intersection of the anodic and cathodic curves is 1.4×10^{-4} A cm^{-2}.

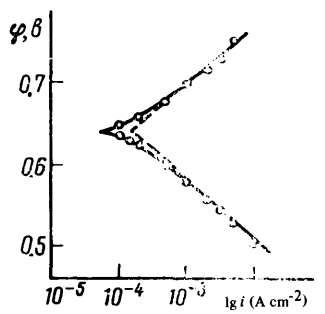

Figure 4. Cathodic–anodic polarisation curves for the solution of 840 g of SeO_2 in 1 litre of 18 N H_2SO_4.[66]

Thus in highly acid solutions the inhibition of the cathodic reaction associated with the depletion of the surface layer of selenium in free electrons, which is characteristic of weakly acid electrolytes, is not observed. The exchange current in highly acid electrolytes is higher by approximately 2 powers of 10 than in weakly acid solutions. The current yield of selenium in concentrated sulphuric and selenic electrolytes is close to 100%.

It is believed[63] that the electrochemical reduction of selenous acid in concentrated sulphuric and selenic acid electrolytes proceeds with participation of the $(H_3SeO_3)^+$ cation, which is formed in accordance with the equilibria

$$H_2SeO_3 \rightleftarrows H^+ + HSeO_3^-, \quad H_2SeO_3 + H^+ \rightleftarrows (H_3SeO_3)^+ .$$

Its concentration increases with the acidity of the electrolyte.

The absence of inhibition in the electrochemical reduction of selenium in concentrated sulphuric and selenic acid solutions is attributed by other workers[66] to the fact that the free electrons involved in the cathodic process are generated in a sufficient amount on the surface of the electrode. Possibly the products of the interaction of selenium with fairly concentrated acids of the H_2SeO_4 and H_2SO_4 type behave as electron generation centres. Despite the fact that there is no direct proof of the formation of these products and there are no data concerning their nature and properties, the polarisation and capacitance measurements as well as the properties of selenium in concentrated solutions[3] suggest that preference should be given to this explanation.

Elemental selenium dissolves readily in concentrated sulphuric acid with formation of $SeSO_3$. The electrolytic reduction of $SeSO_3$ in 98% sulphuric acid solutions proceeds via the reaction

$$SeSO_3 + 6H^+ + 6e \rightarrow Se + S + 3H_2O^{67,68} .$$

The current yield is nearly theoretical. Since $SeSO_3$ is frequently formed in the course of the manufacture of sulphuric acid (when the raw material contains selenium), the electrolytic reduction of $SeSO_3$ can be used for the quantitative separation of selenium from sulphuric acid.

The technology of the electrolytic preparation of selenium from the anodic sludge in the copper refining industry has been described[69]. The sludge is roasted with Na_2CO_3, leached with water, and the solution is saturated with boric acid, filtered, and the pH adjusted to 8–9 by the addition of an aliphatic polybasic alcohol (for example 2-amino-2-methylpropane-1,3-diol). This solution serves as the catholyte, aqueous NaOH or Na_2CO_3 being employed as the anolyte. Selenium is evolved at a potential of 4.5–6 V. The cathode can also be made of iron, copper, titanium, and aluminium and the anode can be made of materials resistant to NaOH solutions.

Selenium is deposited from solutions of alkali metals by hydrogen selenide via the reaction

$$HSe^- + OH^- - 2e \rightarrow Se + H_2O .$$

The anodic oxidation of sodium selenide has been used to coat the plates of rectifiers[70]. The electrolysis was performed at elevated temperatures and a maximum current density of 10 mA cm^{-2}. However, owing to the instability of the selenide solutions, the anodic deposition of selenium has not found wide scale application.

In the electrolysis of alkaline solutions of a selenite, the selenide is formed on the cathode via the reaction $SeO_3^{2-} + 3H_2O + 6e \rightarrow Se^{2-} + 6OH^-$ and can be used for the deposition of selenium on the anode. This process is complicated by the chemical reactions

$$2HSe + {}^1/_2O_2 = 2Se + H_2O, \quad SeO_3^{2-} + 2HSe^- + H_2O = 3Se + 4OH^- .$$

The colloidal selenium formed as a result of this reaction interacts with the selenide and forms polyselenides which are not involved in the electrochemical reaction and merely reduce the concentration of the selenide in the electrolyte. Under certain conditions, sodium selenide is formed in the cathodic compartment in the electrolysis of sodium selenite solutions[71].

2. CATHODIC DEPOSITION OF TELLURIUM FROM ACID SOLUTIONS

In the electrolysis of acid tellurium-containing solutions, coarsely crystalline or fine-grained tellurium deposits are formed on the cathode depending on the electrolysis conditions and the composition of the electrolyte. Spongy deposits are mainly produced in the electrolysis of weakly acid solutions of tellurium. TeO_2, the formation of which is associated with the hydrolysis of tellurium chloride near the electrode, has been found in the spongy tellurium deposits[72].

The best electrolytes for the electrolytic deposition of tellurium from acid solutions are hydrochloric acid solutions. The high positive potential of the Te/Te^{4+} system and the high solubilities of TeO_2 and $TeCl_4$ in hydrochloric acid solutions are extremely favourable for the electrolytic deposition of pure tellurium. The electrochemical behaviour of tellurium in hydrochloric acid solutions has been investigated[25,31,72–76].

Müller and Schlosser[73], who were the first to achieve the electrochemical deposition of tellurium from hydrochloric acid solutions (300 g litre^{-1} Te + 200 g litre^{-1} HCl), noted that pure tellurium is deposited on platinum and titanium cathodes at 30°C.

For the deposition of tellurium with a purity not less than 99.99%, the limiting permissible concentrations of impurities in solution such as selenium, silver, mercury, and gold should not exceed 5 mg litre^{-1} and those of impurities such as aluminium, iron, magnesium, and calcium, and others should not exceed 70–100 mg litre^{-1}.[25] The electrolysis conditions are as follows: $(0.5–2.0) \times 10^{-3}$ M TeO_2 or $TeCl_4$ + $(2.5–5) \times 10^{-3}$ M HCl electrolyte, current density 15–20 mA cm^{-2}, 25–30°C. Such electrolytes can be prepared by the anodic dissolution of technical tellurium in hydrochloric acid solutions[48].

Chlorine in the form of $TeCl_2$ remains in all the tellurium deposits as a mechanical impurity[72]. An increase of the acidity of the solution, the presence of alkali metal chlorides in the electrolyte, and an increase of current density lead to an increase of the $TeCl_2$ content.

A change in the electrolyte temperature has an appreciable influence on the mechanism of the cathodic deposition of tellurium and on the nature of the deposits. A fine-grained grey deposit is formed on the cathode at 25–50°C and current densities of 10–15 mA cm^{-2}. At 75 to 90°C and a current density of 20 mA cm^{-2}, coarse-grained dark-grey deposits are formed, their current yield in relation to Te^{4+} falling from 99% at 25°C to 89% at 90°C.

The formation of $TeCl_2$ is associated with a multistage mechanism of the reduction of Te^{4+} ions by Te^{2+}. Some of the Te^{2+} ions near the electrodes react with Cl^- ions to form $TeCl_2$, which is deposited on the surface of the cathode together with a freshly formed layer of elemental tellurium. Other Te^{2+} ions undergo further electrochemical reaction and disproportionation: $2Te^{2+} = Te + Te^{4+}$.

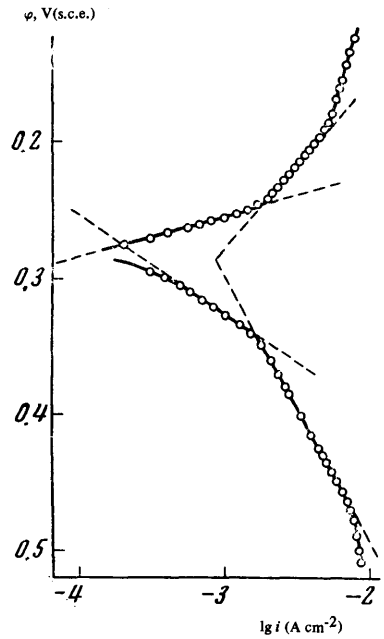

Figure 5. Cathodic–anodic polarisation curves obtained in 2 M HCl + 0.05 M $TeCl_4$ solution[74].

Vigorous formation of Te^{2+} ions and their disproportionation are observed in the anodic polarisation of the tellurium electrode in hydrochloric acid solutions. After the start of electrolysis, the electrolyte near the anode becomes greenish-yellow, then assumes a red tint, and is converted into a dirty-grey turbid suspension, black crystals (pure elemental tellurium) being formed after approximately 30–40 min.

Te^{2+} ions in the solutions after anodic polarisation were detected directly by treatment with an oxidant ($K_2Cr_2O_7$).

The study of the kinetics of the decrease in the amount of Te^{2+} ions in solution after the anodic polarisation of tellurium had ceased and chemical analysis of the solid mass established that (1) Te^{2+} is formed in the anodic dissolution of tellurium in hydrochloric acid solutions; apart from being involved in an electrochemical reaction, Te^{2+} ions subsequently disproportionate and are also deposited in the form of $TeCl_2$ on the surface of the anode; (2) the disproportionation reaction is a second-order process.

The cathodic polarisation curves measured with the aid of the tellurium electrode in hydrochloric acid solutions of tellurium(IV) show the onset of a limiting current, which increases with the concentration of tellurium in the electrolyte, temperature, and the rate of stirring. At an HCl concentration of 2.5–5 M the limiting current varies linearly with the concentration of tellurium in the electrolyte[74]. In this acidity range tellurium is present in solution in the form of the complex ions $TeCl_6^{2-}$.

As the acidity of the electrolyte diminishes, the chlorine in the complex ion is gradually replaced by H_2O or OH^-, tellurous acid is precipitated, and the concentration of Te^{4+} ions in solution falls.

The initial sections of the polarisation curves (Fig. 5) for 2.5–5 M HCl + 0.02–0.25 M Te solutions at 25–50°C show a break and two linear sections with different slopes; $b_{c1} = 0.035$ V, $b_{c2} = 0.12–0.14$ V, $b_{a1} = 0.066–0.070$ V, and $b_{a2} = 0.15–0.20$ V. The exchange currents are $i_{0.1} = 2 \times 10^{-4}$ A cm^{-2} and $i_{0.2} = 1 \times 10^{-3}$ A cm^{-2}.

Comparison of the results of the polarisation measurements with the direct detection of Te^{2+} ions permits the assumption that the cathodic deposition and anodic dissolution of tellurium in hydrochloric acid electrolytes proceed in stages.

The most probable mechanism of the process can be represented in the following form[25]:

$$TeCl_6^{2-} \rightleftarrows TeCl_2^{2+} + 4Cl^-, \quad (1)$$

$$TeCl_2^{2+} + e \rightleftarrows TeCl_2^+, \quad (2)$$

$$TeCl_2^+ + e \rightarrow TeCl_2 \quad (3)$$

$$\text{or } TeCl_2^{2+} + 2e \rightarrow TeCl_2, \quad (4)$$

$$TeCl_2 + e \rightarrow TeCl_2^-, \quad (5)$$

$$TeCl_2^- + e \rightleftarrows Te^0 + 2Cl^- \quad (6)$$

$$\text{or } TeCl_2 + 2e \rightarrow Te^0 + 2Cl^-. \quad (7)$$

If there is only one slow stage in reactions (1)–(7), the sum of the apparent transfer coefficients should be equal to the number of electrons involved in the overall reaction, i.e. $\alpha' + \beta' = 4$, which is not observed experimentally. Therefore one must postulate that the cathodic deposition and anodic dissolution of tellurium in hydrochloric acid solutions occur by more than one slow stage.

The formation of Te^{2+} ions and the increase of their concentration during electrolysis suggest that the slow stage may be reaction (5). On the other hand, reaction (3), whose product can disproportionate and also remain in the solid state apart from being involved in an electrochemical reaction, presumably also has a slow stage.

If one supposes that reactions (3) and (5) and reactions (5) and (3) are slow in the cathodic and anodic processes respectively and that the preceding electrochemical stages are reversible, then, using the characteristics of multistage processes and the proposed reaction mechanism, the following kinetic equations may be derived:

$$i_c = k_{-3}[TeCl_6^{2-}][Cl^-]^4 \exp[-(1+\alpha_3)F\varphi_c/RT],$$

whence $\alpha' = 1 + \alpha_3$, $\beta' = 1 + \beta_5$, $\alpha' + \beta' < 4$, and

$$i_a = k_{+5}[Cl^-]^2 \exp[(1+\beta_5)F\varphi_a/RT].$$

Thus $\alpha' + \beta''$ must be four, which is in fact observed experimentally.

Electrodeposition from tellurium solutions containing tellurium sulphate mixed with ammonium hydrogen tartrate was carried out by Pellini[77]. According to Gallo[78], Pellini's method[77] is unsuitable for the electrochemical deposition of relatively large amounts of tellurium and the electrolysis of pyrophosphate electrolytes is recommended. The electrolytic deposition of tellurium on a lead cathode from a $TeO_2 + HF + H_2SO_4$ electrolyte has been described[79]. However, owing to the corrosive nature of the electrolyte, the method has not found any practical application. It is occasionally recommended for the deposition of thin tellurium films on various metallic surfaces[80]. The conditions governing the electrolytic deposition of tellurium from media described by Mathers and Turner[79] were recently reinvestigated[81] and it was found that a dense deposit of tellurium with a metallic lustre and having a purity of 99.98% is formed on the cathode.

There are data[82] showing that in the electrochemical deposition of tellurium from sulphuric acid electrolytes in an ultrasonic field the limiting permissible current density for the formation of high-grade tellurium deposits is appreciably increased. In sulphuric acid solutions tellurous acid is reduced to elemental tellurium, while telluric acid is not reduced. This property can be used to separate tellurous and telluric acids[54].

The polarisation curves measured with the aid of the tellurium electrode in sulphuric acid electrolytes suggested[83] that the cathodic and anodic processes proceed in stages.

It was established, using buffer solutions in the pH range 7–10, by potentiostatic measurements[84] that at cathodic potentials the tellurium is in a state of cathodic passivation, while at anodic potentials the active state is followed by a state of secondary passivation.

The first studies of the electrochemical behaviour of ultrasmall amounts (10^{-10} M) of tellurium were made by Ghosh–Mazumder and Haissinsky[85]. The authors employed a mixture of tellurium-129 and tellurium-127 isotopes in the form of quadrivalent ions. The experiments were performed in HCl, HBr, and H_2SO_4 media or in solutions of the corresponding salts. With increase of the acidity of the medium, the tellurium deposition potential shifts towards positive values. The nature and state of the electrode surface have an appreciable influence on the tellurium deposition potential. The electrodes can be arranged in the following sequence in terms of the tellurium deposition potential:

platinised Pt > smooth Pt > Pd > Au > Ru.

Tellurium was electrochemically deposited also from nitric acid (0.5–1 M HNO_3) electrolytes at a maximum tellurium concentration of 1.5 g litre^{-1} using platinum electrodes and a current density of 1.2–1.8 mA cm^{-2}.[25] A deposit of grey tellurium firmly adhering to the electrode surface is formed on the cathode; its current yield is close to 100% and appreciable evolution of hydrogen is not observed.

At current densities of 3–5 mA cm^{-2} the deposition of tellurium on the cathode occurs with the evolution of hydrogen and the current yield of tellurium falls to 80%. The tellurium deposited by electrolysis from nitric acid solutions is purer than that deposited from hydrochloric acid electrolytes. In the electrolysis of hydrochloric acid solutions of tellurium the formation of hydrogen telluride is observed only when tellurium is deposited from solutions with very low tellurium concentrations under limiting current conditions at 0–10°C. The mechanism of the formation of H_2Te involves the reaction $Te^{2-} + 2H^+ \rightarrow H_2Te$.[86] Telluride ions are formed initially and then diffuse from the cathode and interact with hydrogen ions migrating to the surface of the cathode. When H_2Te is formed, the evolution of hydrogen ceases; Te^{2+} ions are probably adsorbed on the surface of the cathode and act as a "poison" for the evolution of hydrogen.

The electrolytic method is also used to prepare tellurides[2]. In the electrolysis of sodium sulphate solutions using an anode made of a metal whose telluride is to be obtained and tellurium as the cathode, the products are tellurides. Copper and nickel tellurides have been synthesised in this way. In the synthesis of zinc tellurides, a zinc plate was used as the anode and the cathode consisted of a tellurium–platinum alloy. Nitric and sulphuric acids serve as the electrolyte.

The conditions of the electrolytic deposition of tellurium–silver alloys from nitric acid electrolytes and of tellurium–cadmium alloys from cyanide electrolytes have been described by Klochko and Medvedeva[87] and by Trusova and Chizhikov[88] respectively. The conditions governing the joint electrodeposition of tellurium–copper[89] and tellurium–chromium[90] have also been described.

Using a tellurium cathode and an anode made of other metals in a 1 M $NH_4OH + CH_3COOH$ solution at pH 4.5, CuTe, SnTe, ZnTe, PbTe, and Bi_2Te_3 were synthesised electrolytically[91].

It has been reported[92] that Ag_2Se and Ag_2Te are formed respectively on a silver cathode in the electrolysis of 0.01 M SeO_2 and TeO_2 solutions in 1 M H_2SO_4 at 25°C and a current density up to 0.05 mA cm^{-2}. The electrolysis of acidified $CuSO_4 + H_2SeO_3$,[93,94] $H_2TeO_3 + H_2SeO_3$,[95] $AgNO_3 + H_2SeO_3$,[96] $Bi(NO_3)_3 + H_2SeO_3$,[97] and $CdSO_4 + H_2SeO_3$[98] solutions results in the formation of the corresponding metal selenides on platinum, copper, silver, cadmium, and tellurium cathodes.

The formation of selenides has also been noted[99] in the electrolysis of H_2SO_4, Na_2SO_4, and KNO_3 solutions using a selenium cathode and an anode made of copper, nickel, cadmium, and certain other metals.

3. CATHODIC DEPOSITION OF TELLURIUM FROM ALKALINE ELECTROLYTES

For the electrodeposition of tellurium from alkaline solutions, the electrolyte is usually prepared by dissolving TeO_2 in sodium hydroxide solution.

Apart from simple tellurites of the type Na_2TeO_3, the existence of sodium polytellurites of the type $Na_2Te_3O_7$, $Na_2TeO_5.3H_2O$, and $Na_2TeO_9.5H_2O$ was established in the TeO_2–Na_2O–H_2O system[100]. The reduction of tellurium at the cathode in such solutions is a fairly complex process, the final product of which is elemental tellurium.

A Japanese patent[101] reports the formation of tellurium by the electrolysis of alkaline electrolytes.

In the Soviet Union the preparation of tellurium on an industrial scale was achieved by Gaev et al.[102] The electrolysis was carried out in an electrolyte containing 100 g litre^{-1} of tellurium and 160 g litre^{-1} of free sodium hydroxide. Tellurium is deposited on the cathode in powder form and its purity is 99.5%. Tellurium with a lower impurity content can be obtained by employing a purer electrolyte.

Electrolytic units for the electrolytic isolation of tellurium have been organised in many copper-electrolytic and metallurgical works[103-106], where selenium and tellurium-containing waste accumulates.

At low current densities the electrodeposition of tellurium proceeds with chemical polarisation, while at high current densities concentration polarisation obtains[107]. The cathodic polarisation curves show a limiting current ($i$lim) (Fig. 6). With increase of the concentration of alkali in the electrolyte, the limiting current falls.

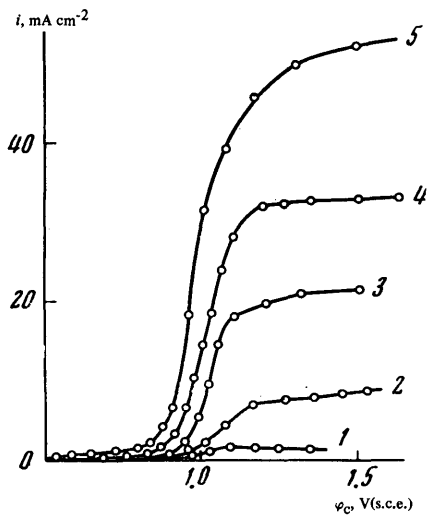

Figure 6. Cathodic polarisation curves for a 4 M NaOH solution containing different concentrations of tellurium (M): 1) 0.016; 2) 0.064; 3) 0.16; 4) 0.25; 5) 0.41.[25]

In an electrolyte with a high concentration of alkali $i$lim varies linearly with the tellurium concentration in the electrolyte and on dilution (in the absence of an excess of alkali) the increase of $i$lim with the concentration of tellurium is faster than would be expected for a direct proportionality. The difference between the values of $i$lim for tellurium in solutions with low and high concentrations of alkali has been attributed[108] to the different nature of the tellurium-containing species being discharged in concentrated and dilute solutions of alkali. In concentrated solutions of alkali the $\varphi - \lg i$ polarisation curves have a single linear section at relatively high current densities (Fig. 7). At low current densities the cathodic curves show a decrease of potential characteristic of the spontaneous dissolution of the metal[109].

Depending on the concentration of alkali in the electrolyte, the overall electrode reaction can be represented as follows:

$$TeO_3^{2-} + 3H_2O + 4e = Te + 6OH^-\ ,$$

$$HTeO_3^- + 2H_2O + 4e = Te + 5OH^-\ .$$

Bearing in mind that in a solution with a high excess of alkali the dominant species are the $[Te(OH)_6]^{2-}$ ions[18], which dissociate via the reaction $[Te(OH)_6]^{2-} \rightleftharpoons Te(OH)_3^+ + 3OH^-$,[109] it follows that, according to the hypothesis put forward[108,109], the electrodeposition of tellurium presumably corresponds to the overall electrode reaction $Te(OH)_3^+ + 4e \rightarrow Te + 3OH^-$, which proceeds in stages via the mechanism

$$Te(OH)_3^+ + e \rightarrow Te(OH)_3\ ,$$

$$Te(OH)_3 + e \rightarrow Te(OH)_3^-\ ,$$

$$Te(OH)_3^- + e \rightarrow Te(OH)_3^{2-}\ ,$$

$$Te(OH)_3^{2-} + e \rightarrow Te^0 + 3OH^-\ .$$

The rate-determining stage is the generation of the last electron. The slope of the linear sections of the $\varphi - \lg i$ curves calculated on the basis of the theory of multistage reactions using kinetic equations is satisfactorily consistent with the experimental results.

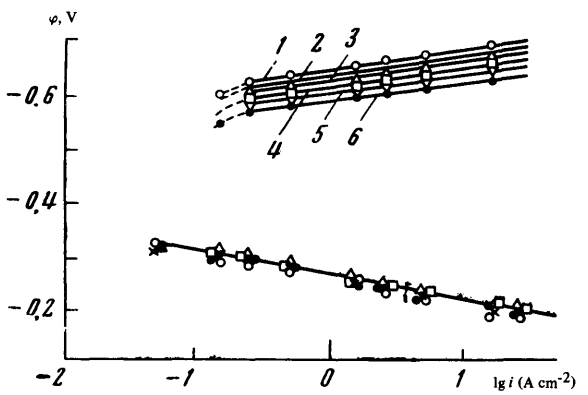

Figure 7. Cathodic–anodic polarisation curves for a 2.5 M NaOH solution containing different concentrations of tellurium (M): 1) 0.0075; 2) 0.015; 3) 0.03; 4) 0.06; 5) 0.12; 6) 0.188.[109]

In the electrolysis of thiotelluride (Na_2TeS_2) solutions tellurium is deposited on the cathode and elemental sulphur on the anode and polytellurides are formed[110]. The accumulation of polysulphides in the electrolyte leads to a decrease of the current yield of tellurium owing to the dissolution of tellurium on the cathode in the polysulphide.

In the course of the electrolysis of alkaline solutions containing tellurium and selenium, tellurium is deposited on the cathode and selenium remains in solution. Optimal conditions have been found whereby the concentration of tellurium in alkaline selenium-containing solutions can be reduced to 5×10^{-5}%.[111] Alkaline electrolytes have also been used in the refining of tellurium[112,113]. All the tellurium deposits obtained by the electrolysis of alkaline or acid solutions containing alkali metal ions contain an admixture of the latter in an amount of 0.01–0.05%.

4. CATHODIC DEPOSITION AND ANODIC DISSOLUTION OF SELENIUM AND TELLURIUM IN NON-AQUEOUS ELECTROLYTES

The conductivities of alcohols, acetic acid, and ethylene glycol increase sharply when $SeCl_4$ or $TeCl_4$ are dissolved in them. The high conductivities of the solutions have been attributed[114] to the presence of H^+ and Cl^- ions formed as the result of the dissociation of HCl produced by the reaction

$$SeCl_4\,(TeCl_4) + nCH_3OH \rightleftarrows Se\,(Te)\,Cl_{4-n} \cdot (OCH_3)_n + nHCl\ .$$

In the electrolysis of alcoholic, acetic acid, and ethylene glycol solutions of $SeCl_4$ or $TeCl_4$, selenium or tellurium is deposited on the cathode. Depending on the electrolysis conditions, primarily on temperature, the selenium deposits can be amorphous or crystalline. Crystalline selenium deposits are obtained from electrolytes heated to 45–60°C. However, under such conditions the nature of the electrolyte changes during electrolysis with formation of an organoselenium compound. Selenium is not electrodeposited from such solutions. Intermediate reduction products were not detected in the cathodic selenium deposits. The current yield of selenium does not exceed 15%. When the electrolyte contains 10% of aromatic hydrocarbons, the current yield of selenium rises to 27%.[115]

As in aqueous hydrochloric acid solutions, the cathodic deposition of selenium in the above solvents proceeds with a high overvoltage, which falls appreciably when the surface of the electrode is illuminated.

At temperatures of 5–10°C and current densities of 5–10 mA cm^{-2}, deposits of metallic tellurium firmly adhering to the surface of the electrode are formed on graphite and titanium cathodes in 0.5–1 M $TeCl_4$ solutions in acetic acid[116], alcohols, and ethylene glycol[25].

A cryptocrystalline tellurium deposit was formed on a platinum cathode in mixed aqueous alcoholic hydrochloric acid electrolytes (water content not greater than 2%) at a current density of 10–20 mA cm^{-2} and a temperature of 15–20°C. Black velvety cathodic deposits are obtained at current densities in the range 10–20 mA cm^{-2}.

Chlorine was detected in all the electrolytic tellurium deposits. Its content depends on the electrolysis conditions and the nature of the electrolyte. The greatest amount of chlorine (up to 7%) remains in deposits which were isolated from acetic acid solutions and the smallest amount (down to 0.04%) was found in deposits from ethylene glycol electrolytes. The chlorine in the electrolytic tellurium deposits is present as a mechanical admixture of tellurium dichloride[25].

Polarisation measurements made with the aid of the tellurium electrode in $TeCl_4$–CH_3OH or $TeCl_4$–C_2H_5OH solutions yield reproducible results (Fig. 8).[117] The cathodic curves show a limiting current section. The limiting current i_{lim} increases with the concentration of tellurium (curves *2*–*4*), temperature, and rate of stirring of the electrolyte, and decreases both with increase of the concentration of chloride ions as a result of the addition of HCl or LiCl to the electrolyte (curves *4* and *6*) and when alcohols with high molecular weights are employed as solvents (curves *4* and *5*).

The initial sections of the cathodic–anodic $\varphi - \lg i$ polarisation curves are described by Tafel equations with o_c = 0.055–0.060 V and o_a = 0.065–0.070 V.

In hydrochloric acid solutions in alcohols, acetic acid, and ethylene glycol both selenium and tellurium undergo vigorous anodic dissolution with formation of a mixture of chlorides. The lowest chlorides are subsequently oxidised to $SeCl_4$ or $TeCl_4$, which react with the solvent, undergoing solvolysis or solvation.

An electrolyte suitable for the electrochemical refining of tellurium can be prepared by the anodic dissolution of technical tellurium in hydrochloric acid solutions in acetic acid.

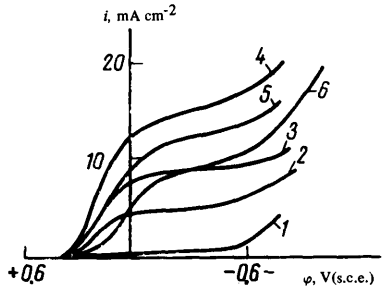

Figure 8. Polarisation curves for amine tellurium-containing solutions: 1) 0.5 M HCl + CH_3OH; 2) ditto + 0.02 M $TeCl_4$; 3) ditto + 0.03 M $TeCl_4$; 4) ditto + 0.05 M $TeCl_4$; 5) 0.05 M $TeCl_4$ + C_3H_7OH + 0.5 M HCl; 6) 0.05 M $TeCl_4$ + 5 M HCl + CH_3OH.[25]

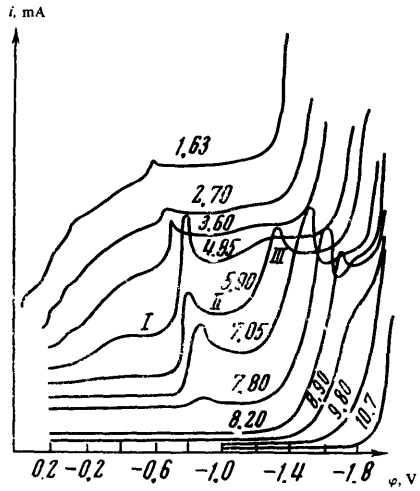

Figure 9. Polarographic curves for a 0.001 M selenium(IV) solution at different pH in the absence of surface-active substances (the pH values are indicated opposite the curves)[123].

An electrolyte with the composition 50% TeO_2 + 25% KCl + 25% LiCl was used for the electrodeposition of tellurium from fused media[118]. This composition was chosen after investigating the properties of certain TeO_2–KCl and TeO_2–LiCl binary systems and also the TeO_2–KCl–LiCl ternary system[119]. The electrolysis was carried out at 650–680°C and a current density of 0.2 A

cm^{-2}. Tellurium reduced to the elemental state accumulated in the liquid form on the bottom of the electrolyser. Impurities collected in the form of a slag on the surface of the deposited tellurium. The impurity content in the cathodic tellurium did not exceed 0.01–0.02%.

When a direct current was passed between two electrodes immersed in fused selenium, some impurities (silver, tellurium, and iron) collected in the cathodic compartment, while others (lead, arsenic, and nickel) collected in both cathodic and anodic compartments. The purest selenium remained in the central part of the cell[120].

In the cathodic–anodic polarisation of liquid selenium in the fused LiCl–KCl eutectic at 400°C, selenium is oxidised at the anode: $2Se + 2Cl^- - 2e \rightarrow Se_2Cl_2$, while the selenide is formed on the cathode: $Se + 2e \rightarrow Se^{2-}$. Under analogous conditions the oxidation of tellurium proceeds up to the formation of Te^{2+} and the cathodic process is limited to the incorporation of lithium in tellurium[121].

IV. POLAROGRAPHY OF SELENIUM AND TELLURIUM

Numerous studies have been made on the polarography of selenium and tellurium[122–178].

Selenium

Depending on the composition of the electrolyte (in the first place on the pH of the medium), the polarogram of selenous acid has up to three waves. A distinct wave, suitable for analytical purposes, appears at potentials between −1.4 and −1.5 V (s.c.e.) in the pH range 8–9. The electrode reaction then proceeds via the mechanism $HSeO_3^- + 6H^+ + 6e \rightarrow HSe^- + 3H_2O$.

There are different interpretations[122–127] of the mechanism of selenous acid reduction in acid solutions at a dropping mercury electrode.

The most likely mechanism of the formation of two waves (Fig. 9) in more acid solutions was given by Lingane and Niedrach[123]. The electrode reaction proceeds initially with participation of six electrons: $SeO_3^{2-} + 6H^+ + 6e \rightarrow Se^{2-} + 3H_2O$. The selenide ions formed at the surface of the mercury drop depolarise mercury anodically, which leads to its oxidation and the formation of a mercury selenide deposit:

$$Se^{2-} + Hg \rightarrow HgSe + 2e\ .$$

The anodic mercury oxidation wave lowers the cathodic selenite reduction wave and the overall process $SeO_3^{2-} + Hg + 6H^+ + 4e \rightarrow HgSe + 3H_2O$ corresponds to a four-electron reaction. As stated by Speranskaya[124], mercury selenide is formed as the result of the involvement of elemental selenium, formed in the reduction of the selenite, in the four-electron reaction

$$SeO_3^{2-} + 6H^+ + 4e \rightarrow Se^0 + 3H_2O,\ Se^0 + Hg = HgSe\ .$$

According to Speranskaya's data[125] the reduction of the selenite ion at dropping bismuth, lead, cadmium, zinc, and sodium amalgam electrodes entails the formation of two waves. The first wave appears at potentials between −0.2 and −0.6 V and is associated with a four-electron process which proceeds with a 100% current yield. At potentials more negative than −0.6 V the selenite is reduced to selenide ions.

According to Brdička and Wiesner[126], the polarographic waves of selenium are due to the reduction of various forms of selenous acid (SeO_3^{2-}, $HSeO_3^-$, H_2SeO_3) to elemental selenium.

In the pH range 2.7–1.6 complex waves are observed for selenium, which are a result of the occurrence of several processes, including the reduction of Se^{4+} to the elemental state and the selenide and the reduction of various forms of selenous acid.

Some information about the polarographic behaviour of selenium(IV) in acid solutions may be found in papers by Jonas[127] and Christian and Knoblock[128].

The selenide ion gives rise to an anodic wave associated with the oxidation of mercury and the formation of mercury selenide[129]. This wave can be used to determine selenides in the presence of sulphides. The electrochemical behaviour of the selenosulphide ion SeS^{2-} at a dropping mercury electrode was investigated by Tornova et al.[130]

In an ammonia buffer solution at pH 8–9.5 a single distinct wave arises on the selenium(IV) polarogram. The diffusion current is directly proportional to the concentration of selenite in solution. This wave is frequently used for a quantitative polarographic determination of selenium[131–135].

The presence of ions of heavy elements in the solutions being analysed interferes with the determination of selenium; they are either separated[136–139] or masked by the addition of suitable complex-forming reagents to the electrolyte[140–142].

The use of modern polarographic apparatus greatly extends the scope and increases the sensitivity of the selenium determination. A vector polarograph with a stationary electrode in the form of a mercury drop permits the determination of 2×10^{-7} mole of selenium or even less[143]. The alternating-current polarographic method has been used to determine selenium in semiconductor materials[144,145]. An oscilloscopic polarographic method for the determination of selenium in germanium selenide has been described[146,147].

Very small amounts of selenium (down to 5×10^{-8} M) can be determined by a pulse polarographic method[137]. Elemental selenium reacts with concentrated sulphuric acid to form $SeSO_3$. In the polarography of sulphuric acid containing selenium, a distinct wave due to the reaction

$$SeSO_3 + 6H^+ + 6e \rightarrow Se + S + 3H_2O$$

is obtained. A polarographic determination of selenium in sulphuric acid has been developed on the basis of this reaction[148].

In an alkali metal sulphite solution elemental selenium forms the selenosulphate ion $SeSO_3^{2-}$ which is reduced at a dropping mercury electrode and gives rise to a distinct wave due to the reaction $SeSO_3^{2-} + 2e \rightarrow Se^{2-} + SO_3^{2-}$.[149] The polarographic method has been used to analyse mixtures of selenothionates[150]. The polarographic determination of selenium as selenosulphate has been described[151].

In acidified solutions of sodium (or potassium) tartrate or lithium citrate at pH 1–5 in the presence of 0.01% of gelatin selenium(IV) gives rise to a distinct wave whose half-wave potential $\varphi_{1/2}$ shifts from −0.55 to −60 V when the pH is raised from 1 to 5.[152,153]

In 0.1 M ammonium acetate solution at pH 6.2 selenium(IV) gives rise to two waves with half-wave potentials of −0.81 and −0.38 V. Deshmukh and Asthana[154]

explained them by the reduction of Se^{4+} to Se^{2+} and elemental selenium. The Se^{2+} state, which was indicated at an early stage by Schwaer and Suchy[122], was not confirmed by Lingane and Niedrach[123].

The polarography of organic selenium compounds is developing successfully. The polarographic behaviour of the selenocystine–selenocysteine system, of certain five- and six-membered cyclic diselenides, and of products of the oxidation of five-membered cyclic diselenides and disulphides has been investigated in detail[155]. Certain inhibition effects of five-membered cyclic diselenides and disulphides have been studied[156]. The polarographic reduction of diphenyl diselenide and diphenyl disulphide has been described by Nygard[157].

When 3,3-diaminobenzidine or *o*-phenylenediamine is added to a solution containing selenium(IV), the product is a diazaselenole which gives rise to a distinct polarographic wave[141]. In 0.1 *N* $HClO_4$ + 0.1 *N* NH_4ClO_4 solution at pH 2.5, phenyldiazaselenole gives rise to two waves with $\varphi_{1/2} = -0.17$ and -0.64 V (s.c.e.). The height of the first wave is proportional to the concentration of selenium. The method was used to determine selenium in sulphur, sulphites, and sulphates.

Tellurium

The telluride ion gives rise to an anodic wave in acid and alkaline electrolytes. In an ammonia buffer solution Te^{2-} is oxidised reversibly to elemental tellurium[129].

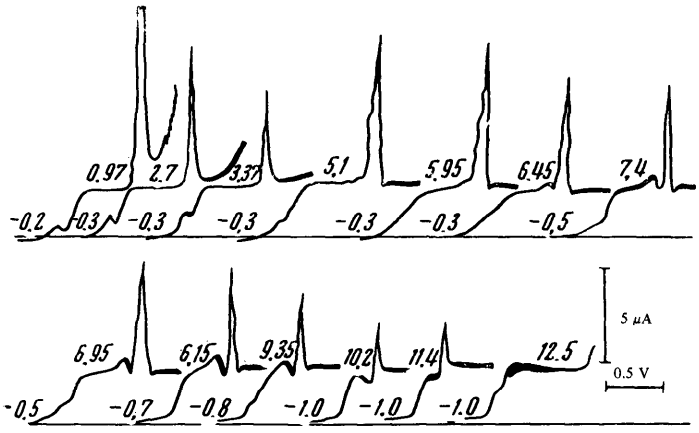

Figure 10. Polarogram for buffer solutions: CH_3COONa + $HClO_4$ + 1.46×10^{-4} M Te, pH ranging from 0.97 to 5.1, and for NaH_2PO_4 + LiOH + 1.46×10^{-4} M Te. The pH values are indicated opposite the curves (pH 5.95–12.5). The numerals at the beginning of the polarogram indicate the potentials at which the polarograms were begun[158].

Depending on the nature of the indifferent electrolyte (as in the case of selenium), there are between 1 and 3 waves on the tellurium(IV) polarogram (see Fig. 10). The mechanism of the formation of the first, main tellurium(IV) wave is similar to that of the formation of the selenium(IV) wave[123,158].

A sharp maximum, differing from the usual polarographic maxima by the fact that it occurs after the attainment of the steady diffusion current of the main wave, arises on the tellurium(IV) polarogram. Its height falls with increase of pH; at pH > 12 it does not appear at all and is readily suppressed by surface-active substances[153]. Various hypotheses have been put forward concerning the reasons for its appearance[158,159,161,162]. At the potential maximum a film of elemental tellurium is observed on the mercury drop.

It has been suggested[158] that under these conditions the anodic dissolution of mercury ceases and telluride ions [formed in the reduction of tellurium(IV)] react with tellurite ions: $2Te^{2-} + 2Te^{4+} \rightarrow 3Te$.

By titrating with hydrochloric acid 0.1 M solutions of $LiClO_4$ containing Na_2TeO_3 which had been made alkaline, it was established[158] that at pH 0.17–2.7 different tellurium species (H_2TeO_3, $HTeO_3^-$, TeO_3^{2-}) exist simultaneously in solution; the polarograms of such solutions have a complex form with several waves.

In contrast to selenium(IV), in the reduction of tellurium(IV) ions in alkaline electrolytes a distinct polarographic wave appears; it is used to determine tellurium in solutions containing selenium[160].

The nature of the reduction of tellurium(IV) and the corresponding half-wave potential depend on the concentration of H^+ ions[163,164]. In acid solutions containing tellurium(IV) catalytic evolution of hydrogen takes place. As the acidity of the electrolyte falls, the evolution of hydrogen is accompanied by partial reduction of tellurium(IV). In neutral and alkaline solutions a single wave with a maximum arises on the tellurium(IV) polarogram. The limiting current of this wave is restricted by the rate of diffusion of tellurium and is proportional to its concentration[163].

The quantitative polarographic determination of tellurium is largely based on the tellurium(IV) wave in the presence of ammonium salts as the supporting electrolyte at pH 6–9; $\varphi_{1/2}$ varies from -0.60 to -0.70 V (s.c.e.). With increase of pH, $\varphi_{1/2}$ shifts towards negative potentials, but the concentration of ammonium salts does not have an appreciable effect[136,165–170].

The polarographic determination of tellurium is interfered with by heavy metal ions (Pb, Zn, Fe, and others). Their influence is eliminated by adding Complexone III to the solution being analysed[171]. In most cases preference is given to the separation of tellurium in the elemental state by the action of reducing agents (hydrazine salts[172], $SnCl_2$,[133] hydroxylamine hydrochloride[173]).

In a tartrate–ammonia buffer solution as the supporting electrolyte, it is possible to determine down to 2×10^{-5} M of tellurium in the presence of lead, iron, and antimony[174]. The maximum arising on the tellurium wave is used for the detection and quantitative determination of microgram amounts of tellurium in selenium[161].

In the presence of large amounts of copper, KCN solutions are used as the supporting electrolyte for the determination of tellurium[175]. Tellurium in semiconductor alloys and in thin films is determined by a pulse polarographic method in the presence of 1 *N* HCl as the supporting electrolyte[176]. The polarographic determination of tellurium in the presence of antimony and gallium has been described[177]. 0.1 M NH_4CNS + Na_2SO_4 solution has been proposed as the supporting electrolyte for the determination of tellurium and selenium[178]. Distinct separate selenium and tellurium waves are obtained in this supporting electrolyte.

It should be noted that only the commonest methods for the polarographic determination of selenium and tellurium were described above. A complete description is outside the scope of this review.

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Optical Methods in Corrosion-electrochemical Studies

A.G.Akimov and I.L.Rozenfel'd

The review discusses problems relating to the technique of optical measurements on the surface of a metallic electrode in an electrolyte solution. Methods for the measurement of the thickness of oxide films on the electrode surface and of the extent of adsorption at the metal-electrolyte interface are examined.
A number of examples of spectroscopic studies on metal-electrolyte and metal-oxide-electrolyte systems are quoted. The usefulness of optical methods for the investigation of the processes on the surface of a metallic electrode in solution is demonstrated on the basis of the data presented.
The bibliography includes 72 references.

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I. INTRODUCTION

The extension and deepening of our knowledge of corrosion processes requires new research techniques. This was already noted in a recently published paper by Bockris et al.[1], who considered the necessity of applying a number of non-electrochemical methods to investigate the electrode surface (phase contrast, interferometric, ellipsometric, and Mössbauer spectroscopic methods).

Indeed many very important corrosion problems, for example inhibition of corrosion, and passivity, require the consideration of adsorption processes and of interactions at a molecular level and hence new methods for the investigation of the electrode surface are needed, since traditional electrochemical techniques do not yield the required information. Methods permitting measurements without disrupting the initial electrochemical system are of greatest value.

Many optical methods meet these requirements. Optical studies can be made directly in the cell for corrosion experiments. The perturbation introduced into the electrochemical system by the light beam may be minimal and, moreover, the absence of measurable photoeffects can serve as a criterion of the smallness of this perturbation. Finally, physical optics, which has been developing vigorously during the last two decades, has now provided fairly powerful theorectical and experimental techniques.

In this review we shall consider certain optical methods for the investigation of a solid electrode in an electrolyte solution, disregarding optical microscopic observations of the surface and optical methods for the analysis of the composition of the solution.

The interaction of an electromagnetic wave and matter, including solids, results in a change of the amplitude and phase of the wave. It is readily seen that this interaction can be described (on the basis of the law of conservation of energy) by means of the universal relation

$$K + R + M = 1 , \qquad (1)$$

where K, R, and M are the coefficients of absorption, relection, and scattering respectively. Thus the study of the changes in any of these coefficients can yield useful information about the properties of the test substance †.

† In the case of specular reflection, scattering may be neglected.

Since metals absorb light strongly over a wide spectral range and their transmittance (absorbance) can be studied only for very thin films (≤ 100 Å), it is clear that the optical methods for the investigation of changes in the electrode surface as a result of electrochemical reactions are mainly those employing the changes in the amplitude-phase parameters of the light reflected from the electrode.

Since in examining corrosion-electrochemical problems we are interested primarily in a number of surface parameters, the optical methods will be classified from this point of view.

II. MEASUREMENTS OF THE THICKNESS OF OXIDE FILMS FORMED ON THE ELECTRODE SURFACE

When the problem of the measurement of the thickness of oxide films on a metallic support is considered, it becomes immediately clear that many optical methods[2-6] are unsuitable for such measurements, since they require the presence of a partly uncoated support and a sharp step at the place where the film terminates.

Many metals (mainly the so called "rectifying metals") form films on anodic oxidation, which give rise to bright interference colours, arising from the partial reflection and refraction of the light incident on the oxide surface. The phase difference between the beams leading to interference is due both to the difference in the paths traversed by the beams and the phase difference arising on reflection. The phase change on reflection is different for the p- and s-components of the light beam (the electric vector of the p-beam is parallel and that of the s-beam is perpendicular to the plane of incidence) except for the case where the beam is incident on the surface at right angles. However, this difference is negligibly small for small angles of incidence: $\alpha \leq 10-15°$.

The simplest interference method for the determination of the thickness of oxide films on metals is based on a comparison of the colour of the film with that of a thin layer of air viewed in transmitted light. The thickness of the air layer must be divided by the refractive index of the material of the film. A very extensive and fairly accurate table of colours of air films was compiled by Rollet[7] and certain additions were made by Menh[8]. However, one must bear in mind that this table was compiled with a number of simplifying assumptions. Firstly, no account is taken of the

dispersion of the refractive index[9]. Secondly, it is assumed that the phase shifts at the boundaries of the layer are zero or π. However, for oxide layers on a metal, the phase shift at one boundary is characteristic of the metal and differs from both zero and π. According to the theory quoted in Methfessel's review[10], the intensity of the light reflected at right angles from a plate has minima corresponding to the thicknesses (d) and wavelengths (λ) which satisfy the relation

$$d = \left(q + \frac{\pi - \delta}{2\pi}\right)\frac{\lambda}{2n} \quad , \qquad (2)$$

where $\delta = \delta_1 - \delta_2$, δ_1 and δ_2 being the phase shifts on reflection from the front and rear surfaces of the film. For an oxide layer on a metal, we evidently have $\delta_1 = \pi$ and $\delta_2 = \delta_m$. The expression for δ_m can be derived from Fresnel's formulae:

$$\tan\delta_m = \frac{-2n_0k}{n^2 + k^2 + n_0^2} \quad , \qquad (3)$$

where k is the absorption coefficient of the metal, n_0 the refractive index of the medium traversed by the light beam, and n the refractive index of the oxide film;

$$q = \frac{\varepsilon}{2\pi} \quad , \qquad (4)$$

where ϵ is the phase difference determined solely by the difference between the optical path lengths. Estimates of the accuracy of this method quoted in Methfessel's review[10] showed that the error in determining the thickness of the layer (the thickness of a layer of silver iodide and silver was calculated) is about 200 Å towards higher values. Thus this method is applicable, if at all, to comparatively thick films giving several interference series. The unsuitability of this method for thin films was demonstrated by the present authors[11] in relation to anodic films on titanium obtained in a dilute solution of alkali. Moreover, both the present authors' investigation and others[10] show that the sequence and tints of the oxide film colours frequently disagree with Rollet's table. This shows that the formation of the film colour can depend on the structure of the film itself.

The fastest and most accurate method employing interference phenomena‡ is the spectrophotometric determination of the wavelengths giving the reflectance minima for a fixed angle of incidence of the light. Fig. 1, taken from Young's review[12], presents a curve of this kind. It shows that the wavelength at the minimum can be determined with a high degree of accuracy. It has been stated[13] that the thickness of the film and the refractive index can be determined in this way to within 1% or better. The accuracy in the determination of the refractive index n and hence of the thickness of the film is said[13] to be related to the error in the measurement of the reflectance R by the formula

$$\frac{dn}{n} = \frac{R^{1/2}}{2(1-R)}\frac{dR}{R} \quad . \qquad (5)$$

If n is known, the geometrical thickness of the film can be determined from the optical thickness corresponding to the singular point on the reflectance curve. It is then necessary to determine the interference series for the observed bands and to take into account the dispersion of the film. One should note that the dispersion of the film will have a significant influence only for thin films (single interference series). Abelès showed for a zinc sulphide film[14] that neglect of dispersion increases the error in the determination of the thickness of the film to 12%.

‡ When absorption of light by the film may be neglected.

A spectrophotometric method for the investigation of anodic films was used by Ellis[15] in a somewhat modified form. The applicability of this method and its great potentialities were confirmed by a recent study[16] whose authors investigated the kinetics of the growth of the oxide on a uranium electrode in an alkaline medium. A fairly rigorous theory of the application of interferometric methods is described by Winterbottom[17] and Heavens[13]. Heavens[13] reviews certain special interferometric methods such as polarisation interferometry and multibeam interferometry.

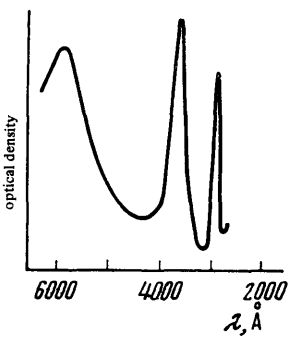

Figure 1. Spectrophotometric curve illustrating the interference minima and the reflection maxima for an oxide film on tantalum. The film is sufficiently thick to obtain several interference series[12].

Apart from studies by reflected light, transmittance measurements can be used to determine the thickness of oxide films. In this case one employs thin semitransparent layers of the metal and the change (increase) in the transmittance of this layer on oxidation is investigated. Light which is not absorbed by the oxide is employed. This method was developed long ago by Steinheil[18], who used it to investigate the oxidation of aluminium. By combining transmittance measurements with reflectance measurements on opaque metallic films *in vacuo* and in air, Hass and coworkers[19-21] established that stable films, formed spontaneously on aluminium in air, have a thickness between 30 and 40 Å and those on titanium are 35 Å thick.

Fig. 2 presents data obtained by Krüger and Yolken[22], who used ellipsometry to investigate the variation of the rate of growth of oxide films on the surface of iron with oxygen pressure. The shape of the curves shows that, even in a high vacuum, iron (and probably all metals except gold) have an oxide film on their surface. Numerous studies have shown that such thin oxide films are in fact present and constitute the main barrier to heterogeneous reactions. Perhaps the only optical method which makes it possible to measure the thickness of such thin oxide films without affecting the experimental conditions is the ellipsometric method.

The physical phenomenon which constitutes the basis of the ellipsometric method is that linearly polarised light incident on an absorbing surface becomes elliptically polarised after reflection from this surface. This method differs from those described above by the fact that measured quantities are not the change in light intensity at the angles, phase differences, and amplitude ratios of the lightwave components. The ellipsometric method is very

accurate in studies of film growth processes; according to Archer and Gobeli[23], the accuracy in the measurement of thickness reaches limits of 0.07 Å.

The method was first used to investigate the kinetics of the growth of oxides by Tronstad[24] and in the USSR elipsometry was used for similar purposes for the first time by Krylova[25], who measured the thickness of films on different metals. The ellipsometer was first applied to corrosion systems in the USSR by Andreeva[26, 27].

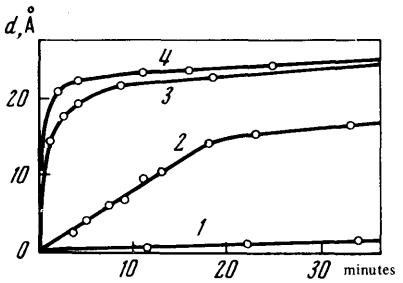

Figure 2. Variation of the thickness of the oxide film with time for iron in an atmosphere of oxygen[22] at different oxygen pressures (mmHg): *1*) 3.5×10^{-6}; *2*) 2.5×10^{-5}; *3*) 2×10^{-4}; *4*) 760.

The ellipsometric method makes it possible to measure also the refractive index of the oxide n. These measurements are simple if the film does not absorb light[28]. However, if the film does absorb light, the measurements of n must be made with a specimen immersed in liquids with different refractive indices[28]. For a fairly thick absorbing film (opaque film), the optical constants can also be determined using a single specimen.

Fig. 3 illustrates graphically the ellipsometric parameters, including the main parameters ψ and Δ.

Suppose that the incidence plane, perpendicular to the plane of the figure, forms a horizontal axis. The light incident on the specimen is initially polarised at an angle of 45° to this plane. The electric vector of the incident wave is 01 and that of the reflected wave is *OR* (Fig. 3). This picture corresponds to a dielectric specimen on which there are no surface films and the reflected light is linearly polarised. The ratio of the components of the *OR* vector corresponding to the polarisation in the incidence plane (r_p) and in the plane at right angles to it (r_s) defines the tangent of the ellipsometric parameter ψ:

$$\tan\psi = r_p/r_s \quad . \tag{6}$$

However, if there is a film on the surface of the support or the support is made of an absorbing material, the magnitude and directions of the r_p and r_s vectors will vary with time and the reflected light becomes elliptically polarised. The direction of rotation of the electric vector is indicated by arrows on the ellipses illustrated in Figs. 3*a* and 3*b*. The phase difference Δ for the r_p and r_s vectors constitutes the second ellipsometric parameter:

$$\Delta = \delta_p - \delta_s \quad , \tag{7}$$

where δ_p and δ_s are the phases of the r_p and r_s vectors respectively. Fig. 3 shows also two other ellipsometric parameters, λ and γ.

The exact theory relating the phase differences Δ to the thickness of the film is very complex; however, provided that the refractive indices of the film and the support are known, the ellipsometric measurements of the film thickness are greatly simplified. In this case it is possible to employ a linear approximation to the exact expressions relating Δ and the film thickness.

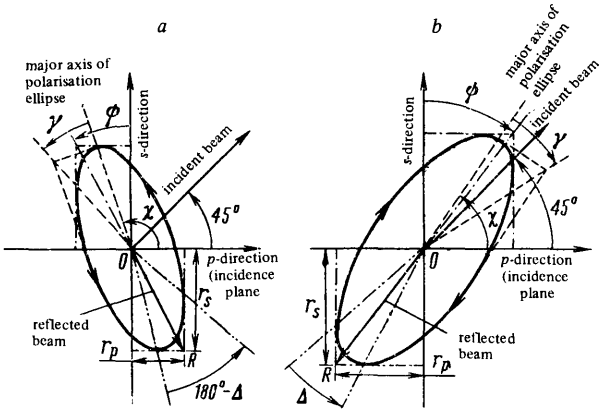

Figure 3. Graphical representation of different ellipsometric parameters: *a*) reflection at an angle of incidence smaller than the principal angle; *b*) reflection at an angle of incidence greater than the principal angle[29].

Starting with Tronstad[24], most investigators over a fairly long period employed Drude's linear approximation, which can be formulated as follows when the surrounding medium has a refractive index $n_2 > 1$:

$$\Delta - \bar{\Delta} = \frac{4\pi}{\lambda} \cdot \frac{\cos\theta \cdot \sin^2\theta\,(n_1^2 - n_2^2)}{(\cos^2\theta - n_2^2\alpha)^2 + n_2^4(\alpha')^2} \cdot [(\cos^2\theta - n_2^2\alpha) \cdot (n_1^{-2} - \alpha) + n_2^2(\alpha')^2] \cdot d \quad , \tag{8}$$

where Θ is the angle of incidence of the beam, n_1 the refractive index of the film, d the thickness of the film,

$$\alpha = \frac{1 - k^2}{\nu^2(1 + k^2)}, \quad \alpha' = \frac{2k}{\nu^2(1 + k^2)^2} \quad , \tag{9}$$

k the absorption coefficient of the metal, ν the refractive index of the metal, and λ the wavelength of the incident beam.

However, comparison of Drude's approximation with the exact theory shows that the error in the determination of the thickness using this approximation is very large and increases markedly with the thickness of the film. Comparison of curves *1* and *3* in Fig. 4, taken from Bennet and Bennet's review[29], shows this clearly. The figure also demonstrates that another linear approximation, proposed

by Archer, is much closer to the exact theory than Drude's approximation. Archer's approximation can be formulated as follows[30]:

$$\Delta - \bar{\Delta} = \frac{1}{[\cos^2\theta - a + \sin^2\theta\,(a^2 - a'^2)]^2 - (a')^2} \cdot \cdot [720\,(d/\lambda) \cdot \cos\theta \cdot \sin^2\theta\,(1 - n_1^2) \cdot \{(a - 1/n_1^2) \cdot \cdot [\cos^2\theta - a + \sin^2\theta\,(a^2 - a'^2)] - (a')^2\}] \quad , \tag{10}$$

where $\bar{\Delta}$ is the phase difference for a surface not coated by a film and $n = n' - jk$ is the complex refractive index of the support:

$$a = (n^2 - k^2)\,(n^2 + k^2)^2 \quad , \quad a' = 2nk/(n^2 + k^2)^2 \quad . \tag{11}$$

On the other hand, if the oxide film absorbs light, the use of approximate expressions for a non-absorbing film [Eqns. (8) and (10)] leads to serious errors in the simultaneous calculation of n_1 and d. This is indicated, in particular, by the experimental data of Chernykh and Yakovleva[31].

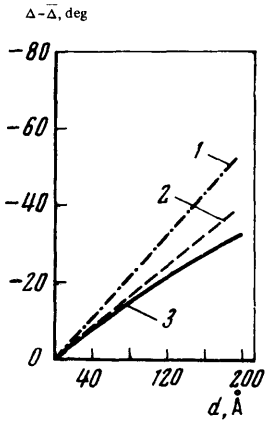

Figure 4. Comparison of Drude's (curve *1*) and Archer's (curve *2*) approximations with the exact theoretical relation (curve *3*). Data for alumina on the surface of aluminium[29].

However, there exist at least two methods, which make it possible to obviate these difficulties. The first involves the determination of the refractive index of the support and the film and of the refractive index of the film alone by independent methods, the ellipsometric method being used only to determine the film thickness in terms of Eqn. (10). Then, even if the film absorbs light, it is possible to obtain fairly accurate film thicknesses[32]. The second method, employed by Chernykh and Yakovleva[31,33] and other investigators, does not require the experimental determinations of the refractive indices and of absorption by the film and support, but in this case difficulties of another kind arise. The method is based on the exact theory of the polarisation of light on reflection and hence requires fairly complicated calculations§. The results permit the plotting of nomograms taking into account the changes in n_1 and k. Analysis of the nomograms[31,33] shows that both ellipsometric parameters, Δ and ψ, depend very significantly on the changes in n_1, k and δ.

Experimental devices permitting the determination of the principal ellipsometric parameters ψ and Δ have been described in many original papers and reviews. One should note that the fundamental scheme of the measurements has changed little since the publication of the first studies by Tronstad. The following units are probably typical for any ellipsometric apparatus: emission collimator (source, slit, collimating lens), polariser, specimen with holder, compensator (quarter-wave plate), analyser, focussing lens, and detector.

Figs. 5 and 6 illustrate schematically two possible ellipsometric systems[29]. The recording can be both visual and photoelectric. Additional components, resembling half-shadow devices which increase the accuracy of visual readings[34,35] or Faraday cells which can be used for accurate photoelectric measurements of angular orientations (the accuracy with which the angles can be read is to within 1 second), can be built into ellipsometric systems similar to those shown in Figs. 5 and 6.[36] Moreover, gas lasers[37], mainly helium–neon lasers, have begun to be used recently as light sources in ellipsometers in order to increase the accuracy of the measurements.

A fairly advanced ellipsometer, a distinctive feature of which is its construction based on a commercial GS-5 goniometer produced in the USSR, was recently built at the Karpov Physicochemical Institute[38]. Four removable units, permitting its employment as an ellipsometer, were specially constructed for this instrument. The instrument has a photoelectric recording system.

Without considering in detail the extensive literature dealing with data obtained by measurements, we would like to quote here as an illustration several studies on the ellipsometry of thin films, which we believe to have a direct bearing on the corrosion-electrochemical behaviour of metals.

Bockris et al.[33] described experimental data obtained in an ellipsometric study of the surface of nickel in sulphuric acid solution. The nickel potential was maintained with the aid of a potentiostat. The observed dependence of the thickness of the oxide film on the electrode potential was of particular interest. However, the interpretation of the results aroused quite justified criticism[39]. The results of ellipsometric studies of the growth of oxide on nickel (in an alkaline medium) were published by Chernykh and Yakovleva[31,40]. They traced the relation between the change in the structure of the oxides and the change in the optical parameters; although some of the conclusions arrived at are controversial, on the whole these studies[31,40] are of great interest.

Goswami and Stachle[41] investigated the kinetics of the growth of passive films on iron and iron–chromium, iron–nickel, and iron–chromium–nickel alloys. The oxide films were formed on anodic polarisation of the electrodes in a borate buffer solution (pH 8.4). Their[41] results show that the dependence of the change in the thickness of the oxide on the potential is greater than would be expected for the inverse logarithmic law. The optical constants of the alloys not coated by oxidates are very close. The growth of films on the electrode surface leads to significant changes of the optical constants. For the same potentials, the film thicknesses on the iron and alloy electrodes are approximately the same. Thus one may suppose that in this case, the rate of the reactions at the electrode–electrolyte interface is determined by the electrophysical parameters of the oxide film and not its thickness.

§ These are simplified when electronic computer techniques are resorted to.

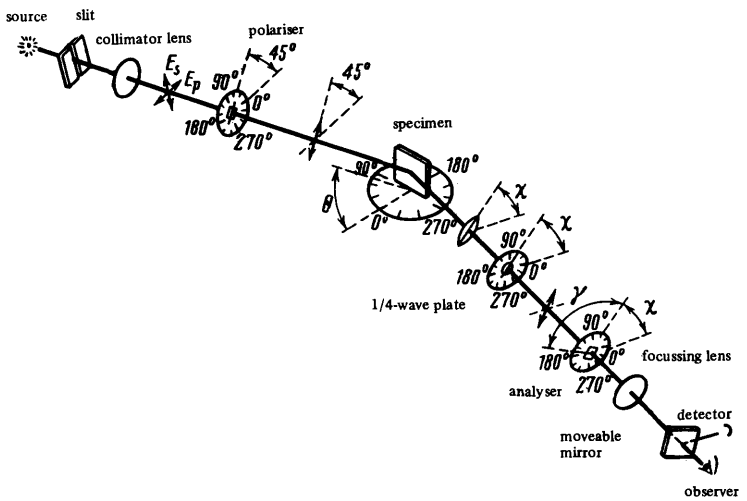

Figure 5. Ellipsometric system for the measurement of Δ and ψ for a 45° orientation of the polariser.

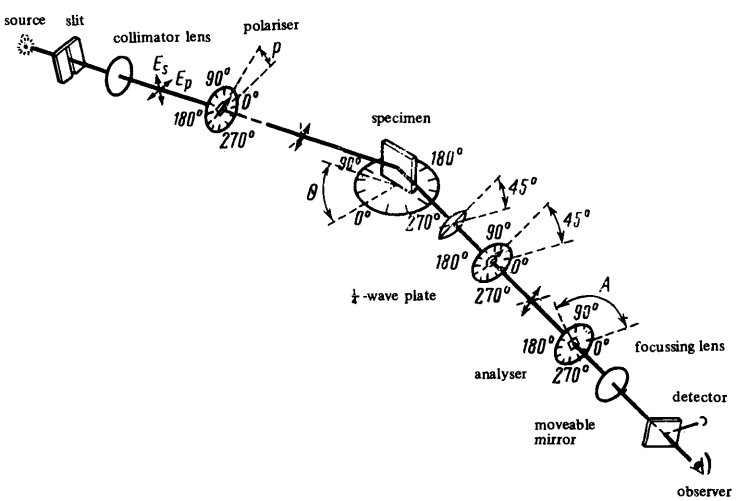

Figure 6. Ellipsometric system with a quarter-wave plate orientated at an angle of 45° for the measurement of Δ and ψ.

A recently published paper by Bockris et al.[42] describes a very extensive study dealing with the mechanism of the passivation of iron in neutral solutions. It was carried out by ellipsometric and coulometric measurements. The part of the investigation describing the methods[42] is of particular interest, since the authors described in detail the technique of the ellipsometric studies. The measured[42] refractive and absorption coefficients of iron oxides agree satisfactorily with other data. The results of the experiments of Bockris et al.[42] led them to the conclusion that at potentials more negative than the passivation potential iron is coated by a film of the hydroxide $Fe(OH)_2$. Very close to the passivation potential, the oxide γ-Fe_2O_3 begins to grow and its molar content in the film increases as the electrode potential shifts towards positive values. A potential shift by 0.5 V leads to complete recrystallisation of the film as γ-Fe_2O_3. According to the authors, the passivation of iron is in fact related to the appearance of the γ-Fe_2O_3 film on the iron surface. A number of studies in which an absorption mechanism of the passivation of iron in neutral solutions was proposed have been criticised.

Two recent studies by Sato and Kudo[43,44] deal with the same problem, namely the passivity of iron in neutral solutions. The first report[43] describes ellipsometric studies on iron in borate solution. It was observed that the oxide film can be completely removed from the electrode surface by cathodic reduction. It is stated that the minimum thickness of the surface oxide on iron is 9 Å. The oxide film exists on the electrode surface also in the region of active dissolution. At potentials between -0.3 and +0.9 V (s.c.e.)

the film thickness increases linearly with potential until the attainment of a thickness of 50 Å. The evolution of oxygen at higher anodic potentials does not disrupt the film. The problem of the distribution of potential in the iron–oxide film–electrolyte system is discussed on the basis of the experimental data obtained. According to Sato and Kudo[43,44], in the passive region the main potential jump is localised in the oxide film. The oxide film, consisting of Fe_3O_4 or γ-Fe_2O_3, was represented[43,44] as a two layer-structure with an outer hydrated layer and an inner non-hydrated layer.

In conclusion of the section dealing with ellipsometric studies on the kinetics of the growth of oxide films on metallic electrodes in electrolytes, noting yet again the extreme importance of these investigations, we should like to make certain critical remarks concerning the interpretation of the results of ellipsometric measurements. For example, Bockris and coworkers[33,42] believe it possible to infer the electronic conductivity of the oxide film from changes in the measured absorption coefficient. This approach is probably not entirely correct. Indeed, it is readily seen that a change in absorption index at a specific wavelength can only indicate a change in the number of electronic transitions from the corresponding level located in the forbidden gap of the oxides¶ and hence a change in the population of this level. In order to relate the change in the population of the level to the change in conductivity, it is necessary to show that the level is at least partially ionised at room temperature and hence can participate in the change of the equilibrium conductivity of the oxide film.

Moreover, it follows from the most general considerations that the electric fields localised in the double layer or in the oxide film can affect the ellipsometric parameters. Nevertheless, these effects are not taken into account in the studies quoted above, although the distribution of potential throughout the system has been discussed[43,44]. However, studies have been published during the last few years in which the effect of electric fields on ellipsometric parameters was in fact used to investigate the structure of the double layer and adsorption on the surface of the electrode. The next section of the review deals with these investigations.

III. ELLIPSOMETRIC STUDIES ON ADSORPTION AT THE METAL–ELECTROLYTE INTERFACE

The first study dealing with certain aspects of the effect of the double layer on the optical properties of the metal–electrolyte interface in relation to ellipsometric measurements was made by Stedman[45]. He chose a simple model of the double layer, whose parameters could be described in accordance with Delahay's theory[46]. Stedman[45] examined the effect of the structure of the double layer on the optical constants of the metal both in the absence and in the presence of specific adsorption. Stedman[45] quotes data obtained for aqueous potassium chloride–mercury and aqueous sodium fluoride–mercury systems. The wavelength of the light in the ellipsometric measurements was 546 nm and its angle of incidence was 70°. The surface charge of the metallic electrode was calculated from the experimental capacitance and potential of the electrode.

¶ One should bear in mind that the width of the forbidden gap in the majority of oxides exceeds 3 eV, while the energy of the light quantum emitted by the light sources usually employed in ellipsometers is less than 3 eV.

Fig. 7, taken from Stedman's paper[45], presents the variation of the ellipsometric parameters Δ and ψ with the electrode charge q_M at different sodium fluoride concentrations in solution. The shape of the curves shows that Δ and ψ depend very markedly on the surface charge, the dependence increasing on dilution of the solution. Thus it was shown that Δ and ψ can vary not only when a new phase grows on the surface of the electrode but also when the surface becomes charged. Moreover, the author points out that the $\Delta - q_M$ and $\psi - q_M$ (Fig. 7) relations have an inflection corresponding to the absence of a surface charge. Possibly this interesting experimental finding will permit the development of a new method for the determination of the zero-charge potential. Stedman[47] considered these problems in greater detail: in particular, he considered separately the effect of the dense and diffuse components of the double layer.

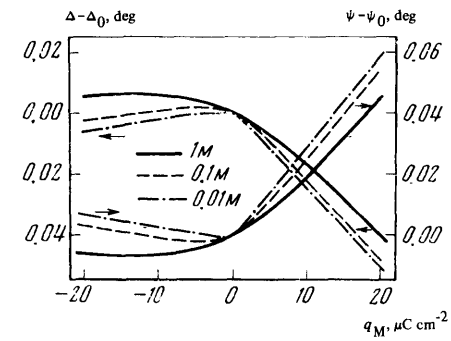

Figure 7. Variation of Δ and ψ with the surface charge of mercury in aqueous sodium fluoride; Δ_0 = 112.893, 113.125, and 113.145 and ψ_0 = 36.821, 36.831, and 36.832 for sodium fluoride concentrations of 1, 0.1, and 0.01 M respectively[45].

The Polish investigators Minc and Herbich[48] studied the influence of the double layer on the optical parameters of the metal–electrolyte interface[48]. They investigated ellipsometrically gold in 0.3 M sodium sulphate solution. To increase the sensitivity of this system, the reflecting element was made in the form of two plane-parallel gold plates between which light was repeatedly reflected. A distinct correlation was discovered between the rate of the electrochemical reactions and the "effective" reflection coefficient. The minima in the reflected light beam correspond to the minimum rates of the electrochemical reactions. Thus this study also confirms the possibility of employing ellipsometry for the investigation of the structure of the double layer.

The above problem was considered in two publications by Bockris and coworkers[49,50]. The first study[49] dealt with the ellipsometric investigation of the adsorption of anions at the solid–electrolyte interface. Silver, gold, rhodium, and nickel test electrodes were employed. The adsorption of Cl^-, Br^-, ClO_4^-, SO_4^{2-}, and OH^- ions was studied. The experimental apparatus consisted of a classical ellipsometer, but a differential recording system was employed. (A phototransistor, whose signal served as the reference signal, was introduced beyond the polariser, which made it possible to increase the sensitivity in the

measurement of the parameter Δ to within 0.002°.) The electrode potential was set by a potentiostat and was varied in 100 mV steps.

In the same study an attempt was made to relate the ellipsometric parameter Δ to the surface charge of the electrode. The authors endeavoured to allow for the electromodulation effect†, according to the interpretation of Hansen and Prostak[51]. Analysis of the equations quoted by Paik Woon-Kie et al.[49] convinced them that the changes in Δ are significantly related to the surface charge of the metallic electrode and depend very little on the charge distribution in the surface layer of the metal. The authors point out that, when the electromodulation effect is disregarded, a significant error may be made in the conversion of Δ into the amount of adsorbed substance. The main equation employed by the authors[49] is

$$\delta\alpha = \delta\Delta_{ads} \cdot (q -) + b\delta q_M \quad , \qquad (12)$$

where Δ_{ads} is the change in the parameter Δ on adsorption, q the amount of adsorbed anions in units of charge, b the electromodulation coefficient tabulated for different metals[49], and q_M the charge of the surface layer of the metal.

Fig. 8 (taken from Ref. 49) presents adsorption isotherms obtained on a gold electrode by the method described above. Similar isotherms were obtained on silver, nickel, and rhodium electrodes. The possibility of deriving such information demonstrates of course the extremely great value of the method.

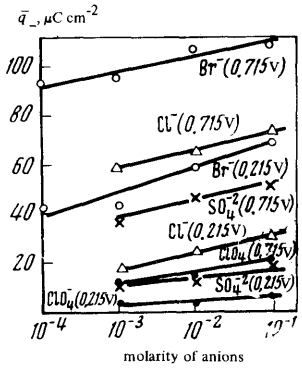

Figure 8. Adsorption isotherms of anions on a gold electrode obtained by ellipsometric measurements[49].

However, the authors themselves point out that the isotherms cannot be obtained in all cases. Thus the Δ–potential relations for the electrodes in hydroxide solutions is anomalous. The authors[49] explain this by the fact that the adsorption of even a monolayer of OH^- ions can (or should) be regarded as a new hydroxide or oxide phase. The fact that the authors[49] based their consideration of electromodulation effects on the model described by the theory of Hansen and Prostak[51] should also be noted. The reliability of the conclusions drawn from this theory is doubtful even as regards the very formulation of the problem of the mechanism of electroreflectance of metals. Moreover certain experimental data[52] disprove the fundamental conclusions of the theory[51]. We shall consider this problem in greater detail in the next section.

Paik Woon-Kie and Bockris[50] describe the results of a detailed experimental study of the joint influence of adsorption and electromodulation of the optical constants on the measured ellipsometric parameters. Although this investigation suffers from the same defects as the previous one, the experimental data and also the conclusions reached by the authors are extremely interesting.

They investigated[50] the variation of the ellipsometric parameter Δ for a gold electrode in 0.01 M NaBr in 0.001 N $HClO_4$‡ solution as a function of the wavelength. The light was made monochromatic using interference filters. The potential change from 0.11 to 0.61 V (s.c.e.). On the basis of the models described above, the authors attempted to calculate the contributions of the two effects — electromodulation and adsorption — and, having summed the two curves, to compare the resulting calculated curve with the experimental curve. A satisfactory agreement was obtained in the wavelength range from 4500 to 5500 Å; at higher wavelengths there was no agreement. The authors state[50] that characteristic contributions by the two effects probably occur for each metal.

One should note that so far experimental data have been obtained which definitely indicate that the change in the order on the electrode surface affects the fundamental ellipsometric parameters and ellipsometry can probably be used as an extremely sensitive method for the investigation of processes leading to such changes. However, so far there is no well-founded and clear theory which would allow a fairly clear-cut interpretation of the observed phenomena. This does not mean of course that studies in this field cannot be regarded as of very great value.

IV. SPECTROSCOPIC STUDIES IN THE ELECTRODE–ELECTROLYTE INTERFACE

The lack of spectroscopic studies on the electrode surface in electrochemical systems (until very recently) can probably be explained both by a number of technical difficulties and by the fact that the urgent need for such investigations arose quite late. Although the number of publications of spectroscopic data on electrodes is small, it is possible to discern a tendency for such investigations to employ the very latest advances in spectroscopy: multiple reflection and modulation methods.

The most promising spectroscopic methods, including those applicable to electrochemical systems, are related to the modulation of the intensity by some kind of external effect (for example an electric field). We then obtain a spectral distribution of the intensity of light reflected from the electrode surface differentiated with respect of this effect, i.e. instead of the I–λ relation, where I is the intensity and λ the wavelength of the light, we obtain the dI/dv–λ relation, where v is the external effect (for example a potential field or an electric field).

It is readily seen that the spectral distribution curves in a differential form have many advantages over the usual curves, primarily as a result of the sharp improvement of resolution. This aspect of the problem in relation to semiconductors and metals has been specially considered in two reviews[53,54]. The first study, dealing with the reflection spectra of metals modulated by an electric field applied in the electrolyte, was that of Feinleib[55], who obtained the electroreflectance spectra of gold and silver.

† The change in the optical constants of the metal when the electrode potential is altered.

‡ The Br^- ions were absorbed.

As regard method, the measurements of electroreflectance do not present fundamental difficulties but the measuring apparatus must be highly selective, since the signal/noise ratio at the input to the amplifier is usually small. A circuit for the measurements of electroreflectance and electroabsorption is presented in Fig. 9.

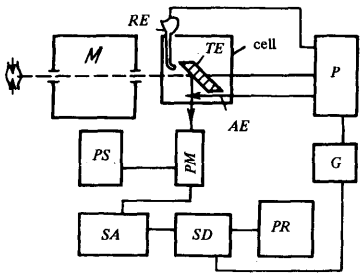

Figure 9. Circuit for the measurement of electroreflectance and electroabsorption in an electrode–electrolyte system.

Polychromatic light from the source passes through a monochromator (*M*) and falls on the surface of the electrode in the cell with the electrolyte §. The light reflected from the electrode falls on a radiation detector — a photomultiplier (PM). In addition to the test electrode (*TE*), the cell contains an auxiliary electrode (*AE*) and the reference electrode (*RE*) and is connected to a potentiostat (*P*). Moreover, a sinusoidal or pulsed alternating current from a generator (*G*) passes through the cell. This variable signal, which modulates the surface field of the electrode, also modulates the light reflected from the surface. Thus at the output from the photomultiplier there are two components of the potential: a constant component proportional to the overall flux reflected from the electrode (*R*) and a variable component proportional to the light flux modulated by the electric field (ΔR). As a rule the variable component is small — the degree of modulation is usually less than 1%. The variable signal at a fixed frequency is therefore amplified by a selective amplifier (*SA*) with a high amplification factor in a fairly narrow amplification band. After amplification the signal is detected synchronously (*SD*) and is recorded with a pen recorder (*PR*). A similar apparatus was described in detail by Akimov[56]. Different authors naturally describe somewhat modified experimental setups, but these modifications do not involve the fundamental and essential units enumerated above.

It is readily seen that the ratio $\Delta R/R$ is independent of the light source intensity spectrum and the light detector sensitivity spectrum but does depend on the changes in the optical and electrophysical (via the change in the local electric fields) properties of the electrode–electrolyte interface.

It was stated above that the electroreflectance effect on metals in an electrolyte was observed for the first time by Feinleib[55] and the mechanism of electroreflectance in this system was formulated by Hansen and Prostak[51], who suggested that the optical constants of the metal are modulated by the electric field owing to the modulation of the surface concentration of electrons (i.e. a change in the Fermi level on the surface of the metal). However, Lazorenko – Manevich and Stoyanovskaya[52], who compared their own data with the conclusions of Hansen and Prostak's theory[51], concluded on the basis of a comparison of the variation of electrode capacitance and electroreflectance with the potential of the gold electrode and the theory[51] cannot account for the mechanism of electroreflectance of metals. They[52] believe that not only the modulation of the surface concentration of electrons but also of their mobility may be the cause of electroreflectance. Incidentally, the value of their work[52] is by no means related to the critism of Hansen and Prostak's theory but is determined by their own experimental results. They obtained the variation of the electroreflectance from a metallic electrode with potential. They investigated gold, platinum, and silver electrodes and showed that the variation of the electrode potential may alter not only the intensity of the spectrum ($\Delta R/R$) but also its shape. In particular, a change in shape was observed in the oxidation of gold at a potential of about 1.5 V. Moreover, it was shown[52] that the shape of the electroreflectance spectrum of gold and silver changes significantly as a result of the specific adsorption of iodide ions from solution. They explained this phenomenon by the formation of chemical bonds between the iodide ion and the metal. The bond energy depends on the nature of the metal.

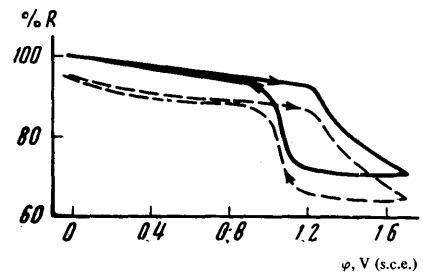

Figure 10. Measurement of the reflectance of gold in 1 *N* $HClO_4$ as a function of electrode potential. Continuous curve — in the absence of benzene; dashed curve — in the presence of benzene. Data for seven reflections are presented[57].

American investigators[57] studied the variation of the reflectance of gold under the conditions of a varying electrode potential. The main electrolyte employed was a solution of $HClO_4$. Single and multiple (sevenfold) reflection was used. The effect of adding benzene to $HClO_4$ on the variation of the reflectance with potential was examined. Fig. 10 shows the variation of the reflectance of the gold electrode with its potential in the presence and absence of benzene. The results[57] are fully consistent with those of Lazorenko – Manevich and Stoyanovskaya[52] in the sense that the variation of the potential changes not only the intensity but also the shape of the spectrum. Moreover, the

§ The requirements which must be met by the optical windows are of the usual kind for measurements of this type.

American workers[57] carried out an extremely useful analysis of the correlation between single and multiple reflection spectra. This relation may be described by the following equation:

$$(1/R)(\partial R/\partial E)_\lambda = (1/nI_n)(\partial I_n/\partial E)_\lambda \quad , \qquad (13)$$

where R is the reflectance of the electrode, $(\partial R/\partial E)\lambda$ a term related to the modulation of R by the applied field at a constant light wavelength λ, and I_n the light intensity after n reflections. It is understood that the shape and value of the (n/R) $(\partial R/\partial E)$–λ curves are independent of the number of reflections.

Mention should be made of the work of Barret and Parsons[58], who investigated the reflection spectra of a platinum electrode and the effect of the adsorption of ions of different substances (O_2, H_2, halogens, methanol, formaldehyde) on the optical constants of the electrode surface.

The data of McIntyre and Kolb[59], who investigated with the aid of reflection spectroscopy thin surface films formed on a metallic electrode, merits a more detailed consideration. They measured the $\Delta R/R$–φ (potential) and $\Delta R/R$–λ relations for platinum, gold and nickel under the conditions of anodic polarisation and the same relations for the adsorption of hydrogen and silver on platinum. Moreover, the results were used with the Kramers – Kronig dispersion relations to calculate the variation of the real and imaginary components of the dielectric constant with the energy of the light quantum. $\Delta R/R$ was calculated[59] as

$$\Delta R/R = [R(d) - R(0)]/R(0) = R(d)/R(0) - 1 \quad , \qquad (14)$$

where $R(d)$ is the reflectance of the metal–surface film–electrolyte three-phase system and $R(0)$ the reflectance of the metal–electrolyte interface. Measurements were made of the $\Delta R/R$–λ relations with light polarised parallel and at right angles to the plane of the electrode. These data permitted the calculation with the aid of equations quoted by McIntyre and Aspens[60] of both components of the dielectric constant of the surface phases. McIntyre and Kolb[59] employed a more complicated experimental apparatus than that used hitherto for analogous measurements. The more sophisticated apparatus permitted the measurement of the $\Delta R/R$ spectra up to 6.5 eV with a sensitivity of about 10^{-5} $\Delta R/R$ for a time constant of 1 s.

Having measured the $\Delta R/R$–φ and $\Delta R/R$–λ relations on platinum in 1 M $HClO_4$, McIntyre and Kolb[59] concluded that the oxide film on platinum consists of PtO (on the basis of the calculation of the absorption coefficient). Moreover, they found that the variation of the absorption coefficient of this layer, $\alpha = 4\pi k/\lambda = 2\pi\epsilon''/n_2\lambda$, has two maxima, the quantum energies of which are 3.4 ± 0.1 and 4.6 eV. At the maxima $\alpha = 5 \times 10^5$ cm^{-1}.

In spectroscopic studies of a gold electrode subjected to anodic polarisation in 1 M $HClO_4$ the authors observed that the oxide formed on gold at a potential of 1.6 V (n.h.e.) is Au_2O_3.

McIntyre and Kolb[59] quote data obtained in an optical study of the anodic oxidation of nickel in 0.1 M KOH. They made a detailed spectroscopic investigation of the surface oxide formed on the nickel electrode at a potential φ = 1.4 V (hydrogen electrode) and observed that the composition of the oxide is NiOOH. Fig. 11 presents curves relating the real (ϵ') and imaginary (ϵ'') components of the dielectric constant of the NiOOH film to the energy of the quantum calculated from the $\Delta R/R$ spectrum obtained for an electrode potential of 1.5 V (n.h.e.) in 0.1 M KOH. The ϵ' maxima corresponding to energies of 3.0 and 4.1 eV agree satisfactorily with data obtained by McClure[61] and Tippins[62] for the absorption of Ni^{3+} ions in corundum. A negative value of ϵ' is characteristic of the metallic conduction of this oxide phase.

The study of McIntyre and Kolb[59] lies at the boundary between spectroscopic investigations of the metal–electrolyte interface and investigations of metal–oxide–electrolyte systems. Below we shall consider studies dealing with systems of the latter type.

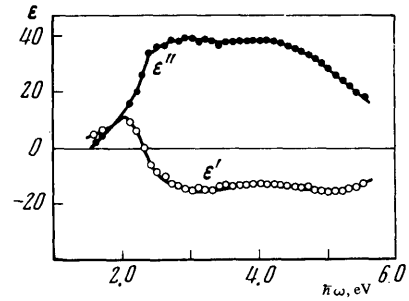

Figure 11. Spectra of real (ϵ') and imaginary (ϵ'') components of the dielectric constant of NiOOH; measurements made at a nickel potential of 1.5 V (s.c.e.)[59].

The paper of Holden and Ullman[63], describing the measurements of electroreflectance of oxidised tantalum and niobium, was published in 1969. An attempt was made to explain the mechanism of the generation of the electroreflectance signal by an interference effect arising in consequence of electrostriction in the oxide film. However, this view was criticised by Frova and Migliorato[64], who showed that the modulation of the interference bands by the electric field in the visible part of the spectrum, observed on tantalum oxide, must be accounted for by the modulation of the refractive index of the oxide. This conclusion was based on the very satisfactory agreement between the calculated and experimental data.

The present authors showed[65] that the spectrum of the light beam reflected from the surface of oxidised titanium and modulated by the field (we treat this effect as electroabsorption) can be interpreted only when the electroabsorption effect $-\Delta I/I$ can be attributed to modulation by the electric field of the optical constants of the surface oxide.

There are at present no theories of electroabsorption and electroreflectance in metal–oxide–electrolyte systems, but for a qualitative treatment one can probably assume that in a number of oxides arising on "rectifying metals" (titanium, tantalum, niobium, zirconium, tungsten, etc.) the mechanism of electroabsorption reduces to the "anomalous" Franz-Keldysh effect[66].

There are two possible research techniques based on electroabsorption in a metal–oxide–electrolyte system. In the first studies on the effect of the electric field on the position of the edge of the intrinsic absorption of crystals[67,68], it was shown that the position of the edge depends significantly on the magnitude of the applied field. This effect is entirely valid also for thin oxide layers formed on the surface of a metal, as shown in our investigation[65]. Thus it was natural to attempt the determination of the change in the electric field strength (potential jump in the oxide) as a function of the electrode potential by measuring the

change in the electroabsorption corresponding to the maximum on the electroabsorption–wavelength curve. The results of experiments of this kind have been published[65,69]. Fig. 12 presents $i-\varphi$, $C^{-1}-\varphi$, and $\Delta I/I-\varphi$ curves which we obtained[69] for a titanium electrode in 5 *N* KOH ¶. The data in Fig. 12 show that $\Delta I/I$ begins to increase on transition from active dissolution to passivation. The main growth of $\Delta I/I$ takes place in the region of passivation potentials. Since according to our data[65] the increase of $\Delta I/I$ is associated with the increase of the field in the oxide film, presumably the redistribution of the components of the overall jump in electrode potential takes place precisely in the region of passivation potentials. The potential jump in the oxide film increases not only as a result of the increase of the anodic potential but also as a result of the change in the location of the Helmholts potential jump, which leads ultimately to the inhibition of the dissolution of the metal. In the passive region the field strength in the oxide remains constant — $\Delta I/I$ is independent of the electrode potential. In the same range of potentials the surface oxide grows (the $C^{-1}-\varphi$ relation is linear). Hence it follows that the growth of the oxide is fully compensated by the increased potential jump in the oxide film due to the anodic potential shift.

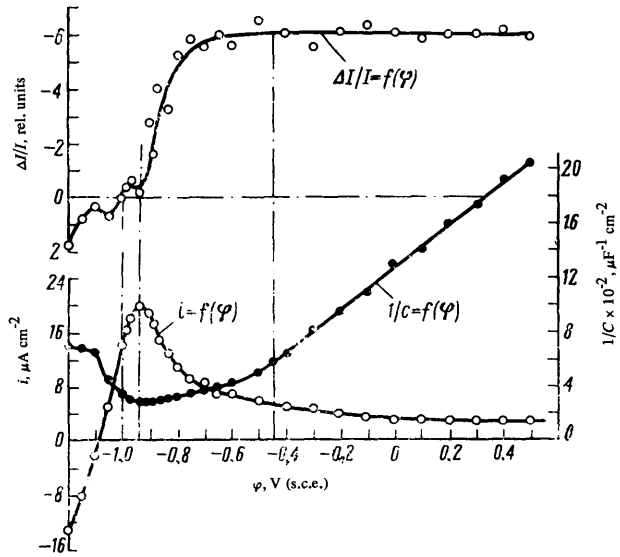

Figure 12. Variation of the current density i, the reciprocal of the capacitance C^{-1}, and the electroabsorption with the potential of a titanium electrode in 5 *N* KOH.

$\Delta I/I$ in a metal–oxide–electrolyte system also has a spectroscopic application. As already stated above, the electroabsorption spectrum has a maximum whose energy corresponds to the edge of the intrinsic absorption — the forbidden gap (ΔE_g) of the crystal. When the electroabsorption in a metal–oxide–electrolyte system is measured, the energy of the electroabsorption maximum on the electroabsorption–λ curve corresponds to ΔE_g for the oxide. Since ΔE_g is related to the main parameters of the oxide lattice, it follows that, having determined ΔE_g, it is often possible to identify the material of the oxide. Thus the maximum in the electroabsorption spectrum of the anodic oxide film on titanium[65] † agreed with ΔE_g for rutile single crystals measured by the same method[66].

The method of measurement of the electroabsorption spectra can probably be particularly useful in the study of structural transformations in surface oxides. Fig. 13 presents electroabsorption spectra which we obtained for a titanium electrode in 2 *N* H_2SO_4. The figure shows that the structure of the spectra changes significantly with the potential. Curves *1–3* (the passivation region) correspond fully to the rutile structure; however, on passing to potentials more positive than the total passivation potential, the absolute value of $\Delta I/I$ (curve with a maximum corresponding to an energy of 3.7 eV) begins to decrease (curves *4–6*) and a new short-wavelength $\Delta I/I$ maximum arises, its magnitude and energy depending on the electrode potential. Curves *7* and *8* corresponding to potentials of 0.2 and 0.5 V (s.c.e.), show that the energy of the new short-wavelength maximum is stabilised and assumes a value of 4.2 eV. We believe that the reason for the observed deformation of the electroabsorption spectra is that at more positive potentials the rutile structure may be replaced by the anatase structure, i.e. at potentials more positive than the passivation potential the rutile–anatase phase transition takes place in the oxide film on the titanium surface. It has been stated[70] that in many cases the anatase structure more readily gives nucleation.

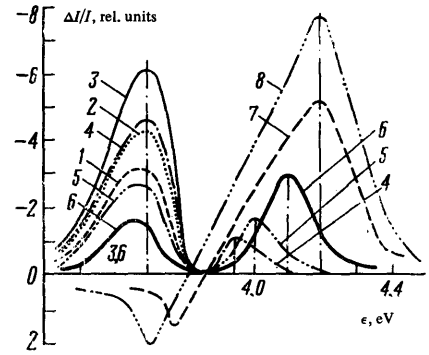

Figure 13. Electroabsorption spectrum obtained for the anodic polarisation of titanium in 2 *N* H_2SO_4 at different electrode potentials [V(s.c.e.)]: *1*) 0.45; *2*) 0.40; *3*) 0.35; *4*) 0.30; *5*) 0.25; *6*) 0.1; *7*) 0.2; *8*) 0.5.

The high sensitivity of the electroabsorption spectra to structural changes in the oxide may be demonstrated by the following example. Fig. 14 illustrates the electroabsorption spectra which we obtained from titanium–niobium alloys with different niobium contents. The measurements were made in 5 *N* KOH at a potential of 0.5 V. It is seen from the figure that the positions of the maxima in the electroabsorption spectrum depend significantly on

¶ Titanium is activated in this electrolyte and its surface oxide has the rutile structure over a wide range of potentials.

† We showed[11] that the oxide films obtained in the anodic polarisation of titanium in alkali have the rutile structure.

the niobium concentration in the alloy, which can be accounted for by the incorporation of impurity Nb^{5+} ions into the main TiO_2 oxide (rutile). Comparison of these data with the TiO_2–Nb_2O_5 phase diagram[71] suggests that the return of ΔE_g to a value characteristic of impurity-free rutile (3.7 eV), which occurs at a niobium concentration of 10%, can be explained by the fact that the initially homogeneous oxide becomes heterogeneous, since the new phase $TiO_2.Nb_2O_5$ appears. The appearance of this new phase can in fact promote the liberation of niobium from rutile.

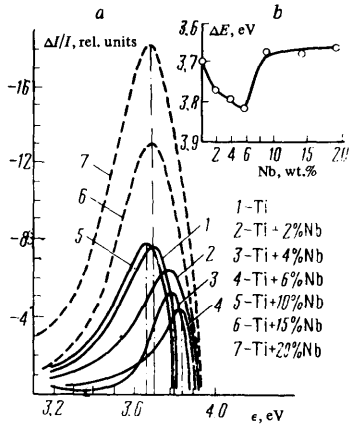

Figure 14. *a*) Electroabsorption spectra for titanium and titanium–niobium alloy electrodes obtained in 5 *N* KOH; *b*) variation of the energy of the electroabsorption maxima with niobium content in the alloys.

Gobrecht et al. [72] made a spectroscopic study of the surface of nickel under the conditions of anodic polarisation in 0.1 *N* sulphuric acid. They employed the electroreflectance method for this purpose and observed a change in the structure of the oxide in the range of potentials between primary and secondary passivation (0.8–1.3 V relative to the saturated calomel electrode). On the basis of a model which considered the inhomogeneity of the oxide film growing on the nickel surface, the authors explained the observed shift of the main absorption edge of the nickel oxide film with increased anodic potential by an increase of the concentration in the oxide film of nickel ions with a valence greater than two. The maximum rate of formation of these ions was observed at a potential of 0.97 V (s.c.e.). Thus, from an anodic potential of 0.76 V (s.c.e.), the outer layer of the oxide film is enriched in Ni^{3+} ions. This hypothesis of the authors is confirmed by a study of the variation of electroreflectance with the frequency of the modulating potential..

The data described above show that the application of various optical methods in the study of corrosion-electrochemical processes in an electrode–electrolyte system is extremely promising and may yield very valuable information about the mechanisms of these processes.

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Extraction Systems with Associated Extractants

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The review examines the characteristics of the extraction behaviour of extractants with pronounced self-association in the organic solution. The importance of the correct choice of the model of the liquid for an adequate description of the properties of the system is discussed.
The bibliography includes 127 references.

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I. INTRODUCTION

The problem of the processing of nuclear fuel and also the necessity of obtaining in large amounts and with a high degree of purity uranium, thorium, the individual lanthanides, and other rare and widely scattered elements to meet the requirements of nuclear power engineering have led to the vigorous development of certain fields of chemical engineering. The need for special purity of the materials led to the large-scale application of the extraction method for the isolation and purification of metal salts. During the last 10–15 years several hundreds of extractants capable of extracting metal salts and inorganic acids from aqueous solutions have been proposed and used on a laboratory and industrial scale. However, the study of the physicochemical properties of these systems has lagged appreciably behind the practical requirements. Many important details of the chemical behaviour of extractants (the effects of the hydration of the initial compounds and products, their solubilities in the organic phase, the effect of the solvent on the selectivity of the extraction and the stability of the complex extracted, the process kinetics, etc.) have been inadequately investigated.

The capacity of many extractants for self association is of special interest. Association in the organic phase is characteristic of extractants such as high-molecular-weight alcohols and phenols [1-13], carboxylic acids [14-20], alkyl- and aryl-phosphoric acids [21-44], and salts of organic ammonium derivatives [45-78]. Examination of the results of numerous studies on the properties of extraction systems including the extractants enumerated above reveals the following fundamental difficulties relating to the association of the extractant.

a. Conflicting data for the degree of association in the same systems or in systems with components of a similar chemical type obtained by different methods.

b. Unexpectedly simple linear concentration variation of the partition coefficients of metal ions (or acids) despite the non-linearity of the variation of the degree of association of the extractant.

c. Inconsistency of the experimental data for the concentration variation of the average degrees of association of the components with the thermodynamic properties of the model of the solution constituting the basis of the interpretation of these data.

The aim of the present reveiw was to examine the physical significance of models of the solution used for the description of extraction systems in connection with the chemical nature of the compounds present in solution, and also to indicate the principal studies in which ways of overcoming the above difficulties have been outlined.

II. GENERAL CHARACTERISTICS OF ASSOCIATED SUBSTANCES

1. Classes of Extractants with a Tendency towards Association

The capacity of particular substances for marked association in organic solvents is related directly to their chemical nature and the nature of the solvent. Thus alcohols, phenols, carboxylic acids, and organophosphorus acids contain both proton-donating and proton-accepting functional groups [OH, COOH, $OP(OH)_2$, etc.], which leads to the formation of a system of hydrogen bonds in the liquid.

A second mechanism of association, which plays a fundamental role for organic derivatives of ammonium salts, is the dipole–dipole interaction of the polar molecules of the extractants in a medium with a low dielectric constant.

As a rule, in real extraction systems the interaction is complex. Molecules of acid extractants and their metal salts usually have high dipole moments [72-79] and alkylammonium salts are capable of combining with "superstoichiometric" inorganic acid molecules via hydrogen bonding:

$$R_4N^+.NO_3^- \ldots HNO_3.$$

Extensive experimental data have accumulated concerning the state of the extractant in the organic solvent. Association equilibria have been investigated by methods based on partition between two liquid phases [14-16,30-45,80,81], cryoscopy [21,25,38-42,50-54,80], ebullioscopy [60,82], measurements of the vapour pressure of the solvent [13,19,22-27,30,38,42,46,60-62,82], potentiometric titration [64,65], conductimetry [15,59,63-65], viscometry [21,23,54,59,63,65], light scattering [57,58,62,71], dielectric constant measurements [20,59,63,65,74,77], infrared, ultraviolet, and Raman spectroscopy of the solutions [6,21,25-27,30,32,38,48,59,63], and NMR and ^1H NMR methods [5,41].

Depending on the chemical nature of the extractant and the solvent, the concentration range considered, and temperature, the average degree of association varies within fairly wide limits, but in general one may say that carboxylic and monobasic alkylphosphoric acids are least associated. Their average degree of association is close to two or a little more at high extractant concentrations [16,21,25,29-31,38]. The degree of association of alcohols and phenols increases with concentration more slowly than that of acids, but it reaches much higher values [2-6,13]. The association of dibasic alkyl phosphate is highest; it has been shown [42,43] to reach values of the order of several tens or above at moderate concentrations. The degree of association of alkylammonium salts depends strongly on the nature of the anion and can sometimes reach equally high values [53,57-59,65,71,82]. Evidently, without a far-reaching study of the properties of associated solutions, it is impossible to understand the complex nature of the extraction processes involving the widely employed associated extractants and to predict correctly the effect of different factors on their extraction capacity.

2. Difficulties in the Quantitative Interpretation of Partition Data in Extraction by Associated Extractants

The quantitative interpretation of partition data is complicated by the multiplicity of the reactions. As a rule, the extractants can form with the extracted species not one but a series of complexes with different contents of the extractant per species extracted. For example, in the extraction of uranium by dialkylphosphoric acids [23,39] the complexes UO_2A_2, $UO_2A_2(HA)_2$, and probably $UO_2A_2(HA)_n$ may be present in the organic phase. Most physicochemical research techniques do not permit a direct determination of the number of species formed in solution, since experimental quantities (vapur pressure of the solvent, partition coefficients between the phases, freezing point, etc.) are functions of the overall concentration of all types of species of the solute. Another fundamental difficulty is the non-ideality of both the aqueous and organic solutions. The solute species (hydrated metal ions or acids in the aqueous phase and the set of complexes of different composition and solvated to different extents in the organic phase) interact with one another and with the solvent, which is formally taken into account by the deviation of the activity coefficients from unity. There is an extensive literature on the activity coefficients of electrolytes in aqueous solutions [83,84], but the available data concerning the activities of the components in the organic phase are scanty and are quoted only for individual thoroughly investigated extractants. With increase of the concentration of the extractant and the extracted compound, there is in many cases a marked change in the dielectric constant of the medium, because the majority of extractants are highly polar substances and their dielectric constants are higher by 10–20 units than that of the pure solvent [49,72-78]. In any description of the chemical interaction in the organic phase account must be taken of the change in the properties of the medium when the range of moderate and high solute concentrations is considered. In order to deduce the reasons for the discrepancies in the experimental degrees of association of the extractant obtained over a wide range of concentration, it is necessary to examine in detail model concepts which constitute the basis of the computational equations.

III. METHODS FOR THE DESCRIPTION OF ASSOCIATED SOLUTIONS

1. Model of the Ideal Associated Solution and the Metrics of the Physicochemical Diagram

In the study of the properties of solutions the concept of the ideal associated solution is widely employed, i.e. of a solution in which all kinds of interaction between the species can be divided into two types: strong "chemical" interactions with energies of the order of 2000–10 000 cal mole^{-1} involving the formation of stable configurations and the interactions between the association complexes and the molecules of the surrounding medium; the energies of interactions of the second type are of the same order as the thermal energy (about 600 cal mole^{-1}) and they do not lead to the formation of stable solvates [85]. It is postulated that such a mixture of monomeric solvent molecules and complexes of the solute constitutes an ideal solution at all concentrations (Prigogine and Defay [86], p. 387). The special case of the ideal associated solution [monomeric solvent–associated extractant (its association complexes can include also a third component—the substance extracted)] is of interest for extraction. The following relations can be formulated for such a system:

$$f_A = \frac{\rho}{\rho_0} \cdot \frac{1}{\frac{X_A}{r} + X_B}, \qquad f_B = \frac{1}{\frac{X_A}{r} + X_B} \qquad (1)$$

where f_A and f_B are the activity coefficients in the symmetrical reference system, X_A and X_B are the mole fractions of the extractant and the solvent respectively, ρ_0 is the mole fraction of monomeric molecules in the pure extractant, ρ the mole fraction of the extractant molecules present in solution in the monomeric form, and r the average degree of association of the extractant molecules. Thus it is possible to describe fully the thermodynamic properties of the system, provided that the degree of association of the pure extractant and the law governing its variation with concentration are known. It is usually assumed that the association reactions obey the law of mass action and that the equilibrium constants remain unchanged at all concentrations.

One can assume approximately, in accordance with Mecke's hypothesis [87], which has been proved from the standpoint of statistical thermodynamics [16], that in the standard state the stepwise association constants K_r are independent of the degree of association, i.e.

$$K_2 \simeq K_3 \simeq K_4 \simeq \ldots \simeq K_r = \frac{X_{r+1}}{X_1 \cdot X_r}, \qquad (2)$$

where X_r is the concentration in solution of the association complex containing r monomeric units.

The ideal associated solution model explains the marked positive deviations from Raoult's law which are characteristic of solutions with an associated component (Prigogine and Defay [86], p. 389), but the model itself is very approximate: the solvent in the model is regarded as an inert medium which does not react in any way with the solute and does not affect its association. The concentration association constants are assumed to be independent of concentration and can be determined by studying the pure associated component. In reality the degree of association depends very markedly on the nature of the

solvent, on its dielectric constant, on its capacity to form hydrogen bonds, etc. In particular, association constants cannot remain invariant at high concentrations, since under these conditions there is a marked change in the dielectric constant of the solution and other characteristics of the medium.

Another fundamental defect of the model is the neglect of the difference between the sizes of the species formed in the system. In the case considered the species differ in dimensions by factors of several tens and even hundreds [42,43,53,57,58,67,71,82,88,89]. In such solutions the entropy component of the excess free energy of mixing is of the same order of magnitude as the thermal component, which means that, for a correct interpretation of the experimental data, it is absolutely essential to take into account the influence of the difference between the dimensions of the association complexes and monomeric species, otherwise the calculated average degrees of association will be much too low.

Finally, when the solution is regarded as an ideal associated system, it is impossible to account for its separation into two organic phases [90], which is frequently encountered and is characteristic of systems containing organophosphorus extractants or alkylammonium salts in a hydrocarbon solvent [54,59,67,91].

2. Methods for the Improvement of the Metrics of the Physicochemical Diagram on the Basis of the Lattice Model of the Solution

The study of the thermodynamic properties of high-polymer solutions led to the development of the so called "athermal" model of the solution proposed initially by Fowler in 1937. [92] Subsequently Fowler's ideas were developed by Chang, Miller [93], and particularly Guggenheim [94]. The liquid is regarded as a quasicrystal in the lattice sites of which molecules are located. This approach makes it possible to take into account readily the differences between the dimensions and shapes of the molecules if one assumes that each site can be occupied by either one monomeric species or by one statistical segment of the association complex macromolecule. The lattice is characterised by a statistical average coordination number (subsequently designated by z). The difference between the dimensions of the component molecules is taken into account by the factor R_A—the number of lattice nodes occupies by monomeric molecules of the associated substance. To a first approximation, R_A is determined from the ratio of the molar volumes of the components. Molecular shape is reflected by the quantity q. The product zq characterises the number of contacts between the molecule and its nearest neighbours. By determining z, R_A, and q for any specific system, it is possible to estimate the number of A–A, A–B, and B–B contacts between the component molecules. If long-range forces are now neglected, which is quite admissible for solutions of organic substances in solvents of low polarity, it is possible to relate the enthalpy and entropy of mixing directly to the interaction energies of the molecules, their structure, and chemical nature.

With the aid of the usual methods of statistical mechanics and the lattice model of liquids, it is possible to obtain expressions for the energy and entropy of mixing or for the activity coefficients of the components in solution. Two cases are of special interest: a regular solution, the excess free energy of mixing in which is largely determined by the heat of mixing and the dimensions of the molecules of the components are assumed to be the same, and the opposite type, the so called athermal solution, in which the heat of mixing is negligibly small and the free energy of mixing is determined by the entropy component.

In a regular solution

$$|h^E| \gg T|s^E|, \tag{3}$$

where h^E is the molar heat of mixing and s^E the excess molar entropy of mixing. In the derivation of the fundamental equations it is assumed that the differences in the intermolecular interaction of species of different kinds are fairly small and the distribution of species in the system is random. The concept of the irregular solution was subsequently extended by Hildebrand and Scatchard to mixtures of molecules having different volumes [95] and semiemperical expressions were obtained for the activity coefficients:

$$\begin{aligned} RT\ln f_A &= v_A^0\left(\frac{v_B^0 n_B}{v_A^0 n_A + v_B^0 n_B}\right)^2 \cdot (\delta_A - \delta_B)^2 \quad , \\ RT\ln f_B &= v_B^0\left(\frac{v_A^0 n_A}{v_A^0 n_A + v_B^0 n_B}\right)^2 \cdot (\delta_A - \delta_B)^2 \quad , \end{aligned} \tag{4}$$

where v^0 is the molar volume of the pure component and n_i the number of moles of component i in the system. Eqns. (4) make it possible to calculate the activity coefficients from data for the pure substances, and the regular solution model has been frequently used to describe extraction systems [44,67,96]. However, according to the significance of the assumptions underlying it, the model can describe satisfactorily only a system with intermolecular dispersion interactions and is unsuitable for systems containing species with large dipole moments which are readily polarised or are capable of forming hydrogen bonds. The second fundamental defect of the regular solution model is the by no means complete allowance for the differences between the dimensions of the species. The introduction of molar volumes or of volume fractions as units of concentration corrects only for the differences between the dimensions of the monomeric species of the components, while the formation of polymeric aggregates or molecular chains in solution is disregarded and yet, for a degree of association $r \geq 5$, the contribution of the formation of association complexes to the excess entropy of mixing frequently becomes decisive.

For an athermal solution,

$$T|S^E| \gg |h^E| \tag{5}$$

and all the deviations from the properties of the ideal solution are determined by the difference between the dimensions and shapes of the species. Typical systems of this kind were described by Meyer [97,98]. They all consist of solutions of substances with large molecular weights and chain molecules in a non-polar solvent such as benzene or hexane and are characterised by a negligible heat of mixing and considerable negative deviations from ideality. Since the heat of mixing is small, the activity coefficients of an athermal solution are almost independent of temperature. Miller [93] showed that, in terms of the $z \to \infty$ approximation,

$$\begin{aligned} f_A &= \frac{N_A + N_B}{N_A + R_A N_B} \cdot \exp\frac{(R_A - 1)N_B}{N_A + R_A N_B} \quad , \\ f_B &= \frac{N_A + N_B}{N_A + R_A N_B} \cdot R_A \exp\left[-\frac{(R_A - 1)N_A}{N_A + R_A N_B}\right] \quad , \end{aligned} \tag{6}$$

where N_i is the number of lattice sites occupied by component i.

Eqn. (6) shows that the activity coefficients are smaller than unity. By a slight extension of Eqn. (6) as a result of the introduction of the parameter q, the physical significance of which was defined above, it is possible to take into account directly not only the dimensions but also the shape of the molecules.

In real systems containing an associated extractant in an organic solvent of low polarity, the intermolecular interactions are much more complex than in the limiting cases of regular or athermal solutions discussed above. There are two methods for the description of real associated solutions involving lattice concepts.

Barker [98,99] developed a pure lattice model in which account is taken not only of the van Der Waals forces but also of directional interactions of the hydrogen bond type, which depend on the mutual orientation of the molecules. In Barker's model the different classes of contact regions, corresponding to functional groups are considered, and the interaction energies of all possible combinations of contact regions are specified, the probability of the formation of each contact pair being determined by the condition of the free energy minimum. In other respects the quasichemical method proposed by Guggenheim is employed. The fundamental defect of Barker's model is a lack of theoretical parameters measured by independent methods. The mutual exchange energies employed in the calculations are essentially converted into empirical parameters and their choice as well as the choice of the geometrical characteristic z, q, and R_i is not unambiguous. The mathematical procedure is complex, requiring the use of computers, despite the approximate nature of the physical model itself (neglect of geometrical factors in the calculation of the probability of the formation of different contact pairs, an overestimate of the degree of order in the liquid, the lack of validity of the condition of constant lattice parameters over a wide range of concentrations, etc.).

Certain difficulties of the pure lattice models of solutions can be obviated by considering separately the strong directional interactions, treating them as ordinary chemical association reactions obeying the law of mass action and specifying the law of association, i.e. the dependence of the stepwise association constant K_r on the degree of association r. Weaker non-directional interactions are treated in terms of the lattice approximation, which makes it possible to take into account the influence of the dimensions and shapes of the species.

A version of this model has been proposed [42,89,100] for the description of solutions of highly associated substances—monoalkylphosphoric acids and alkylammonium salts—in a non-polar solvent (benzene, carbon tetrachloride, etc.). In this case the partition function for a binary system can be formulated as follows:

$$Q = G(N_D, N_T)\prod_D \psi_D^{N_D}\exp\left[-\frac{U(N_D, N_T)}{kT}\right], \quad (7)$$

where the subscripts D and T are general symbols defining the kind of all possible species (including association complexes and solvates) in the system, N_D is the number of species of type D, ψ_D the partition function with respect to the internal states of the molecule, $G(N_D, N_T)$ the number of configurations of the system, and $U(N_D, N_T)$ the configuration energy of the system, which depends on the number and class of contacts of all possible species in the system.

$G(N_D, N_T)$ is calculated from the formula

$$\ln G(N_D) = \sum_D \ln\left(\frac{\rho_D}{\sigma_D}\right)^{N_D} - \sum_D \ln N_D! + \frac{\sum_D N_D(r_D-1)}{\sum_D N_D(r_D-q_D)}\ln\left(\sum_D q_D N_D\right)! - \frac{\sum_D N_D(q_D-1)}{\sum_D N_D(r_D-q_D)}\ln\left(\sum_D r_D N_D\right)! \quad , \quad (8)$$

where ρ_D is the number of ways of distributing molecules of type D among r_D sites for a single fixed unit and σ_D is the molecular symmetry factor. A molecule of type D has in the general case surface regions which are not equivalent as regards energy. Suppose that ϵ and ν are general symbols of the class of contact regions on the molecule; the fraction of contact regions on a species of type D in class ϵ is designated by the symbol v_ϵ^D and can be readily calculated in each specific case. The quantity $U_{\epsilon\nu}$ is the energy of the contact formed by regions of classes ϵ and ν on particles of the same (D) or different (D and T) kinds.

It follows from Eqns. (7) and (8) that the chemical potential of species of type D (cyclic structures of association complexes and solvates are absent) is

$$\mu_D = kT\left\{-\ln\frac{\rho_D}{\sigma_D}\psi_D + \ln N_D - \frac{z}{2}q_D\ln\sum_T q_T N_T + r_D\left(\frac{z}{2}-1\right)\ln\sum_T r_T N_T\right\} + \frac{z}{2}q_D\sum_{\varepsilon,\nu} U_{\varepsilon\nu}\cdot(v_\varepsilon^D v_\nu + v_\nu^D v_\varepsilon - v_\varepsilon v_\nu) \quad . \quad (9)$$

For a specific system, account is taken of the association law $K_r = f(r)$, where K_r is the equilibrium constant of the reaction involving the addition of a monomeric unit to an r-mer of the associated component, and of the shape of the association complex (linear, cyclic, bulky, etc. complexes), whereupon it is possible to obtain from Eqn. (9) the relation between the activity coefficient of the solvent and concentration.

Thus, for the simplest case of an athermal associated solution ($K_2 = K_3 = \ldots = K_r$) and linear association complexes, we have

$$f_B = \frac{1}{1+(R_A-1)X_A}\left\{\frac{\frac{2}{z}h(1-X_A)}{(1-h)[1+(R_A-1)X_A]} + \frac{1+\left(\frac{z-2}{z}R_A-1\right)^{-\frac{z}{2}}}{1+(R_A-1)X_A}\right\} \quad (10)$$

where h is the overall effective concentration of all r-mers in solution:

$$h = \frac{[4K_r X_A(1-X_A)+1]^{1/2}-1}{2K_r(1-X_A)} \quad (11)$$

and X_A is the analytical concentration of the solute.

The advantages of this model consist in the direct allowance for the specific interactions and the simplicity of the estimation of the effect of the difference between the dimensions and shapes of the species on the excess thermodynamic functions of mixing. The empirical choice of the interaction constants constitutes the main defect of the model, although, for example, the average degree of association can be estimated also without employing the association constants.

The defects of the lattice approximation have little influence on the final results, since it is used only to introduce corrections to the van der Waals interaction of the association complexes with one another and with the medium.

An interesting method for the description of systems with associated components was proposed by Zagorets and Ochkin [101], who employed certain conclusions of Mayer and McMillan's theory of liquids [102] for the interpretation

of experimental data obtained in a study of the association of alkylammonium salts in benzene and carbon tetrachloride. They obtained a qualitative explanation of the maximum on the curve relating the degree of association to the concentration of the alkylammonium salt and also of the influence of the dimensions of the cation and anion and of temperature on the degree of association.

However, their assessment of the rigor and universality of the proposed method is open to objection. Thus, two expressions obtained by McMillan and Mayer are used as the initial equations:

$$\ln a = \ln \rho - \sum \nu B_{\nu n} \left(\frac{\Delta a}{\gamma}\right)^{\nu-1} C^n \quad , \tag{12}$$

$$P = P_0 + kT\left[C + \frac{\Delta a}{\gamma} - \sum (\gamma + n - 1) B_{\nu n} \left(\frac{\Delta a}{\gamma}\right)^{\nu} C^n \right] \quad , \tag{13}$$

where ρ and C are the volume concentrations of the solvent and solute respectively, P_0 is the vapour pressure of the pure solvent, $B\nu n$ are the virial coefficients characterising the interactions of ν solvent molecules and n solute molecules, $\Delta a = a - a_0$, a_0 being the activity of the pure solvent, and $\gamma = a/\rho$ (here and below the notation used is that in the original report). The authors claim that "Eqns. (12) and (13) are rigorous, i.e. in their derivation no simplifying assumptions were made concerning the structure of the solutions. This constitutes an advantage of McMillan and Mayer's theory over other statistical theories of solutions (for example the lattice theory)". This is only partly true. Very important assumptions are made in Mayer's theory: the potential energy is regarded as the sum of pair interactions; the energy levels are assumed to be continuous, which is inadmissible for strong directional interactions. Apart from these fundamental simplifications of the initial theory, Zagorets and Ochkin introduced a number of further assumptions: in the expression

$$\frac{C^2}{\rho_0 \ln f_a} = \frac{1}{A_2}\left[1 - \frac{A_3}{A_2} C - \left(\frac{A_4}{A_2} - \frac{A_3^2}{A_2^2}\right) C^2 - \ldots\right] \tag{14}$$

they omitted higher terms, which restricts the applicability of subsequent expressions to low concentrations; moreover, a number of simplifying assumptions were made in the numerical calculations of Ochkin and Zagorets.

Comparison of the version of Mayer's theory proposed by Ochkin and Zagorets and the lattice models shows that both approaches constitute a very rough approximation. The simplifications of the lattice models are clearer and their validity is easier to check, while the consequences of certain approximations in the version under consideration are difficult to assess.

The considerable discrepancies between the calculation of the position of the maximum on the $n = f(m)$ curve from the formula proposed by Zagorets and Ochkin [101],

$$m_{\max} \simeq \sqrt{\frac{A_2}{-A_3 \cdot 10^{-3} M_2}} \tag{15}$$

and the experimental data is very instructive.

A similar attempt to apply a virial expansion to the description of solutions of an associated alkylammonium salt in benzene was made by Danesi et al. [62] As above, the authors make a number of simplifications: (1) they replace the second virial coefficient of the binary system (which depends on the concentrations of the components) by the corresponding coefficient for the pure solvent, (2) they neglect the higher terms of the expansion, and (3) they assume the partial molar volume of the mixture to be equal to the partial molar volume of the solvent.

As a result of these simplifications, they consider essentially the model of an ideal associated solution and, what is more, they assume implicitly its infinite dilution. Evidently the calculation of the average degree of association and other properties on the basis of such simplified models cannot yield a picture describing correctly the complex interactions in a real system.

3. Determination of the Degree of Association of Substances by Methods of Physicochemical Analysis

In order to refine the stoichiometry of the reactions, in the study of extraction equilibria many investigators attempted to determine by an independent method the degree of association of the extractant and its complexes with the metal. For these purposes, they employed cryoscopy [25,39,41,42,50–54,80], ebullioscopy [60,82], measurements of the vapour pressure of the solvent [13,19,22–26,30,32,42,61,82], light scattering [57,58,62,71], and viscosity measurements [21,23,54,59,63,65,70]. Data obtained by different methods for the same systems or systems of similar composition reveal very interesting contradictions. The average degree of association determined by cryoscopy, ebullioscopy, and measurements of the vapour pressure of the solvent proved to be appreciably lower than the value calculated from optical measurements and was inconsistent with the appreciably higher viscosities of such solutions compared with the viscosity of the pure solvent. The discrepancies may be very large. Thus, for trialkylammonium (C_7–C_{12}) nitrate solutions in benzene, cryoscopic measurements and measurements of the vapour pressures of the solvent yielded $r = 1.8$–5.0, whereas according to light scattering data [46] $r \simeq 60$. Similarly, for dialkylammonium sulphate solutions in benzene, light scattering data gave $r = 40$–50, which is higher by a power of 10 than the value derived from cryoscopic measurements [57,58,71].

In the determination of the average degree of association of the solute by methods based on the measurement of the activity of the solvent and of r over a wide range of concentrations, $r = \varphi(X)$ curves with a maximum are frequently obtained [47,52], which conflicts with the thermodynamic condition for the stability of the phase from the standpoint of the representation of the solution as an ideal mixture of all possible compounds (Prigogine and Defay [86], p. 404; Storonkin [103], p. 65):

$$\frac{\partial \mu_A}{\partial X_A} > 0 \text{ and } \frac{\partial^2 \mu_A}{\partial X_A^2} > 0 \quad \text{or} \quad \frac{\partial r_A}{\partial X_A} > 0 \text{ and } \frac{\partial^2 r_A}{\partial X_A^2} < 0 \tag{16}$$

Evidently the properties of the above class of solutions cannot be described by the theory of ideal associated solutions.

The reason for all these contradictions can be readily deduced by considering the model concepts used in the derivation of the equations for the activity of the solute. We shall consider in detail the cryoscopic method (ebullioscopy and tensimetry are based on similar postulates).

In the derivation of the computational formula

$$\Delta T = \frac{RT_{0B}}{L_B} \cdot \frac{M_B}{1000} m_A \qquad (17)$$

the following assumptions were made: (a) the components of the solution are completely miscible in the liquid state and do not form solid solutions; (b) the latent heat of fusion of the solvent is independent of temperature; (c) the solution obeys Raoult's law at all the concentrations considered; (d) the solution is very dilute.

All the deviations from properties of the ideal solution are explained by a change in the number of individual species as a result of chemical interactions:

$$r = \frac{m_A}{m_{A,\,eff}}, \qquad (18)$$

i.e. one uses essentially the model of an ideal associated solution, the fundamental disadvantages of which have already been discussed. Refined cryoscopic formulae proposed by Udovenko or Fomin [104] (p. 45) are valid for a wider concentration range but also only for an ideal associated solution.

A method has been proposed [89] for the calculation of the average degree of association of a substance in a monomeric solvent from the activities of the solvent on the basis of the theory of association equilibria in terms of the athermal approximation whereby account can be taken of the dimensions of the association complexes:

$$r = \frac{X_A}{\frac{z}{2}\left\{\left[\frac{1-X_A}{f_B X_B (1-X_A+R_A X_A)}\right]^{z/2} - 1\right\} \cdot [1+(R_A-1)X_A] + R_A X_A}, \qquad (19)$$

and the results of the calculation of the average degree of association in the trioctylammonium mononitrate–benzene system by Eqns. (17), (18), and (19) have been compared. Table 1 shows that neglect of the negative deviations from Raoult's law due to the formation in the solution of large association complexes reduces r by a power of ten. Calculations by Eqn. (19) agree satisfactorily with light scattering data [46, 57, 58, 71].

Table 1. Average degree of association of trioctylammonium nitrate in benzene according to cryoscopic data [105].

X_A	r_A (17, 18)	r_A (19) with $\begin{cases} R_A=5 \\ z=6 \end{cases}$
0.0090	2.1	2.0
0.021	3.1	5.9
0.041	3.3	32
0.068	2.6	50
0.094	2.1	>50

Similar results were obtained for the mono-n-octylphosphoric acid (MOPA)–carbon tetrachloride system from isopiestic measurements of the vapour pressure [42] (Table 2).

It follows from Tables 1 and 2 that the degree of association of the extractant is frequently found to be too low owing to an incorrect interpretation of the data. This factor must be borne in mind in considering the reactions involved in extraction by highly associated extractants.

IV. EXTRACTION OF SUBSTANCES BY HIGHLY ASSOCIATED EXTRACTANTS

1. Experimental Concentration Variation of the Partition Coefficients of Metals

We shall consider monoalkyl or monoaryl phosphoric acid esters as examples of typical highly associated extractants. The characteristic form of the variation of the partition coefficients of metals between the aqueous and organic phases $\alpha = M_{org}/M_{aq}$ and the extractant concentration in the organic phase S is striking; $\lg \alpha$ varies linearly with $\lg S$ over a wide range of compositions of both aqueous and organic phases [43, 100]:

(a) a unit slope of the concentration curve is observed for cations with different structures of the outer electron shell and in particular with different electrovalences (UO_2^{2+}, Am^{3+}, Np^{4+});

(b) the unit slope persists when the concentration of the inorganic acid in the aqueous phase, the supporting salt, and hence the degree of hydration of the cations are varied;

(c) the variation of the extractant concentration in the organic phase within wide limits (from 0.001 to 1.0 M) does not alter the slope of the concentration curve;

(d) the structure of the hydrocarbon group in the alkylphosphate molecule and the nature of the low-polarity solvent do not influence the slope of the concentration curve.

Table 2. Average degree of association of mono-n-octylphosphoric acid in carbon tetrachloride [42].

X_A	r_A (17, 18)	r_A (19) with $\begin{cases} R_A=1.3 \\ z=6 \end{cases}$
0.108	4.9	8.2
0.151	5.1	17.4
0.395	4.3	18.4
0.471	4.4	21
0.648	3.7	30
0.790	3.0	42

The slope changes only when the condition of a high degree of association of the extractant breaks down and also when solvents causing dissociation into monomers are employed, for example alcohols, or when the concentration of the metal extracted is raised above a certain limit [106]. Concentration curves have been obtained [36] for the extraction of trace amounts of europium and americium by MOPA solutions in various solvents (benzene, carbon tetrachloride, chloroform, n-hexane, and butyl chloride) and it was found that not only is the slope of the concentration curve the same in all cases but the numerical partition coefficients are very close at the same extractant concentrations [36]. This supports the hypothesis of a high degree of order in the distribution of the MOPA chain molecules in its association complexes. The $OPO(OH)_2$ polar groups are probably directed inwards and are surrounded by a stable hydration shell, while the organic groups are directed to the outside of the micelles. During extraction, cations pass from the aqueous phase to the hydration shell linked to the $OPO(OH)_2$ groups. The proposed structure provides a qualitative explanation of the independence of the partition coefficients of the nature of the low-polarity solvent and of the very high water

content in organic MOPA solutions. It has been found[42] that in 1 M MOPA solution in carbon tetrachloride up to 27 moles of water per litre dissolved on saturation, with a sharp increase of viscosity and degree of association (Table 3).

Table 3. Relative water content M_{H_2O}/M_{MOPA} in organic MOPA solutions in equilibrium with 2 M aqueous HNO_3 at 20°C.

Solvent	MOPA mole fraction in organic phase					
	0.0025	0.005	0.01	0.02	0.04	0.08
1-Hexanol	1.4	1.7	2.1	2.1	2.1	2.1
n-Butyl chloride	3.7	4.2	4.5	4.6	4.7	5.1
n-Hexane	7.5	12	13	14	15	16

2. Common Methods for the Interpretation of Experimental Relations

The partition of a substance between two immiscible phases has been used for a long time as one of the methods for the determination of the composition of the complex extracted[51,107-110]. The formation of a single compound in the organic phase is usually considered:

$$M_{(aq.)} + \tau S_{(org.)} \rightleftarrows (MS_\tau)_{(org.)} . \qquad (20)$$

The following relation is valid for this reaction:

$$\alpha = K\frac{(f_S S)^\tau f_M}{f_{MS\tau}}, \qquad (21)$$

where α is the partition coefficient of the substance extracted, K the thermodynamic equilibrium constant, S the concentration of the extractant, and f_S, f_M, and $f_{MS\tau}$ are the activity coefficients. It is assumed that at moderate concentrations the activity coefficients of the uncharged species are close to unity and τ, the number of extractant species involved in the reaction, is determined from the slope of the straight line represented by the equation

$$\lg \alpha = \lg K + \tau \lg S . \qquad (22)$$

The activity of the extractant is either found independently by the usual methods[111-113] or the activity coefficients are assumed to be constant. The method described can of course yield satisfactory results only when the properties of the organic phase differ little from those of an ideal solution. Real extraction systems contain as a rule polar extractants which interact strongly with one another and with the solvent. It can be shown[104] that the association of the extractant or its solvation by the solvent reduce the slope of the curve defined by Eqn. (22) and in the general case the slope becomes a complex function of the extractant concentration and the ratio of the association and solvation constants.

In most studies of the extraction of metal ions by highly associated extractants[105,114-116] the hypothesis that the organic phase in the given concentration range contains only one association complex is employed. Its degree of association is determined independently or simply selected in order to account for the experimental relations. Thus the mechanism

$$M^{l+}_{(aq.)} + \frac{2l}{r}(H_2A)_{r(org.)} \rightleftarrows M[H(HA)_2]_{l(org.)} + l\,H^+_{(aq.)} \qquad (23)$$

was proposed in numerous studies by Peppard and coworkers[25-29,31,33,34,38,40] to account for the characteristics of the extraction of a number of lanthanides and actinides by phosphoric acid monoesters. It explains the extraction of lanthanides with $l = 3$ and of actinides with $l = 4$. The slope of the $\lg \alpha = \varphi(\lg S)$ concentration curve, which is unity, seemingly agreed with the average degree of association of the extractant $r = 6-8$ found by cryoscopic measurements in solutions of mono-2-ethylhexylphosphoric acid (M2EHPA) in dry benzene. However, this mechanism does not explain why the slope is also unity in the extraction of UO_2^{2+},[117] which leads to $l = 4$. Moreover, it has been shown[42] that the degree of association of phosphoric acid monoesters in a non-polar solvent in the presence of water is much higher than 6-8 and changes with the concentration of the extractant. The same authors regard the formation of "infinite" polymers in the organic phase,

$$M^{l+}_{(aq.)} + (H_2A)_{r(org.)} \rightleftarrows M(H_{2r-l}A_r)_{(org.)} + l\,H^+_{(aq.)} \qquad (24)$$

as an alternative mechanism. Although the authors note correctly that in this case the slope of the concentration curve will be unity when $r \to \infty$ if only one cation of the metal extracted is linked to each association complex species regardless of the valence of the cation, they unfortunately did not carry out a quantitative analysis of the proposed mechanism. This led to the incorrect conclusion that the slope of the concentration curve depends on the average degree of association of the extractant which may vary with the concentration of the extractant, temperature, and certain other factors. Another possible explanation of the variable slope of the concentration curves is based on the hypothesis of the presence of several extractable complexes with different component ratios; however, here too there are difficulties when an attempt is made to explain why the slope of the curve decreases with increase of the concentration of the extractant[118].

3. Allowance for the Multiplicity of Interactions in the Organic Phase

In considering the mechanism of extraction by highly associated extractants, one or two, more rarely three, fixed values of r are usually taken into account for the description of the state of the extractants in the organic phase in order to simplify the calculations. The constants for equilibria of the monomer–dimer–polymer type are fitted to give the best agreement with experiment. The approximate nature of the model is evident.

A scheme of interactions taking into account the formation in the organic phase of all possible association complexes of the extractant has been proposed[42,43,119]. When trace amounts of the metal extracted are employed, the overall molar concentration of the extractant is

$$S = \sum_r r[A_r] . \qquad (25)$$

If we introduce the equilibrium constant β for the addition of the cation to a specified reaction centre in the association complex and the statistical factor W_r taking into

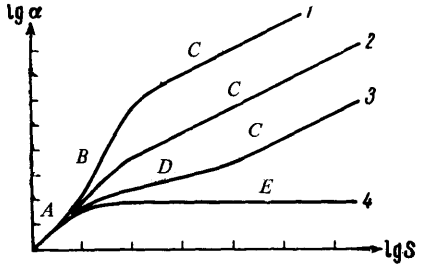
account the number of possible locations of the cation M among the reaction centres of the r-mer, it is easy to obtain the following expression for the partition coefficients:

$$\alpha = \beta f_M \sum_r W_r [A_r] \frac{f_r}{f_{A_r M}}, \quad (26)$$

where $[A_r]$ is the molar concentration of the r-mer and f_M, f_r and $f_{A_r M}$ are the activity coefficients of the M species, the association complex $[A_r]$, and the complex $[A_r M]$. It has been shown[43] that, in terms of the quasi-chemical approximation[94], for a system comprising a solvent and a mixture of r-mers with non-zero mutual exchange energies, $f_r/f_{A_r M} \simeq 1$ provided that $r \geqslant 10$ and $S \leqslant 1$. Moreover, for low concentrations $M_{(org.)}$ the formation of complexes containing several M atoms per association complex $[A_r]$ maybe disregarded. As a result, the following simple expression is obtained for the concentration curve:

$$\alpha = \beta \frac{f_M}{\nu} S, \quad (27)$$

where ν is the number of monomeric units of the association complex $[A_r]$ forming one reaction centre. Eqn. (27) is valid, provided that the condition $S/r \gg M_{(org.)}$ holds, and makes it possible to describe quantitatively the extraction of microconcentrations of metal ions by a highly associated extractant. The limits of the applicability of the ratio $f_M/f_{A_r M} \simeq 1$ depend on the parameters of the specific system; the method of their calculation has been described[119]. When the condition $S/r \gg M_{(org.)}$ breaks down, the relation $\alpha = \varphi(S)$ becomes more complicated and the partition coefficient becomes a function not only of S but also of $M_{(aq.)}$ and, as shown by the same authors[43], analysis of the concentration curve in this case does not lead to determination of the stoichiometry of the reaction.



General form of $\lg \alpha = \varphi(\lg S)$ concentration curves for different values of the parameter b: 1) $b > 1$; 2) $b = 1$; 3) $b < 1$; 4) $b = 0$ ($\partial \lg \alpha / \partial \lg S = \nu$ in region A, $\partial \lg \alpha / \partial \lg S > \nu$ in region B, $\partial \lg \alpha / \partial \lg S = 1$ in region C, $\partial \lg \alpha / \partial \lg S < \nu$ in region D, and $\partial \lg \alpha / \partial \lg S = 0$ in region E).

When the factors influencing the shape of the concentration curves are considered, the problem arises of the influence of the metal ions incorporated into the association complex of the extractant on the bond strength between the monomeric units of the complex[35]. In the general case one can foresee three possibilities: (a) the nature of the bonds in the association complex does not change and the addition of new monomeric units to the complex $[A_r M_i]$ proceeds in accordance with the same law as the addition to the complex without the metal $[A_r]$—the case considered above; (b) the monomeric units in the coordination spheres closest to the metal decrease the strength of bonds with other monomeric units; (c) the bond strength in the association complex increases under the influence of the metal. These effects can be taken into account quantitatively by introducing the bond stabilisation parameter $b = K_i/K_r$, i.e. the ratio of the constants for the addition of a monomeric unit A_1 to the association complex $[A_r]$. As before, the constant K_r is assumed to be independent of the degree of association r. If the bond perturbation zone is assumed equivalent to three coordination spheres closest to the metal atom within which the monomer addition constant $K_i \neq K_r$, the following expression is obtained for the partition coefficient:

$$\alpha = K_{M\nu} f_M \left\{ [A_1]^\nu + \frac{1}{\nu (bK_r)^2} \sum_{j=\nu+1}^{3\nu} j (bK_r)^j [A_1]^j + \frac{b^{2\nu}}{\nu K_r^\nu} \sum_{n=3\nu+1}^{\infty} n [A_1]^n K_r^n \right\}, \quad (28)$$

and

$$S = \sum_{r=1}^{\infty} r [A_r] = \sum_{r=1}^{\infty} r [A_1]^r K_r^{r-1} = \frac{[A_1]}{(1 - K_r [A_1])^2}, \quad (29)$$

where $K_{M\nu}$ is the formation constant of the complex $[MA_\nu]$, $[A_1]$ is the concentration of the monomeric extractant molecules in the organic phase, and j and n are summation indexes; the other symbols have the same significance as before.

The concentration curves calculated for different parameters S, K_r, and b are illustrated in the Figure, which shows that, when the degree of association of the extractant is high, the slope of the concentration curve approaches unity for $b > 0$ owing to the high values of K_r or S. When $b = 0$, the association complex is disrupted by the inserted species and α is independent of S over a wide extractant concentration range. A slope equal to the coefficient ν (the number of monomeric units of the association complex forming a single reaction centre) is obtained only at low concentrations where the degree of association of the extractant is still low. If the bonds in the association complex are appreciably strengthened by the inserted species ($b \gg 1$), the concentration curve shows sections where the slope is higher than ν. It follows from the foregoing that analysis of the shapes of the concentration curves requires a detailed examination of all possible types of chemical interaction in the system over a fairly wide range of concentrations and independent measurements of the degree of association of the extractant and of its solvation by the solvent are necessary.

V. DISTRIBUTION OF ACIDS AND SALTS IN SYSTEMS WITH MODERATELY ASSOCIATED EXTRACTANTS (ARYLAMMONIUM AND ALKYLAMMONIUM SALTS)

1. Certain Contradictions in the Interpretation of Experimental Relations

The considerable success of the methods for the determination of the composition and stability of solvates in extraction systems with neutral organophosphorus and other non-associated extractants left a deep impression on the methods for the interpretation of experimental data obtained with associated extractants. The traditional representation of extraction data in terms of the relation $\lg \alpha = \varphi(\lg S)$, in which the slope is identified with the

solvation number, is transferred without any changes to extraction systems with extractants associated in non-polar solvents such as alkylammonium salts, aryl- and alkyl-phosphoric acids, etc.

It is most surprising that simple linear relations are then obtained. Moreover, the equilibrium distribution of, for example, nitric acid in the extraction system with a trialkylammonium nitrate, may be described [52,120-122,123] by the simple reaction

$$B \cdot HNO_{3(org.)} + H^+_{(aq.)} + NO^-_{3(aq.)} \rightleftarrows B \cdot 2HNO_{3(org.)} \quad (30)$$

(here B = trialkylamine), i.e. seemingly there is no association of the trialkylammonium salt at all. According to the law of mass action, we have for reaction (30)

$$\alpha = K \cdot [B][H^+][NO_3^-] \cdot \frac{f_{\pm}^2 \cdot f_{B \cdot HNO_3}}{f_{B \cdot 2HNO_3}} . \quad (31)$$

However, the condition of a constant f_i usually adopted conflicts with numerous studies on the state of alkylammonium salts in solvents of low polarity. Fairly high association in such systems has been reliably established by cryoscopic [51,53,56] and conductimetric methods [64,65], by dielectric constant measurements [72-74], by light scattering [57,58,71], by viscometric measurements [54,65,70], etc. (particularly if account is taken of the correction for the effect of the difference between the dimensions of the solvent and extractant species on values found by cryoscopic and similar methods). The greater complexity of the equilibria in the extraction of hydrogen halides from aqueous solutions in the form of trialkylammonium salts compared with the simplest reaction

$$B_{(org.)} + H^+_{(aq.)} + X^-_{(aq.)} \rightleftarrows BH \cdot X_{(org.)}, \quad (32)$$

is indicated by the deviation of the $[BHX]_{(org.)} = \varphi\{[B]a_{HX(aq.)}\}$ relation from linearity at fairly low concentrations $[BH.X]_{(org.)} \simeq 0.001$ M, when there is no reason to postulate appreciable changes in f_B and $f_{BH.X}$ due to causes other than association [60,61]. Finally, when no account is taken of the association of the alkylammonium salt, it is difficult to explain the comparatively low capacity of the extractant [124], which deviates appreciably from the capacity expected on the basis of the stoichiometry of reactions (32) and (30).

2. Allowance for the Association of Extractants by a Simplified Procedure

Fomin and Potapova attempted to resolve the contradiction between the results of a cryoscopic study of the trioctylamine–nitric acid–water system and the invariance of the equilibrium constant calculated for reaction (30) without taking into account the association of the extractant. They assume [52] that the reaction equation can be written in the following general form:

$$\frac{y}{x}(BH \cdot NO_3)_{x(org.)} + y\,H^+_{(aq.)} + y\,NO^-_{3(aq.)} \rightleftarrows [B \cdot 2HNO_3]_{y(org.)} \quad (33)$$

and that the equilibrium constant can be expressed thus:

$$K'' = K' \cdot \frac{x^{y/x}}{y} \cdot \frac{1}{[HNO_3]^{2y-2}_{(aq.)} \; [BH \cdot NO_3]^{y/x-1}_{x(org.)}} , \quad (34)$$

where K' is the equilibrium constant for reaction (30). Next it is assumed that, with increase of the concentration of acid in the aqueous phase, the term $[HNO_3]^{2y-2}_{(aq.)}$ will increase and the term $[BH.NO_3]^{y/x-1}_{x}$ will decrease when $x < y$ which leads to the virtually constant value of K' observed experimentally. The main defect of this purely qualitative treatment is that there are no serious grounds for the assumption that the coefficients x and y are constant. They must evidently change with the concentrations of the acid and the amine. In this case too K' and K'' will also be functions of the concentration of the reactants.

Shmidt and coworkers [125] proposed an explanation based on Vanselow's hypothesis [126] according to which the activities of individual groups of the association complex are equal to their fractions relative to all the functional groups of the complex but in the formulation of the fundamental equations account must be taken of the activity coefficients of the association complexes themselves, which was not done by the authors. The conclusion that the degree of association of the alkylammonium salt remains unchanged when it adds to metal salts is also open to objection [69]. This conflicts with statistical considerations, particularly for a high coordination number of the complex-forming agent; Shmidt and coworkers determined the average degree of association of the extractant r by a cryoscopic method, which yielded somewhat low results [89] and, moreover, they failed to examine in detail the important problem of the multiplicity of equilibria, although they do note the constancy of the slope of the concentration curve when the average value of r varies.

Scibona's study [48] is interesting in this respect. The author considers the distribution of a singly-charged anion Y^- or a singly-charged complex anion MX^-_{n+1} between the solution of an electrolyte CX and an organic solution of the corresponding alkylammonium salt RX. The proposed reaction mechanism,

$$\sum_{1}^{I}[RX]_{i(org.)} + t[Y^-]_{(aq.)} \rightleftarrows \sum_{1}^{I}[RY]_{j(aq.)} + \sum_{1}^{A}\sum_{1}^{B}[(RX)_a(RY)_b] + t[X^-]_{(aq.)} \quad (35)$$

takes into account the association of the extractant of the complex extracted. The following equilibria are taken into consideration:

$$[RX]_{(org.)} + [Y^-]_{(aq.)} \rightleftarrows [RY]_{(org.)} + [X^-]_{(aq.)}, \quad K_{(1,X,Y)}, \quad (36)$$

$$i[RX]_{(org.)} \rightleftarrows [RX]_{i(org.)}, \quad K(i, X), \quad (37)$$

$$j[RY]_{(org.)} \rightleftarrows [RY]_{j(org.)}, \quad K(j, Y), \quad (38)$$

$$a[RX]_{(org.)} + b[RY]_{(org.)} \rightleftarrows [(RX)_a(RY)_b]_{(org.)} \quad K(a, b) . \quad (39)$$

An expression was obtained relating the partition coefficient of the anion Y^- to the concentration of the extractant. The authors extrapolated the partition coefficient (using certain auxiliary functions and not the partition coefficients themselves, which does not alter the essential feature of the procedure) to zero extractant concentration and found the constant $K_{(1,X,Y)}$, the deviations from the linear relation $\lg\alpha = \varphi\{\lg[RX]\}$ being regarded as a consequence of association in the organic phase. Although the authors interpret the experimental relations [48,68] in terms of the formation of only one complex, their equations are valid also when the solution contains a multiplicity of complexes of different compositions. Since an ideal associated solution is assumed and the activity coefficients in the organic phase are set equal to unity, the model cannot be valid over a wide range of concentrations and remains essentially semiempirical.

A similar approach has been developed by Högfeldt and Fredlund [66,127]. In their investigations the set of reactions of the associated alkylammonium salts with the complex metal-containing anion, leading to the formation of a continuous series of extractable complexes having structures of different complexity, was treated in terms of the ideal associated solution approximation. The composition of one or several complexes is chosen on the basis of the results of a two-phase potentiometric titration

whereby one can describe satisfactorily the form of the experimental relations. It has been shown [16] that this approach leads to the "discovery" of non-existent complexes or to the assumption that certain complexes are absent, whereas in reality they are formed.

3. Successive Allowance for the Association of Extractants and Extraction Complexes in the Description of Extraction by Amines

In another attempt to account for the known experimental relations governing the extraction of acids and metal ions by alkylammonium salts, taking into account the association in the organic phase, was made by Komarov and Komarov [55]. Account was taken of all interactions of the type

$$B_{r(org.)} + i\,[HA]_{(aq.)} \rightleftarrows B_r(HA)_{i(org.)}, \quad K_{ri}\ , \tag{40}$$

where B_r is an r-mer of the initial alkylammonium salt, HA a monobasic acid, and K_{ri} the thermodynamic equilibrium constant of reaction (40). If each association complex B_r has r energetically equivalent active centres capable of combining with a molecule of the acid HA, the following relation is valid:

$$K_{ri} = \beta^i W_{ri}\ , \tag{41}$$

where β is the equilibrium constant for the addition of the HA molecule to the specified reaction centre and W_{ri} is the statistical factor. It is now possible to find the concentration of each solvate with the aid of the law of mass action:

$$[B_r(HA)_i] = (\beta a)^i W_{ri}\,[B_r] \cdot \frac{f_r}{f_{ri}}\ , \tag{42}$$

where a is the activity of HA in the aqueous phase and f_r and f_{ri} are the activity coefficients of B_r and $B_r[AH]_i$. Bearing in mind that

$$W_{ri} = \frac{r!}{\sigma_r\,(r-i)!\,i!}\ , \tag{43}$$

where σ_r is the symmetry coefficient, it is easy to find the acid concentration C_H and the concentration of the alkylammonium salt C_B in the organic phase:

$$C_H = [HA] + \sum_{i=1}^{r}\sum_{r=1}^{R} (\beta a)^i [B_r] \cdot \frac{f_r}{f_{ri}} \cdot \frac{r!}{G_r\,(r-i)!\,(i-1)!}\ , \tag{44}$$

$$C_B = \sum_{r=1}^{R} r\,[B_r] + \sum_{i=1}^{r}\sum_{r=1}^{R} (\beta a)^i [B_r] \cdot \frac{f_r}{f_{ri}} \cdot \frac{r!\,r}{\sigma_r (r-i)\,i!}\ . \tag{45}$$

In contrast to the studies enumerated above, in this model the organic phase is not regarded as an ideal associated solution. With the aid of the theory of association equilibria, the value of the following function was found by the present authors:

$$\ln\frac{f_r}{f_{ri}} = iR_B\frac{2-z}{2}\left\{\ln\frac{q_s\sum_D r_D C_D}{r_s\sum_D q_D C_D} + \frac{2}{kT}\left[\omega_{as}\left(v_a^2 + v_n v_a - v_a\right) + \omega_{ns}\left(v_n^2 + v_n v_a - 2v_n - v_a\right) - \omega_{an}\left(v_n v_a - v_a\right)\right]\right\} = i\psi(C_H, C_B)\ , \tag{46}$$

where R_B is the number of quasilattice sites occupied by a single molecule of E, z the coordination number of the quasilattice, D a general symbol for a species (solvent molecule, association complex, solvate, etc.), qz the number of nearest neighbours of the species D, C_D the molar concentration of species of type D in the mixture, r_D the number of sites occupied by the corresponding species, a, n, and s are the classes of contact regions (alkyl groups, acid anions, and solvent molecules), v_i is the fraction of contact regions of class i in solution, and ω_{ij} the Guggenheim mutual exchange energy. A numerical estimate of the quantity $\psi(C_H, C_B)$ is possible for specific systems. After carrying out the summation in Eqns. (44) and (45), the following formula is obtained:

$$\beta = \frac{C_H}{(C_B - C_H)\,a}\,e^{-\psi}. \tag{47}$$

Bearing in mind that the multiplier $e^{-\psi}$ is close to unity for low values of C_H, [119] Eqn. (45) can be formally regarded as an expression of the law of mass action for reaction (32), since C_H may be interpreted as the equilibrium concentration of the extractant [B] and $C_B - C_H$ as the equilibrium concentration of the non-polymerised alkyl ammonium salt. It is clear from the above that reaction (30) in no way reflects the entire complexity of the interactions in the system, although simple equations of type (47) are in fact satisfactorily consistent with experimental data.

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The review has demonstrated the exceptional complexity of extraction systems with associated extractants. The authors attempted to emphasise the conflicting nature of the data obtained by different methods for the same systems and to show that this is largely due to the approximate nature of the models of the solution used as a basis for a quantitative interpretation of the results of measurements of macroscopic quantities from the standpoint of the interaction between molecules. In general, one must say that a rigorous interpretation of colligative properties of systems from the standpoint of the determination of the composition and stability of complicated molecular complexes requires also the application of a rigorous theory of the liquid state. However, the only versions of solution theory at present available which meet to the required degree of sophistication are model molecular-statistical theories. Since more rigorous versions of the theory have not been developed at all and have not been used to describe the properties of associated solutions (let alone extraction systems) and in view of their personal preference, the authors attempted to demonstrate that the application of the generalised theory of association equilibria [100] would be definitely useful for the understanding of the characteristics of extraction systems with associated extractants. This standpoint can be readily understood bearing in mind that the models of solutions employed earlier [ideal solution, regular solution (Hilderand model), athermal solution, ideal associated solution, athermal associated solution] are readily described by the fundamental equations of the generalised theory of association equilibria subject to fairly approximate special assumptions concerning the properties of the species in the system.

For example, the general expression for the chemical potential defined by Eqn. (9) has the following properties:

(1) in the absence of specific linkages ($N_i = \sum_{D(i)} N_{D(i)}$, $D(i) \equiv i$, $N_0^i = N_i$) with $r_D = 1$ and $u_{\epsilon\nu} = \frac{1}{2}(u_{\epsilon\epsilon} + u_{\nu\nu})$, the expression describes the chemical potential of the component in an ideal solution;

(2) in the absence of specific linkages with $r_D = 1$ and $u_{\epsilon\nu} \neq \frac{1}{2}(u_{\epsilon\epsilon} + u_{\nu\nu})$, the expression can be readily shown to be equivalent to μ_D in a regular solution;

(3) in the absence of specific linkages with $r_D \neq 1$ and $u_{\epsilon\nu} = \frac{1}{2}(u_{\epsilon\epsilon} + u_{\nu\nu})$, the expression represents the value for an athermal solution;

(4) in the presence of specific linkages with $r_D = 1$ and $u_{\epsilon\nu} = \frac{1}{2}(u_{\epsilon\epsilon} + u_{\nu\nu})$, the expression descibes an ideal associated solution;

(5) in the presence of specific linkages with $r_D > 1$ and $u_{\epsilon\nu} = \frac{1}{2}(u_{\epsilon\epsilon} + u_{\nu\nu})$, the expression corresponds to an athermal associated solution;

(6) in the presence of specific linkages with $r_D > 1$ and $u_{\epsilon\nu} \neq \frac{1}{2}(u_{\epsilon\epsilon} + u_{\nu\nu})$, the expression corresponds to the non-athermal associated solution model.

The study of extraction systems with associated extractants is being rapidly expanded and their practical importance is growing. In this field many surprises and difficulties await the investigator, the overcoming of which may involve a wide-scale employment of modern advances of the statistical theory of solution and an extension of the range of research techniques employed (dielectric constant measurements, Rayleigh light scattering, resonance spectroscopy, diffusion, the dynamo-optical method, measurement of ultrasonic velocities, etc.).

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Effective Size in Quantum-mechanical Systems

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The review presents the results of a number of studies where various integral characteristics of the effective dimensions of quantum-mechanical systems have been derived and justified by interpreting the square of the modulus of the wave function using probability theory. The concepts of the types of electron delocalisation in atoms and molecules and quantities which can serve at its measure as well as hypotheses concerning the integral characteristics of the charge distribution between the effective volume of an atomic-molecular system and the surrounding space are discussed.
The above characteristics have been calculated for a number of specific quantum-mechanical systems, in particular for some of the simplest atoms and molecules.
The bibliography includes 34 references.

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I. INTRODUCTION

This paper presents the result of a number of studies in which various integral characteristics of the effective dimensions of quantum-mechanical systems were derived and their validity was proved. These concepts are related primarily to hypotheses concerning the types and quantities used as measures of electron delocalisation in atoms and molecules and integral characteristics of charge distribution between the effective volume of an atomic-molecular system and the surrounding space.

One of the significant changes introduced by quantum mechanics into the description of an atomic-molecular system was the elimination of the classical concept of an atom or molecule having a specific volume. The square of the modulus of a normalised wave function of an n-particle system is interpreted as the probability density of a $3n$-dimensional continuous random quantity. The electrons of atoms and molecules can be located with a finite non-zero probability in any volume element in a three-dimensiona. pace. For this reason, the pre-quantum-mechanical concept of a definite volume is no longer applicable to an atom or molecule.

Nevertheless the concept of quantities characterising the "effective" dimensions or "effective" volumes of quantum-mechanical systems retains its physical significance and usefulness. As a rule, the methods adopted for the determination of quantities of this kind are related to specific methods for the experimental investigation of the structure of matter.

At the same time it is also possible to justify theoretically the concept of the effective dimensions of an atomic-molecular system. The definition of such concepts uses the generally accepted interpretation of the square of the modulus of the wave function on the basis of probability theory as the probability density of the configuration of the system. In order to characterise completely the distribution, it is generally speaking necessary to know the entire infinite series of its moments. The definition of the concept of the effective dimensions of an atomic-molecular system employs only some of the integral characteristics of the distributions. We shall consider briefly the most important of these characteristics.

Suppose that the state of an n-electron system is described by a normalised function $\psi(\mathbf{x})$, where $\mathbf{x} = (\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_n)$ denotes a set of cartesian coordinates of n electrons and $\mathbf{x}_i = (x_{i1}, x_{i2}, x_{i3})$ denotes the coordinates of the ith particle. We put

$$\rho(\mathbf{x}) = |\psi(\mathbf{x})|^2$$

$\rho(\mathbf{x})$ can then be treated as the density of the distribution of a $3n$-dimensional random vector $\mathbf{X} = (\mathbf{X}_1, \mathbf{X}_2, \ldots, \mathbf{X}_n)$. whose components $\mathbf{X}_i = (X_{i1}, X_{i2}, X_{i3})$ are three-dimensional random quantities with the distribution densities

$$\rho_i(\mathbf{x}_i) = \int \rho(\mathbf{x})\, d\mathbf{x}_1 \ldots d\mathbf{x}_{i-1}\, d\mathbf{x}_{i+1} \ldots d\mathbf{x}_n.$$

Each of the densities $\rho_i(\mathbf{x}_i)$ describes the distribution of the coordinates of the individual ith particle with all other particles in their average positions. We shall denote by $K(\mathbf{X})$ the covariance matrix of the n-particle system:

$$K(\mathbf{X}) = \begin{pmatrix} \mathcal{K}_{11}\mathcal{K}_{12} \ldots \mathcal{K}_{1n} \\ \mathcal{K}_{21}\mathcal{K}_{22} \ldots \mathcal{K}_{2n} \\ \ldots\ldots\ldots \\ \mathcal{K}_{n1}\mathcal{K}_{n2} \ldots \mathcal{K}_{nn} \end{pmatrix},$$

where $\mathbf{K}_{ij}$ is the covariance matrix of the ith and jth particles (see Section III, 5).

The quantity $D(\mathbf{X}) = \det K(\mathbf{X})$ is termed the general variance of the n-electron system. In model problems where the theoretical probability characteristics of a one-dimensional particle are investigated, this quantity is

identical with the variance of a one-dimensional distribution generated by the corresponding wave function. The quantity

$$H(\mathbf{X}) = -\int \rho(\mathbf{x}) \ln \rho(\mathbf{x})\, d\mathbf{x}$$

is termed the entropy of the quantum-mechanical distribution with a density $\rho(\mathbf{x})$ for an n-particle system†. We put $v = \exp H$ and $V = \sqrt{(2\pi e)^{3n} D}$. These quantities are termed respectively the internal and external effective volumes of the n-particle system.

The entropy and external and internal volumes for the distribution of the ith particle or a subsystem of particles with all other particles in their average positions can be defined similarly.

The introduction of general variances makes it possible to extend the concept of the correlation coefficient (describing the relation between two one-dimensional random quantities) to cases where the correlation of particles (i.e. of multidimensional random quantities) is investigated. Namely, if $D(\mathbf{X}_i)$ is the general variance of the ith particle and $D(\mathbf{X}_i, \mathbf{X}_j)$ the general variance of a system of two particles (the ith and jth particles) in an n-particle system, the general correlation coefficient $r(\mathbf{X}_i, \mathbf{X}_j)$ (or the correlation coefficient of two particles) is given by the formula (see Section III, 5)

$$r(\mathbf{X}_i, \mathbf{X}_j) = \sqrt{1 - D(\mathbf{X}_i, \mathbf{X}_j)/D(\mathbf{X}_i)\, D(\mathbf{X}_j)}.$$

Like the usual correlation coefficient, the above coefficient represents a measure of linear correlation. Similarly, the internal correlation coefficient $r_i(\mathbf{X}_i, \mathbf{X}_j)$, introduced in Section III, 6 and defined in terms of the internal volume, also takes into account non-linear correlation.

The entropy and variance reflect, generally speaking, different features of the distribution, significantly supplementing one another. The usefulness of the entropy of a quantum-mechanical distribution together with the variance for the characterisation of the effective size is confirmed by the close relation between this quantity and Heisenberg's uncertainty principle. This principle, together with its variance expression, also permits a formulation in terms of the entropy of distributions. The entropy expression, which is logically stronger and physically more significant, makes it possible to exclude the occurrence of certain situations which are not ruled out by the variance formulation (see Section III, 8).

The formulation of the uncertainty principle is not restricted to a pair of canonically coupled one-dimensional particles such, as, for example, the components of the vector-coordinate $\mathbf{r}_i$ and the corresponding components of the momentum-vector $\mathbf{p}_i$. The uncertainty in the position of a particle or a system of particles can be described not only by one-dimensional characteristics (variances along the coordinate axes), but also by the available volume characteristics such as the covariance matrix, the general variances, and the internal and external volumes. As shown in Section III, 8, the uncertainty principle can be expressed also in terms of all the above volume characteristics. This formulation of the uncertainty principle is stronger than the corresponding one-dimensional formulations.

The calculations of the effective volumes for the simplest atoms and molecules show that these quantities are fairly close to the values found from experimental studies on the viscosities of gases and vapours, which also demonstrates the usefulness of the theoretical definitions of the effective volumes of quantum-mechanical systems.

The variance of the distribution has been used for a long time in quantum mechanics to characterise the uncertainty of the position of the particles. However, the usefulness of the concept of entropy in quantum mechanics was considered for the first time in 1960 by Segal[1]. Hirschman[2] showed that Heisenberg's uncertainty principle can be formulated in terms of the entropies of quantum-mechanical distributions in the coordinate and momentum representations.

Bochvar, Gambaryan, Stankevich, and Chistyakov[3-5] used the concept of the entropy of the distribution to characterise the measures of the delocalisation of electrons and the effective size in atomic-molecular systems.

In a study of studies by Rubanov, Stepanov, and Sedoi[6-9] certain general properties of the entropy functional were investigated and the entropies of the distributions, associated with the wave functions of the simplest quantum-mechanical systems were found.

We shall now consider briefly the contents of this review. Section II deals with the available results of the calculations of the effective volumes of the simplest atomic-molecular systems. The reader interested only in the application of the above concepts of internal and external volumes to specific systems need peruse only this part of the article.

Section III presents a detailed analysis of the concepts of entropy and general variance for the case of many particles. The entropy formulation of the uncertainty principle is discussed in Subsection 8 of Section III.

II. EFFECTIVE DIMENSIONS OF SIMPLEST ATOMIC AND MOLECULAR SYSTEMS

The effective theoretical dimensions of quantum-mechanical systems are interesting from different points of view. One of the significant aspects of the formation of a chemical bond is the redistribution of electron density in the vicinity of atomic nuclei. This redistribution is accompanied by a change in the effective dimensions of the system, its effective internal and external volumes, and the associated change in the normality coefficient N‡.

It is important to have a correct idea concerning the charge distribution in the electron shells of the atoms and molecules between the inner part of the atom or a molecule included in the effective volume and the infinite space external to such volume.

It is interesting to compare the effective theoretical dimensions of atoms and molecules with their effective dimensions determined by the application of various experimental research techniques.

However, one should bear in mind that the entropy H and the general variance D of the distribution are sensitive to the type of wave function employed in the calculation. Therefore serious limitations in the choice of data for the calculations are inevitable. Only fairly accurate wave functions, a further refinement of which no longer has a significant influence on the calculated entropy H and general variance D of the distribution, are suitable for

†We emphasise that this concept must not be confused with the concept of entropy in thermodynamics, as is done, for example, in the book "Dialektika Razvitiya Khimii" (Dialectics of the Development of Chemistry) by V. I. Kuznetsov, Izd. Nauka, Moscow, 1973, pp. 198–199.

‡For a definition of the normality coefficient N, see Section III, 1.

the calculation of the effective dimensions of quantum-mechanical systems.

In this Section the concepts of the entropy and variance refer to the three-dimensional electron density. The information contained in the effective atomic and molecular dimensions, which is of interest primarily from the quantum-chemical point of view, is presented and discussed below. Table 1 gives the results of the calculation of the effective volumes in the ground states of one-electron systems (the H atom, the He^+ ion, and the H_2^+ molecular ion) and the ground states of two-electron systems (the H^- ion, He, Li^+, and H_2). Table 1 also includes the values of v for the H(2s) atom.

Table 1. Effective volumes of the simplest quantum-mechanical systems[a].

System[b]	References	$v\ (a_0^3)$	$V\ (a_0^3)$	N	$r\ (X_1, X_2)$
H (1s)		63.1	70.59	0.894	—
H (2s)		3330.7	3697.6	0.901	—
He^+		7.89	8.82	0.895	—
H_2^+	10	45.15	—	—	—
H^-	11	300.60	443.45	0.678	0.1201
He	11	14.89	17.50	0.851	0.0947
He	12, 13	—	17.71	—	0.0939
He	14	14.88	17.77	0.837	0.0867
Li^+	11	3.50	4.03	0.869	0.0672
H_2	15	50.91	—	—	—
H_2	16	—	54.38	0.936[c]	0.1860

[a] A number of the calculations were made by S. S. Abdullaev.
[b] In the calculation of the effective volumes different approximate wave functions were employed. References are given to studies in which these wave functions were found. Where there are no references, the calculation was made using the exact wave functions. The characteristics of all the systems, with the exception of the H atom, are quoted only for the ground states.
[c] The normality coefficient was found using the internal volume calculated from James and Coolidge's function [15].

The data in Table 1 permit a number of conclusions.

1. For two-electrons spherically symmetrical neutral or positively charged systems, the difference between the external and internal effective radii (R_{ext} and R_{int} respectively) is insignificant. For He and Li^+, $R_{ext}/R_{int} \simeq \simeq 1.05$. With a negative charge, this ratio must of course be somewhat greater than for the corresponding neutral or positively charged systems. Thus $R_{ext}/R_{int} \simeq 1.14$ for H^-. For the hydrogen molecule, the ratio of the average lengths of the effective half-axes of the ellipsoids bounding v is $R_{ext}/R_{int} \simeq 1.02$.

2. For one-centre systems, the addition of a second electron to a one-electron system gives rise to a marked increase of the effective volume v, which also depends on the nuclear charge.

Comparison of H_2^+ and H_2 in the ground states also leads to the conclusion that v increases, although to a smaller extent than for one-centre systems. In this more complex case an effect involving the contraction of the internuclear distance obtains, which partly cancels the increase of v due to electron-electron repulsion.

3. In one-centre two-electron systems an increase of nuclear charge causes a marked decrease of v and V, as can be seen in the series of H^-, He and Li^+ in their ground states. The coefficient N increases—the distribution approaches significantly the normal distribution.

4. The formation of an H_2 molecule from two H atoms entails an appreciable decrease of v compared with the value for the 1s state of the H atom, namely by $11.89a_0^3$.

The fact that $v = 50.91a_0^3$, calculated by Bochvar et al. [17] using the James–Coolidge function [15], is much smaller than the value derived from the wave function of the simple MO-LCAO method [4] ($79.84a_0^3$) merits attention. Table 1 shows that the latter actually exceeds the value of v for the 1s state of the H atom. Hence it follows that the wave functions of the LCAO method in all its versions employing rigid atomic orbitals are unsuitable for a quantitative description of the properties of the electron density distribution in molecules.

5. $v = 45.15a_0^3$ for the ground state of H_2^+, i.e. is smaller by $5.76a_0^3$ than v for the ground state of the H_2 molecule. The overall positive charge and the absence of electron-electron repulsion surpass the effect of the increase in the internuclear distance R due to the weakening of the bond.

6. Comparison of the H_2 and He two-electron systems shows that, whereas v for the He atom in the ground state decreases almost by a factor of two on single ionisation (from $14.88a_0^3$ to $7.89a_0^3$, i.e. by a factor of 1.87), on removal of one electron from the H_2 molecule in the ground state with conversion into H_2^+ also in the ground state v decreases only by $5.7a_0^3$.

The explanation of this fact is that, in the vertical ionisation of H_2, v is reduced by $18.12a_0^3$, i.e. to $32.79a_0^3$ (by a factor of 1.55), but this contraction is partly compensated by the increase of R from $1.4a_0$ to $2a_0$, which leads to an increase of v from $32.79a_0^3$ by $12.36a_0^3$, i.e. to $45.15a_0^3$.

7. The correlation coefficients $r(X_1, X_2)$ for electrons in two-electron systems listed in the last column of Table 1 make it possible to infer the correlation of electrons from the standpoint of probability theory. We note in the first place that, in contrast to the correlation energy, the correlation coefficient of electrons is estimated for any approximate function (poor or satisfactory) without resorting to experimental data or the exact wave function. As the exact wave function is approached, the correlation coefficients should tend to a limit. Calculations show that the values of $r(X_1, X_2)$ for all three fairly satisfactory wave functions of the helium atom yield, to within 0.01, the same value $r(X_1, X_2) = 0.09$. It is noteworthy that (in the present authors' view) the internal correlation coefficient $r_H(X_1, X_2)$ defined by Eqn. (6, 1) allows more completely for the correlation of electrons. According to this hypothesis, $r_H(X_1, X_2)$ calculated from the Hylleraas function [14] is 0.20, which greatly exceeds $r(X_1, X_2) = 0.09$.

Proceeding now to a comparison of the correlations in different systems, we note that in many isoelectronic systems (H^-, He, Li^+) $r(X_1, X_2)$ decreases with increase of the nuclear charge. Its values are respectively 0.12, 0.09, and 0.07. The correlation coefficient of the electrons in the H_2 molecule is 0.186 and is largely determined by the correlations of the z components (directed along the lines of the bond) of both electrons: $|r(z_1, z_2)| = 0.156$.

In many systems the negative charges in regions within and outside the effective volume v were calculated from the data in Table 1. [18] The surfaces bounding the effective volumes v for one-centre systems were naturally regarded as spherical, while for the two-centre systems H_2^+ and H_2 they were assumed to be ellipsoids of rotation with the foci located at the atomic nuclei. The calculation reduced to the integration of the three-dimensional probability

density (corresponding to the three-dimensional charge density) over the corresponding regions. The calculated charges Z_{int} within the effective volumes v and the charges Z_{ext} outside the effective volumes are listed in Table 2. For the two-electron systems He and H_2, Table 2 also includes the unit probabilities defined as the probability sums

$$1 = P^{(2,0)} + P^{(1,1)} + P^{(0,2)}, \qquad (*)$$

where $P^{(2,0)}$ is the probability of finding both electrons within the volume v, $P^{(1,1)}$ the probability of finding one electron in the volume v and the other electron outside this volume, and $P^{(0,2)}$ the probability of finding both electrons outside the volume v. When calculating the charges within and outside the volume v, Eqn. (*) must be multiplied by two and account must be taken of the fact that the situation where one electron is within the volume v and the other is outside it, which has a probability $P^{(1,1)}$, makes different contributions to the charge within the volume v and the charge distributed in the space outside v.

Table 2. Charge distributions for the simplest quantum-mechanical systems (in the ground state).

System	$v\,(a_0^3)$	Z_{int}^{a}	Z_{ext}	$P^{(2,0)b}$	$P^{(1,1)}$	$P^{(0,2)}$
He^+	7.89	0.871	0.129			
H_2^+	45.15	0.893	0.103			
H (1s)	63.1	0.870	0.130			
He	14.88	1.6956	0.3044	0.7080	0.2796	0.0125
H_2	50.91	1.744	0.256	0.7525	0.1280	0.0085

[a] Z_{int} is the charge (in electronic units) in the effective volume v; Z_{ext} is the charge (in electronic units) outside the effective volume v.
[b] $P^{(2,0)}$ is the probability of finding two electrons in the volume v, $P^{(1,1)}$ the probability of finding one electron in the volume v and another electron outside this volume, and $P^{(0,2)}$ the probability of finding two electrons outside the volume v.

The comparatively small range of values of Z_{ext} (per electron) in Table 2, despite the significant differences between many systems, is striking (only from 10.7 to 14.0%). For the H(1s), He^+, and H_2 systems, Z_{ext} (per electron) is almost constant. This finding suggests the hypothesis that significant differences in charge distribution occur only within the effective volumes. Outside the effective volumes, the distributions are similar for different systems, and a spherical distribution is approached more closely the further away one moves from the system of nuclei.

As mentioned above, for the surfaces bounding the internal effective volumes of one-centre systems it is natural to adopt the geometry of the sphere with the centre at the atomic nucleus and, for homonuclear two-centre systems with cylindrical symmetry (H_2^+ and H_2), the geometry of an ellipsoid of rotation with the foci at the atomic nuclei. With these assumptions, it is possible to calculate the effective linear dimensions of the systems.

Table 3 lists the effective diameters d_{ef} of the H and He atoms in their ground states and the effective lengths of the axes $2a_{ef}$ and $2b_{ef}$ of the ellipsoids of rotation for the molecular ion H_2^+ and the molecule H_2, also in their ground states. The average values of d_{ef} obtained from the effective axes of the ellipsoids are also listed for H_2^+ and H_2.

Table 3 also contains (the extreme right-hand column) the effective diameters of He and H_2 calculated from the experimental viscosities of the gases [19] at high temperatures by Chapman's formula [20]:

$$\eta = \frac{1}{\pi\sigma_\infty^2}\sqrt{\frac{kTm}{\pi}},$$

where η is the viscosity of the ideal gas and σ_∞^2 the effective diameter of the species (atom or molecule) of the ideal gas which is assumed to be spherical. The effective external diameter of helium (1.72 Å) is closer to σ_∞ (1.91 Å) than the internal diameter.

Table 3. Effective linear dimensions for the ground states of H, He, H_2^+, and H_2 calculated from the internal volumes.

System	d_{ef}, Å	$2a_{ef}$, Å	$2b_{ef}$, Å	d_{ef}, Å	σ_∞, Å
H	2.62	—	—	—	—
He	1.61	—	—	—	1.91
H_2^+	—	2.50	2.26	2.38	—
H_2	—	2.51	2.39	2.45	2.42

We may note that r_{ef} for the hydrogen atom in the ground state, which is 1.31 Å, exceeds somewhat the van der Waals radius of hydrogen (1.17–1.20 Å). This is quite reasonable, since r_{ef} = 1.31 Å refers to an isolated atom in the ground state, while the van der Waals radius (1.20 Å) corresponds to the state of a hydrogen atom bound in the crystal.

The figures quoted in Table 3 indicate the possibility of interesting relations between the internal (and also external) effective volumes v and the approximate effective volumes of atoms and molecules from other sources (the viscosities of gases, vapours, and liquids, mean free paths in gases, etc.).

According to the foregoing considerations, the internal effective volumes v of the molecular ion H_2^+ and the molecule H_2 in their ground states are smaller than the effective volume v of the H atom in the 1s state. This is understandable, since the formation of a chemical bond should lead to a decrease of the entropy of the three-dimensional distribution of electron density.

However, it is at the same time reasonable to suppose that in each case where a chemical bond is formed there is a certain characteristic one-dimensional density distribution the entropy of which in fact increases. A test of this hypothesis [21] for the ground state of the molecular ion H_2^+ with the exact wave function [10] and for the ground state of the molecule H_2 with the James–Coolidge function [15], in relation to the ground state of the hydrogen atom, is consistent with the above hypothesis, as can be seen from Table 4. In the Table h denotes the entropies of the one-dimensional distribution of entropy density in the H_2^+ and H_2 systems in a direction parallel to the z axis passing through the protons, while for the hydrogen atom it denotes, in view of its spherical symmetry, the entropy of the one-dimensional distribution of electron density in a direction parallel to an arbitrarily chosen diameter.

The situation in the H_2 molecule is more complicated than in the ion H_2^+, since there is the additional effect of the electron-electron repulsion. This last factor tends to increase h and v. On the other hand, in contrast to the attraction of one-electron in H_2^+, the attraction of two electrons to two protons results in a decrease of the distance R between the protons, which tends to reduce h and v. As a result, the effective volume v in the ground state of the H_2 molecule is somewhat smaller than for the ground state of the H_2^+ ion, remaining, however, greater than v for the ground state of the hydrogen atom.

Table 4. One-dimensional effective volumes for the ground states of H, H_2^+ and H_2.

System	h	$v = \exp h$ (a_0)
H	1.39	4.01
H_2^+	1.47	4.35
H_2	1.43	4.18

The entropy of the distribution and the internal volumes for the wave functions in the electron gas model (the lateral cylindrical surface model) for molecules with a "sandwich" type structure were investigated by Bochvar et al.[22] In this study the entropy of the distribution was used as a qualitative characteristic of the degree of conjugation between the carbon rings in molecules of the dibenzene-chromium and ferrocene type.

In conclusion we may mention a number of studies in which the concept of the entropy of a discrete distribution is used for quantum-mechanical systems.

In conformity with studies by Daudel and coworkers[23], who were the first to introduce the concept of the "loge", Aslangul[24] employed the entropy of a discrete distribution to characterise the information which can be extracted from the wave function by considering arbitrary subdivisions of the coordinate space into regions and by assigning to each such region the probability of finding a definite number of electrons in it. The applications of certain properties of the entropy of spin operators have been considered[25].

The definition of the information contained in the state of one quantum-mechanical system relative to the state of another has been discussed[26]. In Zhdanov's book[27] the entropy is used to obtain information about the relative reactivities of conjugated molecules. Primas[28] suggested that the criterion of a minimum in the entropy function be used in certain cases for the derivation of approximate wave functions.

III. THEORY OF EFFECTIVE DIMENSIONS OF QUANTUM-MECHANICAL SYSTEMS

1. Effective Size in a One-Dimensional Quantum-Mechanical System

In order to elucidate the significance of the principal definitions of the theory of the effective volumes of quantum-mechanical systems without complicating the treatment with cumbersome mathematical formulae, we shall consider initially the simplest and most evident case of one-dimensional probability density on the coordinate of a single particle located on an infinite straight line. In this case the wave function $\psi(x)$ is a function of a single variable. Then

$$\rho(x) = |\psi(x)|^2 \tag{1.1}$$

is the probability density of the coordinate for point x on the straight line. The general variance is identical with the usual variance:

$$D = \int_{-\infty}^{\infty} (x - m)^2 \rho(x)\, dx, \tag{1.2}$$

where $m \int_{-\infty}^{+\infty} x\rho(x)dx$ is the expectation value of the coordinate for the distribution $\rho(x)$ and the entropy H is§

$$H = -\int_{-\infty}^{\infty} \rho(x) \ln \rho(x)\, dx. \tag{1.3}$$

Both the quantities D and H characterise the uncertainty in the coordinate of the one-dimensional particle. In order to emphasise the differences between these quantities, we shall resort to an example. Fig. 1*a* represents the density $\rho_1(x)$ of the uniform distribution along a section $[a, b]$ of length L. Fig. 1*b* represents the density of the distribution $\rho_2(x)$ concentrated uniformly on two sections $[a_1, b_1]$ and $[a_2, b_2]$ with an overall length L. The entropies of the distributions $\rho_1(x)$ and $\rho_2(x)$ are equal for any values of $t = a_2 - b_1 > 0$, while the corresponding variances are different, that of $\rho_2(x)$ increasing with increase of the parameter t. This example shows that the entropy is an absolute¶ characteristic of the distribution which reflects the scatter within the regions of the localisation of the distribution regardless of the relative positions of these regions. The variance of the distribution also depends on the relative scatter of the localisation regions. In this sense the variance can be regarded as a relative characteristic of the distribution.

In real problems one can encounter cases more complex than those illustrated in Fig. 1. The distribution densities may not become zero and may have several maxima (corresponding to the localisation regions). The entropy of the distribution characterises, to a rough

§For the logarithmic term in the integrand to be significant, it is necessary that the integrand should be dimensionless. To achieve this, the definition of H must be reformulated as follows[29]:

$$H = -\int_{-\infty}^{+\infty} \rho(x) \ln [\rho(x)\, l]\, dx\ ,$$

where l is a certain length. We shall assume (without restricting the generality of the treatment) that this length is unity. Then H has the significance of the average logarithm of a certain length; in the n-dimensional case H has the significance of the average value of an n-dimensional volume.

¶The absolute nature of the entropy is expressed by the fact that the integrand depends on the coordinate only through the density. This is in fact the cause of the property of entropy considered in this example.

approximation, the overall scatter within the localisation regions and the variance also takes into account the scatter of the localisation regions. The entropy and the variance each reflect the degree of delocalisation of the particle.

Entropy and variance can be used to characterise the effective dimensions of a one-dimensional particle. For this purpose, it is convenient to introduce the concept of effective volumes: the internal effective volume v defined in terms of the entropy by the formula

$$v = \exp H \tag{1.4}$$

and the external effective volume defined in terms of the variance by the formula

$$V = \sqrt{2\pi e D}. \tag{1.5}$$

We may note that, for a uniform distribution on the section $[a, b]$ with a length L (Fig. 1*a*), the internal volume is equal to the length of the section: $v = L$.

For any one-dimensional distribution, the following inequality is valid:

$$H \leqslant \frac{1}{2}\ln(2\pi e D). \tag{1.6}$$

Hence it follows that always $v \leqslant V$†. The equality of these volumes holds only for normal‡ (Gaussian) distribution.

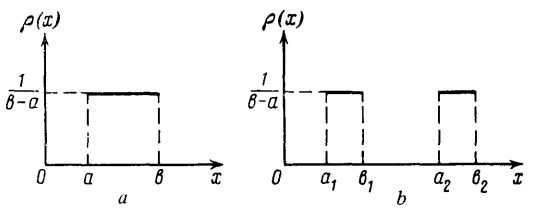


Figure 1.

Fig. 2 presents a plot of D as a function of $H = -\int \rho(x)\ln\rho(x)dx$ for normal distributions. The points located above the curve represent non-Gaussian one-dimensional distributions. When the variance is specified (for example D_0 in Fig. 2), the maximum entropy H_0 holds for the normal distribution. When the entropy is specified (for example H_0, Fig. 2) the minimum variance D_0 holds also for the normal distribution.

Evidently the following inequality is valid for any distribution:

$$v/V \leqslant 1. \tag{1.7}$$

The sign of equality in Eqn. (1.7) holds for normal distributions and only for normal distributions. Therefore it is reasonable to introduce the definition

$$N = v/V$$

and to term the quantity N $(0 \leqslant N \leqslant 1)$ the coefficient of the normality of the distribution. For all normal distributions, $N = 1$. For a uniform distribution, the normality coefficient is a constant quantity of about 0.7. The normality coefficient can be interpreted as the average "degree of population" of the external effective volume of the system with the given distribution. This interpretation presupposes a spatial localisation of the effective volumes v and V involving certain assumptions. These assumptions are chosen in accordance with the nature of the system for which the given distribution is observed. It is noteworthy that, in contrast to the effective volume V, the geometrical interpretation of the effective volume v may show it to be unconnected. We shall consider several examples.

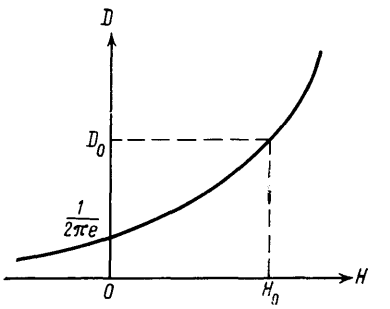


Figure 2.

A one-dimensional particle in a potential well with a finite length L, an infinitely high wall, and a constant potential within the well has a normalised wave function of the type

$$\psi_n(x) = \sqrt{\frac{2}{L}}\sin\frac{\pi n x}{L}, \quad (0 \leqslant x \leqslant L),$$

where n is the quantum number. The entropy H of the electron density distribution $|\psi_n(x)|^2$ is $\ln(2L/e)$ and therefore it depends only on L and is independent of the quantum number n. The variance of the electron density distribution $D(|\psi_n|^2)$ depends on L and n:

$$D(|\psi_n|^2) = L^2\left(\frac{1}{12} - \frac{1}{2\pi^2 n^2}\right).$$

The limiting value of $D(|\psi_n|^2)$ when $n \to \infty$ is $\frac{1}{12}L^2$. Table 5 lists the values of v, V, and the normality coefficient N.

Table 5. Effective volumes of the wave functions of a particle in a one-dimensional potential well.

n	v/L	V/L	N
1	0.736	0.747	0.985
2	0.736	1.098	0.670
30	0.736	1.192	0.617

It shows that the normality coefficient decreases with increase of n and almost attains its limiting value when $n = 30$.

†This relation justifies the terms "external" and "internal" for v and V.

‡The normal distribution has the density $\rho_N(x) = (2\pi D)^{1/2}\exp[-(x-m)^2/2D]$.

As a second example, we present in Table 6 analogous data for the first ten eigenstates of the harmonic oscillator. Evidently the normality coefficient gradually decreases with increase n.

Consider now, a particle localised at the point x_0. Its distribution density is given by the δ-function $\delta(x-x_0)$, the variance is zero, and the entropy is strictly speaking undefined. Nevertheless it is convenient to attribute $H[\delta(x-x_0)] = -\infty$ and the internal volume $v = 0$ to the δ-function, since the entropy tends to $-\infty$ for sequences of the type $\rho_1(x)$ and $\rho_2(x)$ which tend to the δ-function when $L \to 0$ and $D \to 0$. To ensure the validity of the treatment, it will be necessary to show that the entropy tends to $-\infty$ in any δ-sequence.

The introduction of the terms "internal" and "external" for the effective volumes is based on the fact that for specific geometrical interpretations of these quantities, the part of the space representing the entropy volume is contained within the part of the space representing the variance volume or is identical with it for normal distributions§.

Table 6. Effective volumes of the wave functions of a harmonic oscillator.

n	v	V	N
0	2.92	2.92	1.00
1	3.83	5.06	0.76
2	4.47	6.53	0.68
3	4.98	7.73	0.64
4	5.40	8.76	0.62
5	5.79	9.69	0.60
6	6.13	10.54	0.58
7	6.45	11.32	0.57
8	6.72	12.05	0.56
9	6.98	12 74	0.55

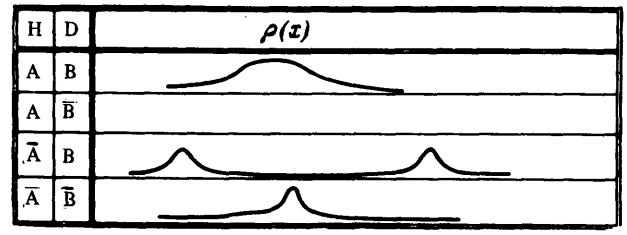
As stated above, in order to characterise fully the distribution it is necessary to know all its moments. However, a rough and purely qualitative classification of one-dimensional distributions with respect to entropy and variance can be formulated as follows: (a) each distribution belongs to one and only one of two classes $\mathbf{A}(H \geqslant 0)$ or $\bar{\mathbf{A}}(H < 0)$; (b) each distribution belongs to one and only one of two classes $\mathbf{B}[D \geqslant (2\pi e)^{-1}]$ or $\bar{\mathbf{B}}[D < (2\pi e)^{-1}]$. Four combinations of the above criteria, corresponding to four classes (one of these classes is empty), are presented in Table 7. The $\rho(x)$ column of Table 7 lists fairly typical distributions of three classes (**A**, **B**), ($\bar{\mathbf{A}}$, **B**), and ($\bar{\mathbf{A}}$, $\bar{\mathbf{B}}$). The normal or Gaussian distribution and a uniform distribution can belong to either of the two classes (**A**, **B**), and ($\bar{\mathbf{A}}$, $\bar{\mathbf{B}}$) depending on their parameters. Linear combinations of Gaussian or uniform distributions are encountered (depending on the parameters) in all non-empty classes. Among the examples of the three classes, two correspond to two sharply different extreme types of particle delocalisation and one to a marked localisation at one centre.

Between the extreme types of delocalisation, there is a continuous series of transitional cases referring, depending on the parameters, to class (**A**, **B**) or to ($\bar{\mathbf{A}}$, **B**).

§Thus the internal effective volume v of the distribution is equal in magnitude to the effective volume of the isentropic normal distribution, which is uniquely defined.

Next we proceed from the one-dimensional case to the consideration of real multidimensional (one- and many-particle) systems. The generalisation of the concept of the internal effective volume does not require additional justification, since the above definition of entropy changes on being extended to the multidimensional case only with respect to the interpretation of the variable integration symbol. However, the usual definition of variance quoted above is essentially one-dimensional. Therefore the concept of the external effective volume cannot be generalised to include multidimensional systems and it is necessary to define not only a more general but formally also a more complex concept.

Table 7. Classification of one-dimensional distributions with respect to the entropies and variances.



2. The Covariance Matrix and General Variance of a particle

We shall now consider a real physical object (the electron¶) in a potential field. Suppose that the state of the electron is described by the wave function $\psi(x_1, x_2, x_3)$ normalised to unity ($\int |\psi(x_1, x_2, x_3)|^2 d\mathbf{x} = 1$)†.

We put

$$\rho(\mathbf{x}) = |\psi(x_1, x_2, x_3)|^2, \tag{2.1}$$

where $\mathbf{x} = (x_1, x_2, x_3)$ are the coordinates of the electron. Then $\rho(\mathbf{x})$ can be treated as the probability density of a three-dimensional random quantity $\mathbf{X} = (X_1, X_2, X_3)$. Its components are one-dimensional random quantities X_1, X_2, X_3, which correspond to the coordinates x_1, x_2, x_3. The densities of the distribution of these one-dimensional random quantities are defined by the formulae

$$\rho_1(x_1) = \iint \rho(\mathbf{x})\, dx_2\, dx_3, \quad \rho_2(x_2) = \iint \rho(\mathbf{x})\, dx_1\, dx_3, \quad \rho_3(x_3) = \int\int \rho(\mathbf{x})\, dx_1\, dx_2. \tag{2.2}$$

We shall employ the probability theory for the description of the delocalisation of a three-dimensional particle. We first recall the definition of the covariance matrix which characterises the deviation of a random quantity $\mathbf{X}$ from a point $M(m_1, m_2, m_3)$ the coordinates of which are given by the formulae

$$m_s = \int x_s \rho(\mathbf{x})\, d\mathbf{x} \quad (s = 1, 2, 3). \tag{2.3}$$

¶Or any other quantum-mechanical particle.

†For brevity we put $dx = dx_1 dx_2 dx_3$ and omit the integration limits. Here and henceforth the integration is from $-\infty$ to $+\infty$ with respect to each one-dimensional variable.

The radius-vector of the point M is called the expectation value of the random quantity X and is designated by $M(\mathbf{X})$. The covariance matrix (or the second moment matrix) is defined as

$$\mathcal{K}(\mathbf{X}) = \begin{pmatrix} k_{11} & k_{12} & k_{13} \\ k_{21} & k_{22} & k_{23} \\ k_{31} & k_{32} & k_{33} \end{pmatrix}, \tag{2.4}$$

the elements of which are

$$k_{st} = \int (x_s - m_s)(x_t - m_t)\,\rho(\mathbf{x})\,d\mathbf{x}. \tag{2.5}$$

The matrix K(X) is symmetrical ($k_{ts} = k_{st}$). Its diagonal elements are the variances $D(X_s) = \sigma_s^2$ of the components X_s and the non-diagonal elements $k_{st} = \mathrm{Cov}(X_s, X_t)$ are the covariances of the components X_s and X_t. The covariance characterises the statistical correlation between the random quantities X_s and X_t. It depends on the choice of scale. In order to eliminate this dependence, the concept of the normalised correlation or the correlation coefficient of two one-dimensional random quantities X_s and X_t is introduced. It is defined by the formula

$$r_{st} = r(X_s, X_t) = \frac{\mathrm{Cov}(X_s, X_t)}{\sqrt{D(X_s)\,D(X_t)}}. \tag{2.6}$$

It can be shown[30] that the following inequality always holds:

$$|r_{st}| \leqslant 1. \tag{2.7}$$

The equality is attained only when the variables X_s and X_t are linearly related. On the other hand, if the random quantities X_s and X_t are independent, then $r_{st} = 0$‡. We shall now determine what information about the delocalisation of the particle can be derived from the matrix K. As already mentioned, the diagonal elements characterise the scatter of the coordinates x_1, x_2, and x_3. In order to determine the scatter in the direction of an arbitrary vector $\mathbf{c}(c_1, c_2, c_3)$, it is necessary to calculate the scaler product of K(X)c and c, i.e.,

$$D_{\mathbf{c}}(\mathbf{X}) = (\mathcal{K}(\mathbf{X})\mathbf{c}, \mathbf{c}) = \sum_{i=1}^{3}\sum_{j=1}^{3} k_{ij} c_j c_i. \tag{2.8}$$

Thus the covariance matrix contains the full information about the delocalisation of the particle in any direction. However, together with the matrix characteristic of the scatter, scalar quantities describing the scatter of a random vector quantity X in terms of a single integral number are of interest.

Before stating these characteristics, we shall elucidate the requirements which they must satisfy. Hitherto, the coordinate system was fixed. On passing to a new coordinate system x_1, x_2, x_3 by an orthogonal transformation (including rotations and reflections)

$$\mathbf{x}' = U\mathbf{x} \tag{2.9}$$

the random quantity X will have the distribution density

$$\tilde{\rho}(\mathbf{x}') = \rho(U^{-1}\mathbf{x}'). \tag{2.10}$$

The substitution (2.9) may be treated as a change to a new random vector (in the old coordinate system)

$$\mathbf{X}' = U\mathbf{X} \tag{2.11}$$

with distribution density

$$\tilde{\rho}(\mathbf{x}) = \rho(U^{-1}\mathbf{x}). \tag{2.10'}$$

The covariance matrix of the random vector X′ (or, what amounts to the same thing, the covariance matrix of the initial random vector in the new coordinate system) is

$$\mathcal{K}(\mathbf{X}') = U\mathcal{K}(\mathbf{X})U^{-1}. \tag{2.12}$$

Since the entire class of random vectors X′ obtained from the initial vector X by all possible orthogonal transformations describes the same state of the particle, the required scalar characteristics must be invariant in the above transformations. Such invariant characteristics are the "spur" of the matrix K(X) (the sum of its diagonal elements)

$$\mathrm{Sp}\,\mathcal{K}(\mathbf{X}) = D(X_1) + D(X_2) + D(X_3) \tag{2.13}$$

and the determinant§

$$D(\mathbf{X}) = \det \mathcal{K}(\mathbf{X}), \tag{2.14}$$

called the general variance of a random quantity X.[30] We shall also call it the general variance of the coordinates of the particle [in the state $\psi(\mathbf{x})$]. We shall now consider the geometrical significance of the above quantities. If we denote by $\Delta\mathbf{X}$ the random vector $\mathbf{X} - M(\mathbf{X})$, then it is readily seen that the spur of the matrix K(X) represents the expectation value of the quantity $|\Delta\mathbf{X}|^2$, i.e. $M(|\Delta\mathbf{X}|^2)$. This quantity has the dimensions of the square of a length. Therefore $\sqrt{M(|\Delta\mathbf{X}|^2)}$ characterises the scatter of the values in the direction of the radius-vector drawn from a point and cannot provide an answer to the question of whether the particle is localised in the vicinity of a plane or a straight line. We emphasise that the quantity $M(|\Delta\mathbf{X}|^2)$ is essentially a one-dimensional characteristic.

In contrast to the quantity $M(|\Delta\mathbf{X}|^2)$ the general variance $D(\mathbf{X})$ characterises a multidimensional scatter. In order to elucidate the geometrical significance of this quantity, we shall consider further the quantity

$$D^*(\mathbf{X}) = D(X_1)\,D(X_2)\,D(X_3). \tag{2.15}$$

The standard deviation $\sigma^*\sqrt{D^*}$ corresponding to this quantity is equal to the volume of a rectangular parallelepiped with the sides $\sigma(X_i) = \sqrt{D(X_i)}$ $(i = 1, 2, 3)$. Thus the quantity $D^*(\mathbf{X})$ characterises the three-dimensional scatter in the direction of all the coordinate axes at once, but it does depend on the choice of the coordinate system. The minimum value of $D^*(\mathbf{X})$ is attained in the coordinate system the unit vectors of which are the eigenvectors of the covariance matrix K(X) and is equal to $D(\mathbf{X})$¶. The coordinate system formed by the eigenvectors of the matrix will be called the intrinsic system of the particle

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‡The converse assertion is incorrect. It does not follow from the equality $r_{st} = 0$ that the random quantities are independent. There are random quantities which are actually linked by a non-linear functional relation, whose correlation coefficient is zero. Therefore Eqn. (2.6) can characterise only a linear relation.

§The remaining invariant characteristics are not considered here.

¶A maximum value of D^* also exists and is $D_{\max}(\mathbf{X}) = (\frac{1}{3}\mathrm{Sp}\mathbf{K})^3$. With the aid of the quantities $D_{\max}(\mathbf{X})$ and $D(\mathbf{X})$, it is possible to define a measure of the anisotropy of the distribution: $[D_{\max}(\mathbf{X}) - D(\mathbf{X})]\sqrt{D_{\max}(\mathbf{X})D(\mathbf{X})}$.

coordinates†. In this coordinate system the covariance matrix is of the diagonal form, i.e. the components of the random vector X are not correlated.

Thus the geometrical significance of the quantity $D(\mathbf{X})$ becomes clear: it is the general variance of the particle equal to the product of the one-dimensional variances in the directions of the axes of the intrinsic coordinate system of the particle, i.e. to the product of the eigennumbers of the covariance matrix. It follows from the condition for an extremum in $D^*(\mathbf{X})$ that the following inequality always holds:

$$D(\mathbf{X}) \leqslant D(X_1) D(X_2) D(X_3), \tag{2.16}$$

where the equality sign obtains only when the components X_1, X_2, and X_3 are not correlated.

3. The Covariance Matrix of an n-Particle System

We shall now consider a quantum-mechanical system of n particles. Suppose that the state of the system is described by the normalised wave function $\psi(\mathbf{X})$, where $\mathbf{x} = (\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_n)$ denotes a set of cartesian coordinates of n particles and $\mathbf{x}_i = (x_{i1}, x_{i2}, x_{i3})$ denotes the coordinates of the ith particle. We put

$$\rho(\mathbf{x}) = |\psi(\mathbf{x})|^2. \tag{3.1}$$

Then $\rho(\mathbf{x})$ can be treated as the probability density of a $3n$-dimensional random vector:

$$\mathbf{X} = (\mathbf{X}_1, \mathbf{X}_2, \ldots, \mathbf{X}_n). \tag{3.2}$$

The components of the vector are three-dimensional random quantities $\mathbf{X}_i = (X_{i1}, X_{i2}, X_{i3})(i = 1, 2, \ldots, n)$ with the distribution densities

$$\rho_i(\mathbf{x}_i) = \int \rho(\mathbf{x})\, d\mathbf{x}_1 \ldots d\mathbf{x}_{i-1} d\mathbf{x}_{i+1} \ldots d\mathbf{x}_n. \tag{3.3}$$

Each density describes the distribution of the coordinates of the individual ith particle with all other particles in their average positions. The expectation value of the sth component of the ith particle is given by the formula

$$m_{is} = \int x_{is} \rho(\mathbf{x})\, d\mathbf{x}, \tag{3.4}$$

and the covariance matrix $\mathbf{K}_{ii}$ of the ith particle is defined by formulae of type (2.4) and (2.5). The covariance of the sth component of the ith particle and of the tth component of the jth particle is given by the formula

$$\mathrm{Cov}(X_{is}, X_{jt}) = \int (x_{is} - m_{is})(x_{jt} - m_{jt}) \rho(\mathbf{x})\, d\mathbf{x}. \tag{3.5}$$

Thus the covariance matrix of the coordinates of a system of n particles [i.e. of the random vector (3.2)] is of order $3n$ and can be represented by the block matrix

$$K(\bar{\mathbf{X}}) = \begin{pmatrix} \mathcal{K}_{11} & \mathcal{K}_{12} & \ldots & \mathcal{K}_{1n} \\ \mathcal{K}_{21} & \mathcal{K}_{22} & \ldots & \mathcal{K}_{2n} \\ \ldots & \ldots & \ldots & \ldots \\ \mathcal{K}_{n1} & \mathcal{K}_{n2} & \ldots & \mathcal{K}_{nn} \end{pmatrix}, \tag{3.6}$$

where $\mathbf{K}_{ij}$ is the covariance matrix of the ith and jth particles comprising the elements of the matrix (3.5) with $s = (1, 2, 3)$ and $t = (1, 2, 3)$. The matrix $K(\mathbf{X})$ is symmetrical. Therefore the "elements" symmetrical relative to the main diagonal are linked by the relation $\mathbf{K}_{ij} = \mathbf{K}'_{ji}$, where the prime denotes transposition. On the basis of the considerations set out in Section III, 2, one can speak of the general variance of the coordinates of an individual particle $\mathbf{x}_i$ in an n-particle system. This variance is given by the formula

$$D(\mathbf{X}_i) = \det \mathcal{K}_{ii}. \tag{3.7}$$

The general variance of the coordinates of the entire system,

$$D(\mathbf{X}) = \det K(\mathbf{X}) \tag{3.8}$$

and the general variance of the coordinates of an arbitrary subsystem of μ particles,

$$D(\mathbf{X}_1, \mathbf{X}_2, \ldots, \mathbf{X}_\mu) = \det K_\mu, \tag{3.9}$$

where K_μ is a block matrix comprising the elements of the matrix $\mathbf{K}_{ij}$ designated by the numbers of the isolated particles, can be defined by analogous formulae.

For the system as a whole (as well as for any of its subsystems), it is possible to select the intrinsic coordinate system, i.e. the coordinate system in the $3n$-dimensional space in which the covariance matrix of the entire system (called the subsystem) is diagonal. If not all the elements of the matrix $\mathbf{K}_{ij}$ are zero, the set of the intrinsic coordinate systems of the individual particles need not coincide with the intrinsic coordinate system of the n-particle system (or subsystem).

4. Effective Volumes of Quantum-Mechanical Systems

Just as the uncertainty of the position of a one-dimensional particle is described by the variance D and the entropy H, the uncertainty of the position of a real particle or a system of n particles is described by the general variance (3.8) and the entropy:

$$H(\mathbf{X}) = H(\mathbf{X}_1, \mathbf{X}_2, \ldots, \mathbf{X}_n) = -\int \rho(\mathbf{x}) \ln \rho(\mathbf{x})\, d\mathbf{x}. \tag{4.1}$$

As in the one-dimensional case, the entropy characterises the uncertainty of the position of the particles in the regions of their "localisation", while the general variance takes into account also the scatter of the localisation regions. Therefore the concepts of the internal and external volumes can be naturally extended to the multidimensional case as follows. The internal volume of an n-particle system is given by the formula

$$v(\mathbf{X}) = v(\mathbf{X}_1, \mathbf{X}_2, \ldots, \mathbf{X}_n) = \exp H(\mathbf{X}), \tag{4.2}$$

and the external volume by the formula

$$V(\mathbf{X}) = V(\mathbf{X}_1, \mathbf{X}_2, \ldots, \mathbf{X}_n) = \sqrt{(2\pi e)^{3n} D(\mathbf{X})}. \tag{4.3}$$

The usefulness of the definition of the internal volume by Eqn. (4.2) is confirmed by the following facts. If the system is concentrated in a finite region Ω and the density of its distribution is uniform, then the internal volume of such a system is equal to the volume of the region Ω. On the other hand, if the distribution of the system in the region Ω is non-uniform, its internal volume is smaller than that of the region Ω.

It follows from the properties of the general variance and the definition of the one-dimensional external volume (size) that the external volume of the particle is equal to the product of the one-dimensional external sizes in the

†It is assumed that the particle is in a fixed state $\psi(\mathbf{x})$.

directions specified by the intrinsic coordinate system of the particle. The following inequality for the external volume follows from inequality (2.16):

$$V(\mathbf{X}) \leqslant V(X_1)\,V(X_2)\,V(X_3). \tag{4.4}$$

A similar assertion is valid also for a system of n particles. It is then found that the external volumes of the particles‡ and of the system as a whole are linked by the inequality

$$V(\mathbf{X}) = V(\mathbf{X}_1, \mathbf{X}_2, \ldots, \mathbf{X}_n) \leqslant V(\mathbf{X}_1)\,V(\mathbf{X}_2) \ldots V(\mathbf{X}_n), \tag{4.5}$$

where the equality sign obtains only when the particles are not correlated, i.e., all the elements of all the matrices $\mathbf{K}_{ij}$ $(i \neq j)$ are zero.

The situation is somewhat different when one-dimensional and multidimensional internal volumes are compared. We shall demonstrate this using as an example a single particle. If $\rho(x_1, x_2, x_3)$ is the distribution density of the particle, the distribution densities of the components X_i are given by Eqns. (2.2) and the one-dimensional entropies and internal volumes are given by the equations

$$H(X_i) = -\int \rho_i(x_i) \ln \rho_i(x_i)\, dx_i \tag{4.6}$$

and

$$v(X_i) = \exp H(X_i). \tag{4.7}$$

The quantity $v^*(\mathbf{X}) = v(X_1)v(X_2)v(X_3)$ depends on the choice of the coordinate system. It has a minimum $v^0(\mathbf{X})$ which satisfies the inequality

$$v^0(\mathbf{X}) \geqslant v(\mathbf{X}), \tag{4.8}$$

where the equality sign is obtained for normal distributions. Thus the relation between one-dimensional and multidimensional internal volumes is given by the inequality

$$v(\mathbf{X}) \leqslant v(X_1)\,v(X_2)\,v(X_3). \tag{4.9}$$

Similarly the internal volume of an n-particle system is linked to the volumes of its constituent particles§ by the inequality

$$v(\mathbf{X}) = v(\mathbf{X}_1, \mathbf{X}_2, \ldots, \mathbf{X}_n) \leqslant v(\mathbf{X}_1)\,v(\mathbf{X}_2) \ldots v(\mathbf{X}_n). \tag{4.10}$$

The last two inequalities are of the same form as inequalities (4.4) and (4.5). However, the equality sign is not generally speaking attained in formulae (4.9) and (4.10) even for non-correlated components¶. This finding suggests that the entropy (and hence the internal volume) is a more refined concept which takes correlation into account more fully. We shall consider this in greater detail in Section III, 6.

As already mentioned, among distributions concentrated in a restricted region Ω the uniform distribution has the maximum internal volume. Among distributions which are not concentrated in a limited region and have a specified external volume V, the normal distributions have the maximum internal volume v (equal to V). The converse is also true; among distributions which are not concentrated in a restricted region and have a specified internal volume v, the normal distributions have the minimum external volume (equal to v).

‡The external volume of an individual particle in a system of n particles is defined in terms of the variance $D(\mathbf{X}_i)$ given by Eqn. (3.7).

§The internal volume of an individual (ith) particle is defined in terms of the entropy of the distribution with density $\rho_i(\mathbf{x}_i)$ specified by Eqn. (3.3).

¶Systems with the normal distribution density are an exception.

5. The General Covariance Matrix

The introduction of the concepts of a general variance and an external volume makes it possible to assign a definite geometrical significance to covariance and the correlation coefficient. Consider a covariance matrix $\mathbf{K}(\mathbf{X})$ specified by Eqns. (2.4) and (2.5). An arbitrary non-diagonal element k_{ij} $(i \neq j)$ of this matrix expresses the correlation of the coordinates x_i and x_j of a particle [in a state with the distribution density $\rho(x_1, x_2, x_3)$]. The covariance matrix of a two-dimensional random vector (X_i, X_j) has the form

$$\begin{pmatrix} D(X_i) & k_{ij} \\ k_{ij} & D(X_j) \end{pmatrix}. \tag{5.1}$$

The general variance of an arbitrary t-dimensional random vector is defined as the determinant of its covariance matrix [Eqns. (2.14), (3.8), and (3.9) represent special cases of this definition]. The general variance of the two-dimensional random vector (X_i, X_j) is thereby expressed by the formula

$$D(X_i, X_j) = D(X_i)\,D(X_j) - k_{ij}^2 .$$

Hence it follows that the covariance modulus k_{ij} can be put in the form

$$|\operatorname{Cov}(X_i, X_j)| = |k_{ij}| = \sqrt{D(X_i)\,D(X_j) - D(X_i, X_j)}, \tag{5.2}$$

and the modulus of the correlation coefficient in the form

$$|r(X_i, X_j)| = \frac{|\operatorname{Cov}(X_i, X_j)|}{\sqrt{D(X_i)\,D(X_j)}} = \sqrt{1 - \frac{D(X_i, X_j)}{D(X_i)\,D(X_j)}}. \tag{5.3}$$

By analogy with Eqn. (4.3), the external volume of a two-dimensional random quantity is given by the formula $V(X_1, X_2) = 2\pi e\sqrt{D(X_1, X_2)}$. It is therefore possible to express the modulus of the correlation coefficient in terms of the external volumes:

$$|r(X_i, X_j)| = \sqrt{1 - \left[\frac{V(X_i, X_j)}{V(X_i)\,V(X_j)}\right]^2}. \tag{5.3'}$$

We shall now elucidate somewhat the geometrical interpretation of covariance and the correlation coefficient using as an example two one-dimensional random quantities.

Suppose that $\rho(x_1, x_2)$ is the distribution density of a two-dimensional random quantity. In order to express the nature of the distribution, it is useful to outline the lines of the $\rho(x_1, x_2)$ density levels on the plane of the variables x_1 and x_2. As an example, Fig. 3 presents the density levels for a two-dimensional normal distribution. The point O' with the coordinates $(m_{\mathbf{X}_1}, m_{\mathbf{X}_2})$ characterises the "centre of gravity" of the distribution and the uncertainty of the position of the two-dimensional random quantity in the directions x_1 and x_2 is characterised by the standard deviations $\sigma(X_1) = \sqrt{D(X_1)}$ and $\sigma(X_2) = \sqrt{D(X_2)}$. The "volume" characteristic of the uncertainty of the position of the two-dimensional random quantity can be expressed, without taking into account the correlation of the components,

by the area of the rectangle $ABCD$, the "centre" of which is at point O', the sides are parallel to the coordinate axes, and their lengths are $2\sigma(X_1)$ and $2\sigma(X_2)$.

We shall now find the eigenvectors of the matrix (5.1) and, assuming them to be the unit vectors of a new coordinate system with origin at the point O', we obtain the intrinsic coordinate system (x_1^0, x_2^0) of the two-dimensional random quantity. The uncertainty of its position with respect to the intrinsic directions is characterised by the standard deviations $\sigma(x_1^0)$ and $\sigma(x_2^0)$, while the "volume" uncertainty is expressed by the area of the rectangle $A^0B^0C^0D^0$ with the centre at the point O' having sides with lengths $2\sigma(x_1^0)$ and $2\sigma(x_2^0)$ which are parallel to the axes x_1^0 and x_2^0 (respectively). If such rectangles are plotted for any orthogonal coordinate system, it is found that among them there is one whose area is an extremum. The area of the rectangle $A^0B^0C^0D^0$ is the smallest of all the possible values. This follows from the following inequality for a two-dimensional random quantity X:

$$D(\mathbf{X}) \leqslant D(X_1)\, D(X_2). \tag{5.4}$$

which is analogous to inequality (2.16).

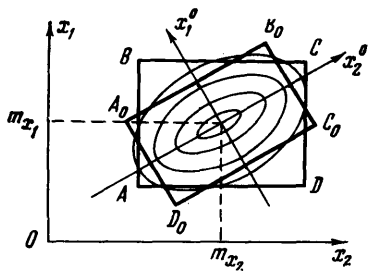

Figure 3.

We may mention further that the length of the sides of the triangles may be made proportional to the standard deviations. In particular they can be made equal to the external dimensions $V(X_i)$. In all cases the ratio of the areas of the rectangles $A^0B^0C^0D^0$ and $ABCD$ will be the same and equal to

$$s = \frac{\sigma(X_1, X_2)}{\sigma(X_1)\,\sigma(X_2)} = \frac{V(X_1, X_2)}{V(X_1)\,V(X_2)}. \tag{5.5}$$

The quantity s will be called the non-correlation coefficient. It is readily seen that its values lie in the range

$$0 \leqslant s \leqslant 1. \tag{5.6}$$

The quantity s is a maximum for non-correlated components. Indeed, in this case the equality sign obtains in formula (5.4) and consequently $s = 1$. The minimum value of s occurs when there is a linear correlation between X_1 and X_2. The minimum eigenvalue $D(X_1^0)$ of the covariance matrix then becomes zero, so that $s = 0$.

Formula (5.3) or (5.3′) shows that the relation between the correlation coefficient r and the non-correlation coefficient s is given by

$$r^2 + s^2 = 1. \tag{5.7}$$

If one remembers further that $\sigma(X_1, X_2) = \sigma(X_1^0)\sigma(X_2^0)$ and $V(X_1, X_2) = V(X_1^0)V(X_2^0)$ characterises the "volume" of the scatter of the non-correlated random quantities X_1^0 and X_2^0, one may conclude that the quantities r and s reflect the change in the "volume" uncertainty of the position of the two-dimensional random quantity on passing to the intrinsic coordinate system.

We shall now turn to the consideration of an n-particle system with the distribution density $\rho(\mathbf{x}) = \rho(\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_n)$. As already mentioned, the covariance matrix $K(\mathbf{X})$ of such a system has the form of the block matrix (3.6). This matrix contains the complete information about the uncertainty of the position of the $3n$-dimensional random vector $\mathbf{X}(\mathbf{X}_1, \mathbf{X}_2, \ldots, \mathbf{X}_n)$ in terms of the approximation defined by the second moments. However, in order to estimate the correlation between the particles (ith and jth), it is useful to have a scalar quantity as well as the matrix $\mathbf{K}_{ij}$. From physical considerations, it should be independent of the choice of the coordinate system of the particles and should reflect the correlation between the particles†.

The above considerations suggest the necessity to extend the concept of correlation based on probability theory to the case of a pair of particles or a system of particles. Therefore our immediate problem is to construct the covariance matrix Q of quantum-mechanical particles in an n-particle system which would constitute a natural extension of the usual covariance matrix‡.

One of the possible generalisations (seemingly the most natural generalisation) was proposed by Del-Re et al.[31] It is based on Eqn. (2.5), where the vectors $\mathbf{x}_s$ and $\mathbf{x}_t$ must be substituted in place of the variables x_s and x_t and the vector product must be regarded as a scalar quantity. As will be shown below, this definition of covariance is defective as regards physical significance.

Another possible generalisation of the covariance matrix was proposed by ourselves on the basis of the concept of general variance. Indeed the general variances $D(\mathbf{X}_i)$ characterising the uncertainty of the position of the coordinates of the ith particle

$$q_{ii} = D(\mathbf{X}_i), \tag{5.8}$$

are adopted as the diagonal elements of the matrix Q. The non-diagonal elements q_{ij} of the matrix Q, i.e. the covariances of the coordinates of the ith and jth particles, are determined, by analogy with Eqn. (5.2), from the formula

$$q_{ij} = \mathrm{Cov}(\mathbf{X}_i, \mathbf{X}_j) = \sqrt{D(\mathbf{X}_i)\,D(\mathbf{X}_j) - D(\mathbf{X}_i, \mathbf{X}_j)}, \tag{5.9}$$

where the plus sign was chosen for the square root term, since the correlation interaction is characterised by the

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†We may note that in the term "correlation energy" employed in quantum chemistry the word correlation means in fact the part of the electron correlation which depends significantly on the choice of the approximate method of calculation used and the term "correlation energy" itself denotes a correction to the energy calculated by the approximate method. The correlation energy is usually understood as the difference between the energy calculated by the Hartree–Fock method and the exact energy of the system.

‡In contrast to the initial covariance matrix K of order $3n$, the generalised covariance matrix Q is of order n.

modulus of the correlation coefficient. The term correlation coefficient for two particles in an n-particle system ($n \geq 2$) will be given to the quantity

$$r(\mathbf{X}_i, \mathbf{X}_j) = \frac{\mathrm{Cov}(\mathbf{X}_i, \mathbf{X}_j)}{\sqrt{D(\mathbf{X}_i)\,D(\mathbf{X}_j)}} = \sqrt{1 - \frac{D(\mathbf{X}_i, \mathbf{X}_j)}{D(\mathbf{X}_i)\,D(\mathbf{X}_j)}}. \qquad (5.10)$$

Using Eqn. (4.3), it is possible to express the correlation coefficient in terms of external volumes:

$$r(\mathbf{X}_i, \mathbf{X}_j) = \sqrt{1 - \left[\frac{V(\mathbf{X}_i, \mathbf{X}_j)}{V(\mathbf{X}_i)\,V(\mathbf{X}_j)}\right]^2}. \qquad (5.10')$$

Therefore r will also be called the external correlation coefficient in contrast to the internal correlation coefficient defined below. Eqns. (5.10) and (5.10′) constitute natural extensions of Eqns. (5.3) and (5.3′). The concept of the non-correlation coefficients can also be evidently extended to the case of a pair of particles:

$$s(\mathbf{X}_i, \mathbf{X}_j) = \frac{\sigma(\mathbf{X}_i, \mathbf{X}_j)}{\sigma(\mathbf{X}_i)\,\sigma(\mathbf{X}_j)} = \frac{V(\mathbf{X}_i, \mathbf{X}_j)}{V(\mathbf{X}_i)\,V(\mathbf{X}_j)}. \qquad (5.11)$$

Therefore the correlation coefficient of the particles $r(\mathbf{X_i}, \mathbf{X_j})$ and the non-correlation coefficients $s(\mathbf{X_i}, \mathbf{X_j})$ have the same significance as the usual coefficients r and s: they reflect the degree of condensation of the two-particle subsystem. It is easy to verify the following properties of the correlation coefficient.

1. $r(\mathbf{X_i}, \mathbf{X_j}) = 0$ if the ith and jth particles are independent, i.e. their density is represented by the product $\rho(\mathbf{x_i})\rho(\mathbf{x_j})$.

2. $r(\mathbf{X_i}, \mathbf{X_j}) = 1$ if there is a linear relation between the coordinates of the ith and jth particles§; the converse assertion is also valid: if $r(\mathbf{X_i}, \mathbf{X_j}) = 1$, there is at least one linear relation between the coordinates.

3. The correlation coefficient satisfies the inequality

$$0 \leqslant r(\mathbf{X}_i, \mathbf{X}_j) \leqslant 1.$$

The above properties are fully analogous to those of the usual correlation coefficient. Thus, for the usual correlation coefficient property(1) is irreversible, i.e. when $r(\mathbf{X_i}, \mathbf{X_j}) = 0$, the given particles need not necessarily be independent. There can even be a functional relation between them. This factor and property (2) suggest that the correlation coefficient (the usual and extended coefficient) should be more correctly called the linear correlation coefficient.

The analogue of the correlation coefficient for the approximation of a non-linear functional relation is discussed in Section III, 6.

In conclusion of this subsection we emphasise that the quantities $D(\mathbf{X_i})$, $D(\mathbf{X_i}, \mathbf{X_j})$, $\mathrm{Cov}(\mathbf{X_i}, \mathbf{X_j})$ and $r(\mathbf{X_i}, \mathbf{X_j})$ satisfy the requirement of invariance in relation to the orthogonal transformations of the coordinate systems of the individual particles. We may note that the definitions of covariance and correlation coefficient proposed by Del-Re et al.[31] do not satisfy this invariance condition.

§This means that there is a functional relation of the type:

$$a_1 x_{i1} + a_2 x_{i2} + a_3 x_{i3} + b_1 x_{j1} + b_2 x_{j2} + b_3 x_{j3} = 0.$$

6. Non-Linear Correlation. Internal Correlation Coefficient

When we speak of a statistical relation for random quantities, we are interested primarily in the possible similarity of the given statistical relation to a functional relation. To assess this similarity, it is necessary to determine a quantity characterising its measure. The linear correlation coefficient cannot serve as such a measure since, as already shown, there exist distribution in which the variables are linked by a functional relation, while the correlation coefficient is zero.

We recall that the modulus of the correlation coefficient defined by Eqn. (2.6) for two one-dimensional random quantities is expressed in terms of the external volumes by Eqn. (5.3′). The formal replacement of the external by internal volumes permits the introduction of the quantity

$$r_H(X_i, X_j) = \sqrt{1 - [v(X_i, X_j)/v(X_i)\,v(X_j)]^2}, \qquad (6.1)$$

which we shall call the internal correlation coefficient¶. The subscript H means that this quantity is defined in terms of the entropy, namely

$$r_H(X_i, X_j) = \sqrt{1 - \exp[2H(X_i, X_j) - 2H(X_i) - 2H(X_j)]}.$$

We shall now consider the properties of the internal correlation coefficient. In the first place it follows from the inequality[29] $H(X, Y) \leqslant H(X) + H(Y)$ that the quantity $r_H(X, Y)$ also varies in the range $0 \leqslant r_H \leqslant 1$. The minimum value is reached for independent X and Y, i.e. when the probability density of the two-dimensional random quantity is a product of the densities of the quantities X and Y: $\rho(x, y) = \rho_1(x)\rho_2(y)$. Indeed for the independent quantities $H(X, Y) = H(X) + H(Y)$, $\exp[2H(X, Y) - 2H(X) - 2H(Y)] = 1$ and hence $r_H(X, Y) = 0$. On the other hand, if the random quantities are linked by a functional relation $Y = \varphi(X)$, then $r_H(X, Y) = 1$.

We shall prove this assertion. For simplicity, we shall assume that the function φ has a converse function $X = \theta(Y)$. Then the density of the joint distribution of two random quantities is of the form

$$\rho(x, y) = f(x)\,\delta(y - \varphi(x)) = f(x)\,\delta(x - \theta(y)), \qquad (6.2)$$

where the function f satisfies the condition $\int f(x)dx = 1$. In addition the convergence of the integrals is postulated:

$$H[f] = -\int f(x) \ln f(x)\,dx,\quad H[f(\theta)] = -\int f[\theta(y)] \ln f[\theta(y)]\,dy.$$

The functional of the entropy has not been defined for the density (6.2). It must be additionally defined as the limit of the functionals of the entropy H_n for the densities $\rho_n(x, y) = f(x)g_n[y - \varphi(x)]$, where g_n is a δ-sequence. We have

$$H_n = -\int\int \rho_n(x, y) \ln \rho_n(x, y)\,dx\,dy = -\int\int f(x)\,g_n(y - \varphi(x)) \ln f(x)\,dx\,dy -$$
$$-\int\int f(x)\,g_n(y - \varphi(x)) \ln g_n(y - \varphi(x))\,dx\,dy = -\int f(x) \ln f(x)\,dx -$$
$$-\int f(x)\,dx \int g_n(y - \varphi(x)) \ln g_n(y - \varphi(x))\,dy = H[f] + H[g_n].$$

By virtue of the hypothesis made in Section III, 1 concerning the entropy of the δ-function and the condition for $H(f)$, we have $\lim_{n\to\infty} H_n = H[f] + \lim_{n\to\infty} H[g_n] = -\infty$.

¶On the other hand the usual correlation coefficient, which is expressed in terms of the external volumes, can also be reasonably called the external correlation coefficient.

Moreover, $\rho_1(x) = \int f(x)\delta[y - \varphi(x)]dy = f(x)$ and $\rho_2(y) = \int f(x)\delta[x - \theta(y)]dx = f[\theta(y)]$. Therefore $H(X) = H[f]$ and $H(Y) = H[f(\theta)]$. Since both these quantities are finite, it follows that $\exp[2H(X, Y) - 2H(X) - 2H(Y)] = 0$ and therefore $r_H(X, Y) = 1$.

The definition (6.1) can be naturally extended to the multidimensional case. The internal correlation coefficient of two particles will be defined as

$$r_H(X_i, X_j) = \sqrt{1 - [v(X_i, X_j)/v(X_i)\,v(X_j)]^2}. \qquad (6.1')$$

The properties of this quantity are as follows.

1. $r_H(X_i, X_j) = 0$ if the quantities X_i and X_j are independent, i.e. $\rho(x_i, x_j) = \rho_i(x_i)\rho_j(x_j)$.

2. If there is a functional relation between the coordinates of the vectors x_i and x_j, then $r_H(X_i, X_j) = 1$; conversely if $r_H = 1$, the internal volume of a system of two particles (the ith and jth particles) is zero.

3. For any distribution density $\rho(x_i, x_j)$, the quantity $r_H(X_i, X_j)$ satisfies the inequalities

$$0 \leqslant r_H(X_i, X_j) \leqslant 1.$$

The equality $r_H(X_i, X_j) = 1$ is not a characteristic property of the functional relation. It is characteristic of the situation where the internal volume becomes zero.

7. Many-Particle Correlation

As stated above, electron correlation is usually estimated from the energy standpoint. Below we quote formulae for the estimation of many-electron correlation in the language of the concepts of probability theory. They are obtained by a natural extention of the formulae for two-particles.

The external correlation coefficient of a subsystem of μ particles ($2 \leqslant \mu \leqslant n$) will be defined as

$$r(X_1, X_2, \ldots, X_\mu) = \left[1 - D(X_1, X_2, \ldots X_\mu) \Big/ \prod_{i=1}^{\mu} D(X_i)\right]^{1/2}. \qquad (7.1)$$

This quantity can evidently be expressed also in terms of external volumes:

$$r(X_1, X_2, \ldots, X_\mu) = \left\{1 - \left[V(X_1, X_2, \ldots, X_\mu) \Big/ \prod_{i=1}^{\mu} V(X_i)\right]^2\right\}^{1/2}.$$

The internal correlation coefficient is defined similarly:

$$r_H(X_1, X_2, \ldots, X_\mu) = \left\{1 - \left[v(X_1, X_2, \ldots, X_\mu) \Big/ \prod_{i=1}^{\mu} v(X_i)\right]^2\right\}^{1/2}. \qquad (7.2)$$

The properties of these quantities are as follows.

1. If one of the particles $x_1, x_2, \ldots, x_\mu$ is independent of the others, then $r(X_1, X_2, \ldots, X_\mu) = r_H(X_1, X_2, \ldots, X_\mu) = 0$.

2. If there is a functional relation between the coordinates of the particles $x_1, x_2, \ldots, x_\mu$, then $r_H(X_1, X_2, \ldots, X_\mu) = 1$†; if this relation is linear, then also $r(X_1, X_2, \ldots, X_\mu) \leqslant 1$.

3. Both quantities satisfy the inequalities $0 \leqslant r(X_1, X_2, \ldots, X_\mu) \leqslant 1$ and $0 \leqslant r_H(X_1, X_2, \ldots, X_\mu) \leqslant 1$.

†Nothing can be said about the quantity $r(X_1, X_2, \ldots, X_\mu)$. It may even be zero.

8. The Uncertainty Principle

As noted in the introduction, the concepts of entropy, variance, and effective volumes are very closely related to one of the most important principles of quantum mechanics—the uncertainty principle.

For a quantitative expression of the uncertainty principle, the variances (or standard deviations) of canonically coupled quantities are usually employed as measures of their uncertainty. We shall consider initially the case of a one-dimensional particle and shall examine two quantities: the coordinate x and momentum p‡. Heisenberg's uncertainty principle is expressed in terms of Weyl's inequality:

$$D_x D_p \geqslant \tfrac{1}{4}(\text{at. units}) \qquad (8.1)$$

where D_x and D_p are the variances of the coordinate and the momentum respectively. Suppose that D_x is "small" which corresponds to the localisation of the coordinate of the particle; then the variance of the momentum must be large, i.e. $D_p \geqslant 1/4D_x$. Otherwise inequality (8.1) will not hold. However, the method of expressing the uncertainty principle in the form of inequality (8.1) suffers from an important disadvantage.

Suppose that is it known that the particle is localised in fairly small regions around two or a greater (finite) number of centres. The variance of this distribution can have any value, as can be seen, for example, from Fig. 4. Weyl's inequality will not rule out in this case the possibility of determining the momentum with a fairly high degree of accuracy. Nevertheless this type of situation is in reality excluded. The uncertainty principle formulated in the entropy form [2,32,33],

$$H_x + H_p \geqslant C > 0 \qquad (8.2)$$

shows that in our example the distribution density of the momentum not only cannot be fully concentrated in a small region around a certain point but it cannot be localised even in the vicinity of a finite number of points.

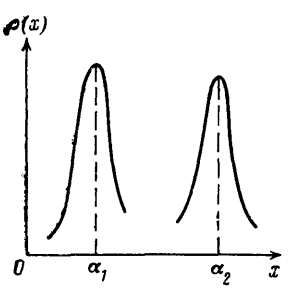

Figure 4.

Indeed if the particle is localised in a small region Ω around a certain point, then $f(x) > 1$ for $x \in \Omega$ and $f(x) = 0$ for $x \notin \Omega$. Therefore $f(x)\ln f(x) \geqslant 0$ and consequently the entropy integral is negative. The greater the degree of localisation the smaller the entropy and the smaller the

‡If the state of the one-dimensional particle in the coordinate representation is described by a wave function $\psi(x)$, then in the momentum representation it corresponds to the wave function $\psi(p) = (1/\sqrt{2\pi})\int \psi(t)e^{-ipx}dx$.

effective size. It follows from inequality (8.2) that the quantities H_x and H_p cannot assume simultaneously values so small that $H_x + H_p < C (C > 0)$.

In the general case the functionals D and H do not define one another unambiguously. However, they are linked to one another by inequality (1.6). It follows from this inequality that the expression of the uncertainty principle in the entropy form (8.2) is stronger than in the variance from (8.1), since

$$0 < C \leqslant H_x + H_p \leqslant \frac{1}{2} \ln (2\pi e D_x D_p). \tag{8.3}$$

This factor in fact makes it possible to investigate certain general physical aspects of the uncertainty principle which are not embraced by Weyl's inequality.

The problem of the value of the constant $C (C > 0)$ in inequality (8.2) is of fundamental importance. If $C = \ln \pi e$, the implication is that the two characteristics of uncertainty in the phase space $D_x D_p$ and $v_x v_p / 2\pi e$ assume identical minimum values. There is every reason to suppose that this does indeed happen and that the minimum uncertainty is achieved with Gauss functions. However, there is at present no rigorous proof of this assertion.

The derivation of inequality (8.1) has been frequently discussed in the literature and therefore we shall not consider it in detail. We shall only mention that, in order to prove Weyl's inequality, it is sufficient to employ the most general properties of the Fourier transformation in the Gilbertian space $L_2(-\infty, \infty)$§.

We shall consider briefly the proof of inequality (8.2). Let $\varphi(x) \in L_r(-\infty, \infty)$ and let $\psi(t)$ be its Fourier transform. Then $\psi(p) \in L_q(-\infty, \infty)$, where $q = r/(r-1)$. Babenko[34] showed that for even values of q the following inequality holds

$$\| \psi \|_q \leqslant M(r) \| \varphi \|_r,$$

where

$$M(r) = \left(\frac{r}{2\pi}\right)^{\frac{1}{2r}} \left(\frac{q}{2\pi}\right)^{\frac{1}{2q}}.$$

Using the Riesz theorem, the present authors showed[32] that for $r \in [4/3, 2]$ we have

$$\| \psi \|_q \leqslant M^{2(r/2-1)} \| \varphi \|_r, \tag{8.4}$$

where $M = 0.592$¶. On taking logarithms in inequality (8.4), we obtain

$$\frac{1}{q} \ln \int |\psi|^q \, dp \leqslant 2 (2/r - 1) \ln M + \frac{1}{r} \ln \int |\varphi|^r \, dx. \tag{8.5}$$

Consider the function

$$\chi(r) = \frac{1}{q} \ln \int |\psi|^q \, dp - \frac{1}{r} \ln \int |\pi|^r \, dx - 2 \left(\frac{2}{r} - 1\right) \ln M.$$

§Henceforth the following notation will be employed: $L_r(-\infty, \infty)$ is defined as a set of functions $f(x)$ of a single real variable x for which the values of the integral $\int |f(x)|^r dx = I_r$ are finite. The quantity $(I_r)^{1/r}$ is designated by $\| f(x) \|_r$ and is called the norm of the function $f(x)$.

¶The constant is quoted to within 0.001.

Then it follows from inequality (8.5) that $\chi(r) \leqslant 0$ for $4/3 \leqslant r \leqslant 2$. Moreover, $\chi(2) = 0$. Therefore $\chi'(2 - 0) \geqslant 0$. Formal differentiation of the function $\chi(r)$ leads to the expression

$$\chi'(r) = \frac{1}{r^2} \ln \int |\psi|^q \, dp - \frac{1}{r(r-1)} \frac{\int |\psi|^q \ln |\psi| \, dp}{\int |\psi|^q \, dp} +$$

$$+ \frac{1}{r^2} \ln \int |\varphi|^r \, dx - \frac{1}{r} \frac{\int |\varphi|^r \ln |\varphi| \, dx}{\int |\varphi|^r \, dx} + \frac{4}{r^2} \ln M.$$

Bearing in mind that $\| \varphi \|_2 = \| \psi \|_2 = 1$ we obtain for $r = 2$ the inequality

$$- \int |\psi|^2 \ln |\psi|^2 \, dp - \int |\varphi|^2 \ln |\varphi|^2 \, dx + 4 \ln M \geqslant 0.$$

and hence the entropy expression for the uncertainty principle can be formulated as $H_x + H_p \geqslant C$, where $C \simeq 2.100$.

We have considered hitherto the uncertainty principle in terms of a one-dimensional treatment. We shall now proceed to a real physical system—a quantum-mechanical particle or a system of such particles.

The uncertainty of the position of the coordinates of an n-particle system [in the state $\psi(x_1, \ldots, x_n)$] is characterised by the covariance matrix $K(\mathbf{X})$, the general variance $D(\mathbf{X})$, and the entropy $H(\mathbf{X})$. The one-dimensional uncertainty in the direction of the $3n$-dimensional vector $\mathbf{c}$ is expressed by the quantity $[K(\mathbf{X})\mathbf{c}, \mathbf{c}]$ and the "volume" uncertainty is expressed by the quantities $D(\mathbf{X})$ and $H(\mathbf{X})$.

In the momentum representation the same state of the n-particle system is described by the wave function $\tilde{\psi}(\mathbf{p}) = \psi(\mathbf{p}_1, \mathbf{p}_2, \ldots, \mathbf{p}_n)$, which is a Fourier transform of the initial function

$$\tilde{\psi}(\mathbf{p}) = \frac{1}{(2\pi)^{n/2}} \int e^{-i(\mathbf{p}, \mathbf{x})} \psi(\mathbf{x}) \, d\mathbf{x}.$$

The distribution density of the momenta $|\tilde{\psi}(\mathbf{p})|^2$ is also normalised to unity, which makes it possible to treat it as the distribution density of a $3n$-dimensional random quantity $\mathbf{P} = (\mathbf{P}_1, \mathbf{P}_2, \ldots, \mathbf{P}_n)$, where the random three-dimensional vector $\mathbf{P}_j$ corresponds to the momentum of the jth particle. The covariance matrix $K(\mathbf{P})$ of the random vector $\mathbf{P}$ characterises the uncertainty of the positions of the momenta in the n-particle system and the general variance $D(\mathbf{P})$ and the entropy $H(\mathbf{P})$ characterise their "volume" uncertainty.

The above characteristics of multidimensional quantum-mechanical systems based on probability theory permit the formulation of the Heisenberg uncertainty principle directly in the multidimensional form. Indeed, it is possible to prove the validity of the inequalities

$$H(\mathbf{X}) + H(\mathbf{P}) \geqslant \ln (2\pi)^{3n} \tag{8.6}$$

and

$$D(\mathbf{X}) D(\mathbf{P}) \geqslant (1/4)^{3n} \text{ (at. units)} \tag{8.7}$$

which constitute natural generalisations of inequalities (8.2) and (8.1) respectively. The uncertainty relations, expressed in terms of the internal and external volumes

$$v(\mathbf{X}) v(\mathbf{P}) \geqslant (2\pi)^{3n} \text{ (at. units)} \tag{8.8}$$

and

$$V(\mathbf{X}) V(\mathbf{P}) \geqslant (\pi e)^{3n} \text{ (at. units)} \tag{8.9}$$

follow from inequalities (8.6) and (8.7). All the inequalities (8.6)–(8.9) express the fact that the volume uncertainty of an n-particle system cannot

be fairly small in the coordinate and momentum representations simultaneously. We may note that inequality (8.2) or, what amounts to the same thing,

$$D(\mathbf{X}) - {}^1/_4 D^{-1}(\mathbf{P}) \geqslant 0$$

can be generalised also in terms of the covariance matrices. It is found that the matrix

$$T = K(\mathbf{X}) - {}^1/_4 K^{-1}(\mathbf{P})$$

is positively defined, i.e. for any $3n$-dimensional vectors c we have the inequality

$$(Tc, c) \geqslant 0. \qquad (8.10)$$

It is possible to show that inequality (8.10) follows from the uncertainty relation in the variance form for each pair of canonically coupled variables (one-dimensional variables).

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Reactions of Silicon and Germanium with Halogens, Their Hydrides, and Organic Halogen Derivatives

A.I.Gorbunov, A.P.Belyi, and G.G.Filippov

Results published up to 1972 inclusive on the kinetics and the mechanism of the reactions of silicon and germanium with halogens, their hydrides, and organic derivatives are summarised. The kinetics and the mechanism of formation of the most important organic and halogenated derivatives of silicon and germanium, which have found wide industrial application, are discussed. Published data are analysed in the light of modern views on the progress of heterogeneous catalytic reactions. A list of 163 references is included.

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I. INTRODUCTION

The interaction of silicon or germanium with a halogen, its hydride, or an organic derivative is a complicated heterophase catalytic process, in which a gaseous halide reacts with a solid in the presence of a catalyst with the formation mainly of gaseous reaction products. The kinetics of such "gas–solid" processes, including the gasification of coal[1], remained for a long period a little studied field.

During the past decade, however, the reactions of silicon and germanium with halogenated hydrocarbons have found wide application in the preparation of organometallic monomers[2-4] for the industrial production of novel oligomers and polymers possessing valuable technical properties. The halogenation and the hydrohalogenation of silicon and germanium are used also in various branches of semiconductor technology[5,6].

The practical significance of these reactions has arisen during recent years from extensive investigations of the kinetics and the mechanism of the formation of silicon, germanium, organosilicon, and organogermanium halides. Thorough study of this branch of chemistry became possible when elementary silicon and germanium of the required purity became available in the necessary quantities for kinetic experiments.

The reactions of silicon and germanium with halogens and organic halides appear a fortunate example for elucidating general aspects of the reactivity of solids on treatment with gaseous reactants to form volatile products—the effects of impurities and catalytic additives, the nature of the halogen, and other factors on the activation energy, the kinetic order of the reaction, etc.

Study of the kinetics and the mechanism of several preparations of silicon and organosilicon halides, forming the basis of large-scale production[7-12], has been connected with the development of modern methods of design of reaction vessels and the modelling of chemical processes[13,14].

Earlier surveys[15-19] were concerned mainly with the reactions of silicon with alkyl chlorides and hydrogen chloride, and ignored data on reactions with other halides, as well as information on the corresponding reactions of germanium—an analogue of silicon—about which a large number of publications had already appeared. It has become necessary to analyse and generalise results on the kinetics and the mechanism of the formation of silicon, germanium, organosilicon, and organogermanium halides, which is the purpose of the present Review. The chemical properties and the methods of preparation of these compounds are not dealt with, since several special publications have appeared on this aspect[2-4,20,21].

II. KINETICS OF REACTIONS

1. Reactions of Silicon and Germanium with Halogens X_2

The reaction of halogens with silicon and germanium provides the simplest method for preparing the halides. These elements form compounds of types MX_4 and MX_2, as well as polyhalogenated silanes and germanes M_nX_{2n+2}.[21,22] Quadrivalent compounds are more characteristic of silicon; germanium typically forms both quadrivalent and bivalent halides. Under normal conditions polyhalides are formed in small quantities.

Fluorination. Silicon reacts with fluorine even at room temperature to form gaseous silicon tetrafluoride. A detailed gravimetric study of this reaction has been made on single crystals of silicon[23-25]. Initially the process is slow because of the presence of an oxide film on the surface. With a fluorine pressure of 20–150 torrs the reaction on the (111) face at 20°C is of the first order with respect to fluorine[24]. Study of the fluorination of silicon plates (99.9% pure) over the pressure range 2.8–52.5 torrs at temperatures of 75–900°C established[25] that at low temperatures (120–150°C) the activation energy was 12 kcal mole^{-1} and the order with respect to fluorine $n_{F_2} = 1$. At high temperatures the effect of external diffusion lowered the activation energy to 1.3 kcal mole^{-1} and the kinetic order to $n_{F_2} = 0.6$.

No published data are available on the kinetics of the fluorination of germanium.

Chlorination. Investigations of the chlorination of silicon and germanium[26-30] have established that the purity of the solid reactant and the presence of catalytic additions of copper influence the kinetics[26,27]. At low temperatures tetrachloro-derivatives are the main products. Table 1 lists the kinetic parameters of their formation. The results show that additions of copper to pure specimens

and impurities in technical silicon tend to enhance the reactivity of the solid. This is apparent in a sharp drop in the temperature at which reaction begins, a decrease in activation energy, and a raising of the kinetic order with respect to chlorine. The activation energies of reactions with silicon (mono- and poly-crystalline specimens with added copper) are usually higher than those for comparable specimens of germanium.

Table 1. Kinetic parameters of the formation of silicon and germanium tetrahalides.

Contact mass	Conditions of expt. T, °C	Conditions of expt. P_{X_2}, torrs	Reaction order n_{X_2}	Activation energy, kcal mole^{-1}	Ref.
fluorination					
Monocryst. Si	20	20—150	1.0	—	24
Polycryst, Si (99.9%)	120—150	3—52	1.0	12	25
chlorination					
Monocryst. Si					
Polycryst. Si (99.9999%)	20—580	—	2.0	35	28
	254—292	12—64	0.4	24.4	26
Chemically purified Si (99.8)	320—370	—	—	18	29
Technical Si (98%)	180—240	12—82	1.0	15.1	26
Polycryst. Si-Cu alloy (10% Cu)	96—115	20—68	0.6	11.6	27
Monocryst. Ge	175—258	15—160	0	25.0	30
Polycryst. Ge (99.999%)	115—142	19—70	0.4	18.1	27
Polycryst. Ge-Cu alloy (13.5% Cu)	117—160	16—70	0.7	8.4	27
iodination					
Polycryst. Ge (99.999%)	300—550	10^{-2}—10^{-4}	—	18.5	31
Polycryst. Ge	—	—	0.5	31	32

Bromination. Studies have been made on single crystals, technical silicon, and ferrosilicon (15% of iron)[33,34]. Added metals (copper, iron, cobalt, nickel, silver) lower the temperature at which bromination of monocrystalline silicon begins. Additions of copper and its bromides also enhance the reactivity of technical silicon and ferrosilicon, and tend to increase the yield of tetrabromosilane. No kinetic data have been published on the bromination of silicon or germanium.

Iodination. No kinetic data have appeared on the iodination of silicon, and results for that of germanium are contradictory. Over the temperature range in which the reaction is not complicated by diffusion the activation energy is 31 kcal mole^{-1} and the kinetic order $n_{I_2} = 0.5$.[32] The reaction on the (110), (100), and (111) faces of germanium has been ascribed[31] activation energy 18.5 kcal mole^{-1} and reaction order $n_{I_2} = 1.18$, whereas other workers[35] give $n_{I_2} = 0$. These differencies are probably due to experimental inaccuracy, since similar specimens of germanium were used and closely similar temperature ranges (280–460° and 300–500°C).[31,32]

2. Reactions of Silicon and Germanium with Hydrogen Halides HX

The main products are di-, tri-, and tetra-halogenated silicon and germanium derivatives H_2MX_2, HMX_3, and MX_4, under certain conditions with a small quantity of the monohalogeno-derivatives. The composition of the products depends on the temperature of preparation, the purity of the solid, and additions of copper, whose catalytic effect on reactions with hydrogen chloride had been noted long ago by Combes[36].

Hydrochlorination of silicon

The first kinetic study of the process was made by Trambouze[37]. The activation energy of the formation of trichlorosilane was found to be 3 and 10 kcal mole^{-1} for pure silicon and for a silicon–copper alloy. However, the higher value of 28 kcal mole^{-1} has since been obtained by Joklik and Bažant[38], who used a mixture of powdered technical silicon (98% Si) and copper (Si : Cu = 11 : 1) to prepare trichlorosilane under similar conditions over the range 180–220°C. Such contradictory values of the activation energy are due to errors of method in the earlier work[37]: experimental results obtained at the high temperatures of 250–600°C were probably distorted by diffusion factors.

Especial attention has since been paid[39-41] to improving the experimental method, and the effect of pressure has also been studied. At low temperatures silicon reacts with hydrogen chloride mainly with the formation of trichlorosilane. The variation in the surface of the solid reactant and the effect of this variation on the reaction velocity have been examined[41]. The reactivity of silicon is significantly affected by the presence of impurities. The temperature at which reaction begins and the activation energy fall as the impurity content of silicon increases in the sequence

pure (99.9999%) > purified (99.8%) > technical (98%).

In spite of a substantial difference in reactivity, the composition of the products in the region of the temperature at which reaction began was almost identical for these samples of silicon: the content of trichlorosilane in the condensate was 93–98%.

The composition of the reaction products is significantly affected by the addition of copper to the silicon. Each purity grade silicon has a definite temperature range within which the dichlorosilane content increases[41]. In the presence of copper this content rises to 30–35%.[43] The temperature ranges for the selective formation of dichlorosilane are 420–440°, 250–320°, and 220–320°C respectively for pure silicon, technical silicon, and all types of silicon in the presence of copper[43,44].

The kinetic order with respect to hydrogen chloride is close to zero with specimens of pure and purified silicon, but 0.5 with technical silicon. The reaction products —hydrogen and trichlorosilane—have no effect on the rate of the process, and the order with respect to them is zero[40].

Since the formation of trichlorosilane is almost irreversible[42], the rate equation can be written

$$r = k \cdot P_{HCl}^{n_{HCl}} .$$

The kinetic parameters of the process are affected even by small additions (0.001–0.04%) of copper to pure silicon: the temperature at which reaction begins is lowered almost by 100 deg (Table 2) and the activation energy by 6–10 kcal mole^{-1}, while the order of reaction with respect to hydrogen chloride is raised[43-45]. Table 2 reveals no correlation between the copper content and the kinetic parameters E and n_{HCl}: thus specimens with a tenfold difference in copper contents (0.04 and 0.3%) have almost the same kinetic parameters. This is probably

connected with the way in which copper is distributed during preparation of the alloys. Comparison of the reactivity of silicon of different degrees of purity showed[44] that the specific rates with pure and with chemically purified silicon are respectively around 0.01% and 1% of those with technical silicon and silicon–copper alloys.

Table 2. Effects of impurities in silicon and additions of copper on kinetic parameters of the synthesis of trichlorosilane[43–45].

Contact mass	Reaction starts at °C	Reaction order n_{HCl}	Activation energy, kcal mole^{-1}	Specific rate*, mmole m^{-2} min^{-1}
Pure Si (99.9999%)	300—320	0.0—0.1	34.4	$2.8\cdot10^{-5}$
Chemically purified Si (99.8%)	220—240	0.0—0.1	27.0	$7.1\cdot10^{-3}$
Technical Si (98.0%)	180—200	0.45—0.5	20—23	$2.7\cdot10^{-2}$
Pure Si alloyed with Cu (%)				
0.0013	250	—	27.0	—
0.04	200	0.65	24.0	—
0.08	200—240	0.24	28.4	—
0.3	180—200	0.54	24.5	—
Alloy of pure Si and Cu (%)				
2.4	180—200	0.21	29.0	$1.5\cdot10^{-1}$
8.6	180—200	0.43	23.0	$3.6\cdot10^{-1}$

*Specific rate calculated for 250 °C and p_{HCl} = 450 torrs.

Hydrochlorination of germanium

Use of copper both as an alloy[46] and as a powdered mechanical mixture[47] has a marked affect on the kinetics: the temperature at which reaction begins is lowered, and the yield of the main product (trichlorogermane) is raised. The content of tetrachlorogermane increases with rise in temperature. Formation of dichlorogermane is not observed.

Table 3. Kinetic parameters of the hydrochlorination of germanium[46,163].

Contact mass	Reaction starts at, °C	Reaction order n_{HCl}	Activation energy, kcal mole^{-1}
Pure Fe (99.9999%)	340	0.35	22—24.0
Mixture of Ge and Cu (10%) powders	300	1.0	12.5
Ge–Cu alloy (30% Cu)	180	0.8	11.4—12.3
Ge–Cu alloy (3% Cu)	210	1.3	10.2—13.1

Copper is still more effective in corresponding processes with germanium than with silicon[46]: the activation energy is roughly halved, and the kinetic order with respect to hydrogen chloride is raised from ~0.35 to 1.0 (Table 3). The value n_{HCl} = 0.8 given[46] for pure germanium is probably incorrect: repetition of the measurement has shown that n_{HCl} = 0.35.

Closely similar activation energies were obtained for reaction with germanium–copper alloys and with powdered mixtures, but reaction began at different temperatures. A more extended reactive surface of contact between copper and germanium could be regarded as most likely in the former case, or else the addition of copper tends to increase the pre-exponential factor in the reaction rate constant.

The rate of entry of germanium into reaction increases as it is consumed[18]. This is probably due to an increase in the surface area of germanium during the reaction, as was established for the hydrochlorination of silicon[41].

Hydrobromination of silicon and germanium

These processes occur similarly to hydrochlorination. Impurities in the solid reactant and additions of copper have marked effects on the kinetics. Results obtained under comparable conditions are given in Table 4. The temperature of the start of reaction and the activation energy are markedly lower in the presence of copper, while the kinetic order with respect to the gaseous reactant is higher.

Table 4. Kinetic parameters of the hydrobromination of silicon[48] and germanium[49].

Contact mass	Reaction starts at, °C	Specific rate*, mmole m^{-2} min^{-1}	Reaction order n_{HBr}	Activation energy, kcal mole^{-1}
Silicon				
Pure (99.9999%)	320	$1.2\cdot10^{-5}$	0.06—0.2	35—37
Pure Si + 10% Cu from CuCl	220	$2.9\cdot10^{-2}$	0.6—0.8	20—22
Technical (98%)	220	$1\cdot10^{-2}$	0.55—0.51	24—25
Technical Si + 10% Cu from CuCl	185	—	0.6—0.63	18.0
Germanium				
Pure (99.9999%)	325	—	0.1—0.15	24—25
Pure Ge + 10% Cu from CuCl	175	—	0.75—0.8	12.0

*At 250 °C and p_{HBr} = 300 torrs.

The value given in Table 4 for the activation energy with a pure specimen of germanium (25 kcal mole^{-1}) differs from that obtained in Ref. 50 (19 kcal mole^{-1}), the probable reason being differences in experimental conditions, primarily the higher temperature range (400–600 °C) used in this work. Raising the temperature of the hydrobromination of germanium gives rise to appreciable quantities of the tetrabromide accompanying tribromogermane[51]. The rate estimated in this paper from the loss in weight of germanium during the reaction therefore represents actually the rate of formation of two products ($HGeBr_3$ and $GeBr_4$).

Hydroiodination of germanium

Kinetic investigation of the reaction of hydrogen iodide with germanium (single crystal, (111) face) showed[52] that n_{HI} = 1 and E = 16.6 kcal mole^{-1}.

3. Formation of Organosilicon and Organogermanium Halides

The reaction of organic halides with silicon and with germanium in the presence of catalysts forms the basis of the so called direct synthesis of halogenated alkylsilanes and alkylgermanes, the chief method of obtaining organosilicon [16,22,53] and organogermanium [54,55] monomers. A mixture of products of types RMX_3, R_2MX_2, R_2MX, and $RMHX_2$ is obtained, where R = CH_3, C_2H_5, C_6H_5, etc. X = Cl, Br, and M = Si, Ge.

Highly selective preparation of these derivatives is extremely difficult in comparison with the halogenation and hydrohalogenation of silicon or germanium. Only the dimethylsilicon and dimethylgermanium dihalides can be obtained in high yields (90–95%) under fairly mild conditions. Dimethyldichlorosilane finds wide application in industry, and obviously kinetic investigations of its formation are most fully represented in the literature.

Table 5. Kinetic parameters of the synthesis of dimethyldichlorosilane.

No.	Contact mass Si + Cu (9:1)	Pressure, atm	Reaction order n_{MeCl}	Activation energy, kcal mole^{-1}	Ref.
1.	Mixed powdered Si (99.9%) + Cu	0.1—0.6	1.0	25.3	56
2.	Mixed powdered Si (98%) + Cu	1—7	1.0	20.1	57
3.	Mixed powdered Si (99.0%) + Cu from CuCl	1	1.0	26.6	16,58
4.	Si (99.98%)-Cu with added Al + Zn	4.6—12.7	1.0	25.8	16,58,59
5.	Mixed powdered Si + Cu	—	4.0	20.0	60
6.	Mixed powdered Si (99.0%) + Cu	1	1.85	9.0	61
7.	Mixed powdered Si (99.9999%) + Cu	0.15—0.9	0.96—1.1	29.0	62
8.	Mixed powdered Si (99.85%) + Cu	0.15—0.9	0.96—1.2	25.0	62
9.	Mixed powdered Si (98%) + Cu from CuCl	0.15—0.9	0.91—0.96	21.0	62
10.	Mixed powdered Si (98%) + Cu from $Cu(OH)_2$	0.15—0.9	1.1	19.2—20.0	63

Early kinetic investigations of the formation of dimethyldichlorosilane [15,56–61] disregarded the effect of the purity of the silicon, which might have been very substantial, as is evident from the above data on chlorination and hydrochlorination. Probably also because of other procedural errors, kinetic parameters obtained by different investigators varied considerably: thus values from 1 to 4 have been obtained for the order of the reaction with respect to methyl chloride, and from 9 to 27 kcal mole^{-1} for the activation energy. Although this reaction order seems [62] almost independent of the purity of the silicon, this factor nevertheless affects the activation energy (Table 5, Nos. 1, 2, and 7–9). Results for contact masses based on technical silicon, obtained by reducing copper(I) chloride and copper(II) hydroxide (Nos. 9 and 10), indicate that the chemical composition—the purity of the initial components—is of primary importance, not the mode of preparation of the contact mass.

The above experimental data are consistent with a kinetic equation of the type

$$r = K \cdot P_{MeCl}$$

for the formation of dimethyldichlorosilane. The very widely used kinetic equation proposed by Bažant et al.[56]

$$r = \frac{K \cdot P_{MeCl}}{[1 + a_{Me_2SiCl_2} \cdot P_{Me_2SiCl_2} + \sqrt{a_{MeCl} \cdot P_{MeCl}}]^2},$$

which contains the adsorption coefficients a of methyl chloride and of the product, can in several cases be considerably simplified. Kinetic data indicate first-order dependence on methyl chloride, so that the term $(a_{MeCl}P_{MeCl})^{1/2}$ can be neglected. Experimental results for the reaction under dynamic conditions with variation of P_{MeCl} from 1 to 6 atm at a low temperature could be well represented by the simplified equation [56,57], although the above term had to be taken into account with rise in temperature. This term evidently represents formally deactivation of the contact mass with rise in temperature, when the organic group undergoes appreciable pyrolysis. Published data on the retarding effect of the product $a_{Me_2SiCl_2}P_{Me_2SiCl_2}$ are contradictory. No effect of the product on reaction velocity was detected in special experiments [18] using mixtures of methyl chloride and up to 50 vol.% of dimethyldichlorosilane.

Hydrogen chloride, introduced into the reaction zone from outside [63–65] or obtained by the pyrolysis of methyl chloride [66,67] has a decisive effect on the selective formation of methyldichlorosilane under conditions of direct synthesis. Use of a mixture of methyl and hydrogen chlorides enabled the kinetics of its formation to be investigated [68] under comparatively mild temperature conditions, when the content of methyldichlorosilane in the condensate lay in the range 86–95%. The activation energy of formation of this compound from silicon of different degrees of purity was almost the same in the presence of copper (Table 6).

Table 6. Kinetic parameters of the synthesis of methyldichlorosilane [68] and ethyldichlorosilane [18].

Contact mass	Reaction order n_{RCl}	Activation energy, kcal mole^{-1}
methyldichlorosilane		
Technical Si	0.9—1.25	18.3—21.5
Technical Si + 10% Cu (mixed powders)	1.2	24.2
Technical Si + 10% Cu from CuCl	0.85	19—22
Pure Si (99.9999%) + 10% Cu from CuCl	0.9—1.1	18—20.5
ethyldichlorosilane		
Technical Si	1.2	18.3
Pure Si (99.9999%) + 10% Cu from CuCl	0.9—1.04	18—22

Technical silicon, which is sufficiently reactive for the preparation of trichlorosilane even without the addition of copper, is reactive also in the formation of methyldichlorosilane. The reaction order with respect to methyl chloride is independent of the type of contact mass and is approximately $n_{MeCl} \simeq 1$, while the activation energy lies in the range 18–24 kcal mole^{-1}.

The activation energies of formation of methyltrichlorosilane and tetrachlorosilane were estimated [18], from the

temperature dependence of the ratio of their rates of formation in the preparation of methyldichlorosilane[68], when they are present in small quantities (4–5%) among the reaction products, as respectively ~40 and 3–6 kcal mole^{-1}.

Organogermanium compounds containing hydrogen could not be obtained[68] by the reaction of germanium with methyl chloride in the presence of hydrogen chloride, and there is no information on their direct synthesis.

Voorhoeve et al.[67] obtained interesting kinetic data on the formation of methylchlorosilanes by the reaction of methyl chloride with silicon in the presence of catalytic amounts of tin and lead. In experiments with a silicon–tin contact mass (9% and 17% Sn) between 300° and 500°C the main products were methyltrichlorosilane (80–90%) and tetrachlorosilane (~10%). The activation energy of the formation of methyltrichlorosilane under these conditions was 15.6 kcal mole^{-1}.

Highly selective formation of dimethyldichlorogermane[69] results from the interaction of germanium and methyl chloride in the presence of copper. Its content in the mixture at 320–400°C is 90–98%, and is independent of the state or content (in the range 3–30%) of copper in the contact masses. The mode of preparation of the contact mass (alloy or mixture of powered germanium and copper) has no appreciable effect on the principal kinetic parameters of the process, as with silicon[62]. The kinetic order with respect to methyl chloride is n_{MeCl} = 1.5, and the activation energy 24–27.5 kcal mole^{-1}.

Comparatively little investigation has been made of the kinetics of the formation of ethylchlorosilanes. The reason is that interaction between ethyl chloride and silicon–copper contact masses yields several products in considerable quantities, which complicates interpretation of the experimental results and calculation of the kinetic parameters of the process.

Furthermore, ethyl chloride breaks down during the reaction to form ethylene and other hydrocarbons. The reaction products contain not only diethyldichlorosilane but also a large quantity of ethyldichlorosilane. The total rate of conversion of ethyl chloride on a silicon–copper contact mass is of the first order with respect to ethyl chloride[70,71]; under dynamic conditions the process is well described by the equation of Frost and Panchenkov[72]. Later Bažant and Kraus[73], on the assumption that ethylchlorosilanes and hydrocarbons (ethane and ethylene) are formed by parallel reactions, estimated activation energies respectively of 18 and 25 kcal mole^{-1} for the two overall processes.

A kinetic examination has been made also of the formation of ethyldichlorosilane as an individual reaction product on specimens of technical silicon and pure silicon in the presence of copper[18]. As with the preparation of methyldichlorosilane, a mixture of ethyl and hydrogen chlorides was used. The content of ethyldichlorosilane in the reaction products was 90–95%. The order of the reaction with respect to ethyl chloride was n_{EtCl} = 0.9–1.2, and the activation energy 18–22 kcal mole^{-1} (Table 6). As with the preparation of methyldichlorosilane, the kinetic parameters of the process are independent of additions of copper, provided that the silicon is sufficiently active in forming trichlorosilane.

No quantitative kinetic investigation has been made of the interaction of chlorobenzene with silicon–copper contact masses. Only a few data have been published on the parallel formation[15,74] of the main reaction products—phenyltrichlorosilane and diphenyldichlorosilane—and the secondary products—benzene, biphenyl, and tetrachlorosilane. Some idea of the nature of the reaction between an aryl halide and silicon can be obtained from kinetic data on the formation of phenylbromosilanes[75]. The experiments were made in a flow-type apparatus at bromobenzene pressures of 0.3–19 atm. The main product was diphenyldibromosilane, the activation energy of whose formation was 22.8 kcal mole^{-1}.

Studies[76,77] of the effect of substituents in the aryl bromide on the rate of formation of diaryldibromosilanes and aryltribromosilanes in the presence of a silicon–copper contact mass at 400°C established a linear dependence of the logarithm of the relative initial rates on the Hammett constants for the individual substituent (*p*-fluoro, *p*-chloro, hydrogen, *m*-methyl, *p*-methyl, *p*-t-butyl, and *p*-isopropyl). Kinetic equations were also obtained for the formation of di-*p*-fluorophenyldibromosilane and *p*-fluorophenyltribromosilane, regarded as occurring by parallel reactions.

Topochemical processes occurring in the solid phase are of great importance in the direct synthesis of organosilicon and organogermanium halides. Various products can be formed by interaction of copper and the solid reactant in the contact masses depending on their method of preparation. Before reaction a silicon–copper alloy consists of two phases—silicon and an intermetallic compound Cu_3Si (η-phase)[37,78–82]—the latter being formed also in contact masses from a mixture of silicon and copper(I) chloride during preliminary reduction, as well as during synthesis as the copper chloride is formed on breakdown of the organic chloride, especially in the initial (induction) period of the reaction[79,80]. It was suggested in these papers that organosilicon chlorides are indeed formed by interaction of the organic chloride with silicon liberated by breakdown of the η-phase.

The reaction of silicon–copper alloys with methyl chloride was used as example to study the kinetics of the breakdown of the η-phase[83,84], the quantity of silicon that had reacted to form methylchlorosilanes being taken as the rate of the process. It was assumed that only silicon from Cu_3Si underwent reaction. An activation energy of 16 kcal mole^{-1} was obtained; this fell to 8–10 kcal mole^{-1} in the presence of additions of 0.2% of antimony and 0.5% of arsenic, but 0.5% of titanium raised it to 28 kcal mole^{-1}. These values are extremely tentative, since silicon not combined as Cu_3Si may take part in the reaction.

Changes occurring in a silicon–copper alloy (24.7% Cu) during reaction with ethyl chloride between 280° and 360°C were monitored[81,82,85] by X-ray examination. Breakdown of the η-phase was shown to have a fairly high activation energy (30 kcal mole^{-1}) and to obey a first-order kinetic equation. The lower activation energy obtained for conversion of the ethyl chloride (20 kcal mole^{-1}) was attributed to the catalytic effect of the resulting copper.

Under conditions of direct synthesis the contact masses undergo not only structural and chemical changes but also changes in texture (grain size), specific surface, and porosity[41,86]. At higher temperatures pyrolysis of the organic groups becomes important[87–89]. Unfortunately, hardly any kinetic study has been made of the pyrolysis of organic chlorides of silicon–copper contact masses. Investigations by Bažant et al.[15,87–89] suggest a stepwise conversion of organic groups on the contact masses with the formation of polymeric products (polymethylenes, polyphenylenes, etc.).

Some data on the kinetics of the decomposition of methyl chloride on copper under dynamic conditions

appeared in a paper by Trambouze[37], who found the activation energy to vary from 4 to 7 kcal mole^{-1} depending on the type of copper. However, methane was not detected in this investigation, and a scheme was suggested in which the methyl group decomposed into carbon and hydrogen. This conclusion is inconsistent with results obtained by Bažant[89], Anderson[90], and Ivanova et al.[91] The decomposition of methyl chloride on the surface of a pure copper film sublimed in a vacuum[90] yielded hydrogen, methane, and other hydrocarbons. The activation energy of the decomposition was estimated[90,91] to be considerably lower on a silicon–copper alloy than on technical and pure silicon (respectively 14.9, 24.2, and 44 kcal mole^{-1}).

III. MECHANISM OF REACTIONS

1. Nature of Reactions

With respect to the state of aggregation of reactants and products, direct synthesis is a heterophase process. Until recently it was not clear whether the process was purely heterogeneous, occurring on the surface of the solid or heterogeneous–homogeneous, with reactive intermediates formed on the surface, passing into space, and reacting further in the gas phase.

Hurd and Rochow[92] assumed direct synthesis to be a heterogeneous–homogeneous process. They investigated the interaction of methyl chloride with silicon and copper, and suggested the formation, on the contact surface, of the reactive species CH_3 and CH_3Cu, which migrated into the gas phase and reacted with reactive silicon–chlorine intermediates (SiCl and $SiCl_2$) to give the final products. The function of copper in the suggested mechanism was to form intermediate compounds (CH_3Cu and CuCl) to act as alkylating and chlorinating agents. Rochow subsequently extended this scheme to the direct synthesis of other organosilicon halides.

An alternative view, put forward by Klebanskii and Fikhtengol'ts[78], Trambouze[37], Bažant[15], and Voorhoeve[93], regards direct synthesis as involving heterogeneous–catalytic reactions, occurring solely on the solid surface.

Certain aspects of Hurd and Rochow's mechanism appeared in several papers. At one time Andrianov et al.[94] assumed the participation of free radicals formed by dissociation of the intermediate methylcopper chloride CH_3CuCl. Holzapfel[95] considered that intermediate chlorinated compounds of silicon reacted in the gas phase. Even in the fluorination of silicon[25] it was regarded as possible that certain stages occurred in the gas phase and involved SiF and SiF_2.

The investigations of Andrianov, Golubtsov, and their coworkers[96-101] have shown that appreciable quantities of intermediate compounds of the type SiCl, $SiCl_2$, $SiCl_3$, $HSiCl_2$ may be formed in the gas phase in the reactions of copper(I) chloride and of gaseous hydrogen chloride with silicon. Thermodynamic calculations, as well as direct investigation of dichlorosilane $SiCl_2$ by mass spectrometry and ultraviolet spectroscopy, indicate comparatively high concentrations of this intermediate in the reduction of copper(I) chloride by silicon in the temperature range of direct synthesis (180°C and above)[96,97,100-102].

Attempts were made[103] to study the interaction of intermediate products in the chlorination of silicon ($SiCl_2$) with methyl chloride in the presence of copper. Ascribing great importance to copper(I) chloride, as in Hurd and Rochow's mechanism, and also allowing for the possible formation of $SiCl_2$, Andrianov, Golubtsov, et al. suggested a scheme of direct synthesis[103] in which an important part was assigned to the hypothetical compound RCl.Cu, which reacted with $SiCl_2$ to give R_2SiCl_2 and $RSiCl_3$, regenerating CuCl and Cu respectively. It is not clear from the paper where the main stages occur, in particular whether those involving $SiCl_2$ take place on the surface or in the gas phase. Alkylation stages involving R or CuR are excluded. Yet Czernotsky[104], from a study of the effect of additions of dimethyl ether on the formation of methylchlorosilanes, concludes that dimethyldichlorosilane is formed by the interaction of dichlorosilene with methyl radicals, which according to Müller and Gumbel[105] are formed from methyl chloride and copper.

Many objections have been raised against a radical mechanism of direct synthesis[15,16,93]. Special experiments in which donors or acceptors of radicals—nitric oxide[106], iodine[15], azomethane[15,58]—were introduced into the reaction mixture in the synthesis of methylchlorosilanes also did not support a radical mechanism. Comparative analysis[107] of products of the pyrolysis of chlorobenzene and by products not containing silicon also makes participation of free phenyl radicals in the synthesis of phenylchlorosilanes improbable.

Direct assessment of the homogeneous component in homogeneous–heterogeneous processes—by a method of separate calorimetry—has been used to settle the question of the nature of the reactions involved in the synthesis of silicon and germanium halides and their organic derivatives[26,27,44,108-110]. In the formation of trichlorosilane[44,110] good agreement was shown by a quantitative comparison of the rise in temperature calculated theoretically for a purely heterogeneous synthesis and observed experimentally. Consequently no significant exothermic stages take place in the gas phase. The chlorination of silicon[26], the chlorination[27] and hydrochlorination[18] of germanium, and the formation of methylchlorosilane[108,109], germanes[18], and ethylchlorosilanes[18] have been studied similarly. The results also indicate the absence of homogeneous exothermic reactions.

Thus the main stages in most of the processes investigated—for which, moreover, the most complete kinetic data are available—must be regarded as heterogeneous, taking place solely on the surface of the solid reactant.

2. Intermediate Surface Chemical Interaction

With purely heterogeneous reactions the first stage—adsorption of the gaseous reactant—may be of the most important. Rostsishevskii[113] made the first attempt at a qualitative estimate of the adsorption of methyl chloride on silicon–copper contact masses. Adsorption was found to be slight below 230°C, and was larger on alloy contact masses (15% Cu) than on a mixture of silicon and copper powders.

Bažant et al.[56] showed that methyl chloride is not adsorbed at 100°C, either on copper or on silicon, although adsorption occurs on a silicon–copper alloy (10% Cu), and at 200 torrs reaches the improbably (to the Reviewers) high value of 3.5×10^{-5} mole g^{-1}, which corresponds to roughly nine monolayers of adsorbed methyl chloride.

The adsorption of methyl chloride was studied in greater detail by Müller and Gumbel[105], who concluded that considerable adsorption occurs on the surface of a silicon–copper contact mass containing silicon–chlorine and copper–chlorine bonds (after preliminary chlorination

or remaining from the conditions of preparation of the mass). Appreciable adsorption is observed also on copper(I) chloride, which may be present in chlorine-containing contact masses. The paper contains no information on the specific surfaces of the adsorbents, and the experiments were made only at one, fairly high temperature (245–250°C), when investigations of adsorption may have been complicated by the occurrence of chemical reaction on the surface.

Contradictory views are held on the nature of the adsorption bonds holding RX to the contact masses. The concept of the dissociative adsorption of RCl is widely used in the literature on direct synthesis without adequate experimental justification. Thus adsorption on two centres of the type

is assumed by Trambouze[37] and by Bažant et al.[15]; whereas Voorhoeve[58] and Klebanskii and Fikhtengol'ts[78] take into account the electronegativity of the elements and suggest adsorption of the type

Several authors have considered the chemisorption of RCl on silicon–copper contact masses in terms of the band theory of solids. Thus Trambouze[37] used Dowden's well known views[111] concerning catalysis and chemisorption on metals. Dragojevic[112] explains chemisorption and the effect of copper and other additives in silicon on the basis of Vol'kenshtein's semiconductor theory[114], but direct experimental confirmation of the authors' conclusions is lacking; the former ignores the specific character of silicon, which has a quasi-insulated surface. Yet the discussion of adsorption on silicon–copper contact masses containing 10–20% of copper in terms of the electronic theory of semiconductor catalysis is incorrect, because such adsorbents are already strongly alloyed, degenerate semiconductors.

Work published during recent years enables a fuller assessment to be made of the character of the adsorption. Boonstra, Van Ruler[115,116], and Bootsma[117] established by a volumetric method, and Podgornyi et al.[118–124] from the contact potential difference[126], two characteristic types of adsorption of hydrogen chloride on pure polycrystalline silicon and on germanium: the γ-form involves rapid adsorption and has a lower activation energy; the β-form involves slow adsorption and requires a larger activation energy[116,119–121]. Hydrogen bromide and hydrogen iodide are adsorbed similarly[116,117]. Extremely low heats of adsorption were estimated by a chromatographic method for the low-temperature and the activated adsorption of hydrogen chloride on technical (98%) silicon[127]. The adsorption of hydrogen chloride on silicon was found to be strongly dependent on its purity, the presence of impurities, and catalytic additions of copper, the last of which promote the type of adsorption having a higher activation energy[123].

Studies have been made also of the adsorption of gaseous chlorine, chloromethane, and chloroethane[118–121] on silicon and germanium[120], as well as of chlorobenzene, vinyl chloride, and allyl chloride on silicon[122]. As with hydrogen chloride, the two forms of adsorption are found with chlorine and methyl and ethyl chlorides on pure polycrystalline silicon; but very slight adsorption effects are observed with alkyl chlorides compared with hydrogen chloride and chlorine.

Since the chemisorption of the adsorbates studied is reversible and extremely rapid even at room temperature, both on silicon and on germanium, it is evidently not the limiting stage.

With regard to the nature of the chemisorption bonds, hydrogen, methyl, and ethyl chlorides are adsorbed mainly in molecular form on silicon at room temperature[118–124]. The adsorption bond is assumed to be formed through the chlorine atom of the RCl molecule: the β-form of adsorption is effected by the donation of a pair of $3p$ electrons of the chlorine atom to a d orbital of silicon (or germanium), i.e. by a donor–acceptor bond; the γ-form corresponds to formation of a bond in which electrons from the adsorbent are directed to a $3d$ orbital of the chlorine atom. It is noteworthy in this connection that the adsorption of hydrogen halides on silicon and germanium has been assumed[115,116] to be dissociative in character.

The lack of adequate data on the first stage of surface chemical interaction—adsorption of the gaseous reactant RX—introduces some uncertainty, of course, into the description of subsequent reactions of the surface compounds on silicon (or germanium) before formation of the final products.

Two approaches have been adopted towards the stages of surface chemical interaction: the first assumes the presence of a stage limiting the whole process, and the second a steady state with no limiting stage. Thus adsorption of RX is the limiting stage in the formation of trichlorosilane and methylchlorosilanes according to Trambouze[37], and in that of ethyl-, phenyl-, and vinylchlorosilanes according to Voorhoeve[16]. However, Bažant and his coworkers[15] regard the adsorption step as extremely rapid in several processes of direct synthesis (of hydrogen-containing chlorosilanes[38], dimethyldichlorosilane[56,57], dimethyldibromosilane[127], and phenylbromosilanes[75]), assuming that the reaction velocity is limited by the surface reaction of adsorbed RX in dissociated form. Similar views were held by Müller and Gumbel[105]. The above adsorption results indicate that the opinions of the latter authors are quite well founded. Nevertheless, the hypothesis of dissociative adsorption of RX has no direct experimental support, as noted already. It has therefore been assumed in a recent series of papers[119–124] that methyl chloride is adsorbed in molecular form quite rapidly and reversibly both on silicon–copper[119] and on germanium–copper[120] contact masses. Kinetic data[62,69] on the formation of dimethyldichlorosilane (for the order with respect to methyl chloride see Section II) indicate that the activated complex of the limiting stage contains one molecule of chemisorbed methyl chloride, but in the case of dimethyldichlorogermane two methyl chloride molecules are present[18,19].

Even the simpler processes—the halogenation of silicon and germanium—are also viewed in different ways. The fluorination of silicon has been regarded[25] as limited by the adsorption stage. The iodination of germanium to the di-iodide has been represented[32] by a four-stage scheme involving dissociated forms of chemisorbed molecular iodine I_2 and bulk and surface current carriers in the crystal. The initial period of the chlorination of silicon produces linear polymeric chlorosilane molecules attached to surface atoms[128–130]. In the chlorination of germanium[30] the surface is assumed to be completely covered with the chemisorbed gaseous reactant, and the limiting stage is conversion of the surface germanium–chlorine compound; an important role is attributed to current carriers in the semiconductor.

The reactions of silicon and germanium with hydrogen halides have been more thoroughly studied. At temperatures close to the start of the reaction the hydrochlorination and the hydrobromination both of silicon and of germanium involve formation of the trihalogeno-derivative HMX_3 as main product. On the basis of adsorption data and investigations of the kinetic isotope effect in the reactions of silicon [34,131] and germanium [34,46] with HX and DX (where X = Cl, Br), and also kinetic data (Section II), the slow stage is assumed to be a surface chemical reaction of the chemisorbed hydrogen halide in molecular form. The HX molecule in the activated complex is deformed differently depending on the reactivity of the solid reactant: on highly active specimens (containing copper or an impurity) the H–X molecule is present in the activated complex essentially in a dissociated form (with the establishment of M–X and M–H bonds); on relatively inactive specimens (high-purity silicon and germanium) the state of the H–X molecule in the activated complex is similar to adsorption.

A mechanism suggested [52] for the action of hydrogen iodide on germanium, when the main product is the di-iodide GeI_2, involves as limiting stage desorption of the product formed by reaction between the surface compound HGeI and gaseous hydrogen iodide.

Alkyldichlorogermanes $RGeHCl_2$ cannot be obtained by direct synthesis [4]. Thus the desired results could not be obtained from the interaction of mixtures of methyl and hydrogen chlorides with germanium–copper contact masses over a wide range of temperatures [68]. This is probably because the surface compound GeHCl reacts rapidly with hydrogen chloride to form the surface dichloride $GeCl_2$, which reacts with methylchloride to give the final product CH_3GeCl_3. Formation of a bond with hydrogen in the direct synthesis of alkyldichlorosilanes is more probable with silicon than with germanium, owing to the specific character of the surface compound SiHCl.

Thus the first approach in interpreting surface chemical interaction in formation of the corresponding gaseous derivatives of silicon or germanium is usually based on adsorption data, but in some cases with recourse to kinetic results (type of kinetic equation representing formation of an individual product). No use at all is made of data on the selectivity of the process, which is its important characteristic [162].

In practice, however, e.g. in hydrohalogenation, the synthesis of alkyldichlorosilanes, etc., several products are very often formed simultaneously [68]. Thus, in the synthesis of methyldichlorosilane from mixtures of hydrogen and methyl chlorides, silicon tetrachloride is formed at a closely similar rate to trichlorosilane. Similarly, trichlorosilane and dichlorosilane are formed at similar rates in the hydrochlorination of silicon over a certain temperature range. In these cases, therefore, it is impossible to describe the surface chemical interaction in terms of the concept of a limiting stage.

Such more complicated situations have been discussed in recent years in terms of the Horiuti–Temkin theory of stationary reactions [132,133], which has already been widely used to describe surface chemical interaction in complicated heterogeneous catalytic reactions [13,134]. This second approach has proved extremely useful for interpreting the mechanism of the reactions

$$HCl + Si \rightarrow \text{Products}$$
$$HCl + MeCl + Si \rightarrow \text{Products} \quad .$$

It may evidently be quite effective in examining the direct synthesis of methylchlorosilanes and other organosilicon monomers [19].

It was assumed in this work that the gaseous reactant is adsorbed in molecular form, and that the intermediate surface compounds do not contain copper. A multistage mechanism was proposed for the hydrochlorination of silicon, which involved the assumed formation of the intermediate surface compounds (ZHCl), (ZHCl.HCl), (ZHSiCl), $(ZSiCl_2)$, $(ZSiCl_3)$, and (ZH), where Z denotes an active centre on the surface [133]. The process is represented by a nine-stage scheme with three independent paths

$$Si + 2HCl = H_2SiCl_2$$
$$Si + 3HCl = HSiCl_3 + H_2$$
$$Si + 4HCl = SiCl_4 + 2H_2 \quad .$$

The suggested mechanism agrees satisfactorily with kinetic data (Section II) and experimental data indicating a linear dependence of the selectivity $S = r_{II}/r_I$, the ratio of the rates by the second and first routes, on the reciprocal p_{HCl}^{-1} of the partial pressure of the gaseous reactant.

The mechanism of the more complicated reaction

$$HCl + MeCl + Si \rightarrow \text{Products}$$

has been analysed similarly [132]. Consideration is given not only to the above intermediate surface compounds but also to molecules (ZCH_3Cl) adsorbed on the silicon surface. The mechanism comprises ten stages with four independent routes

$$MeCl + HCl + Si = MeSiHCl_2$$
$$MeCl + 2HCl + Si = H_2 + MeSiCl_3$$
$$3HCl + Si = H_2 + HSiCl_3$$
$$4HCl + Si = 2H_2 + SiCl_4 \quad .$$

The kinetic equation obtained for the formation of the methyldichlorosilane is consistent with the observed first order with respect to methyl chloride. The expression for the selectivity $S = r_I/r_{IV}$ (the ratio of the rates by the first and fourth routes) was a linear function of the ratio of the partial pressures of the gaseous reactants p_{HCl}/p_{CH_3Cl}, in good agreement with experiment.

Since either (ZHCl) or (ZHSiCl) may be formed by the pyrolysis of methyl chloride, we can try to extend the multistage mechanism of the process

$$MeCl + HCl + Si \rightarrow \text{Products}$$

to the process

$$MeCl + Si \rightarrow \text{Products} \quad .$$

In particular, a possible scheme of formation of dimethyldichlorosilane may comprise the stages [19]

$$MeCl + Z \rightleftarrows ZMeCl$$
$$ZMeCl + ZMeCl \rightleftarrows ZMeCl \cdot MeCl + Z$$
$$ZMeCl \cdot MeCl + Si \rightarrow Me_2SiCl_2 + Z \quad .$$

The appearance of such byproducts as tri- and di-methylchlorosilanes can be explained by the presence of the stages

$$ZMeCl + ZMeSiMe \rightarrow Me_3SiCl + 2Z$$
$$ZMeCl + ZMeSiH \rightarrow Me_2SiHCl + 2Z \quad .$$

However, this leaves unanswered the question of the stages which will lead to formation of the intermediates (ZCH_3SiCH_3), (ZCH_3SiH), $(ZHCH_3Cl)$, and $(ZSiCl_2)$. More detailed investigations are required here on the mechanism of the pyrolysis of alkylchlorosilanes on a silicon–copper contact mass.

The idea of the formation of symmetrical derivatives such as dichlorosilane and dimethyldichlorosilane via intermediate compounds from two molecules of the gaseous

reactant is expressed in several papers, as already noted above. However, the qualitative aspect—the nature of the active centre Z—was the main concern. Thus Voorhoeve[16] suggested that the active centre in the direct synthesis of methylchlorosilanes contains two copper atoms and one silicon atom. In a series of later investigations Golubtsov et al.[135] considered that the active centre in this process is a group of the type SiCl. The theory of stationary reactions permits a quantitative approach to the inclusion of intermediate compounds of the type (ZRCl.RCl) in a multistage scheme, since its consequences can be tested experimentally. On the assumption, for example, that dichlorosilane is formed at the stage

$$ZHCl+ZHSiCl\rightarrow H_2SiCl_2+2Z,$$

in the hydrochlorination of silicon, the above selectivity $S = r_{II}/r_I$ would in general not have depended on the partial pressure of hydrogen chloride, which would have been contrary to experience.

The nature of the active centre in the kinetic analysis of multistage schemes is not significant in the Horiuti–Temkin method, since the surface is assumed to be in a steady state.

Role of copper and impurities

Comparison of kinetic data on the chlorination and hydrochlorination of silicon and germanium with data on their interaction with methyl chloride and bromide reveals the features reported below.

(*a*) Syntheses involving germanium have smaller activation energies than those involving silicon.

(*b*) A higher kinetic order with respect to the gaseous reactant is observed with germanium–copper contact masses than in the case of silicon.

(*c*) Impurities and additions of copper have a marked effect on the kinetics, lowering considerably the activation energy, and this effect is larger for reaction with germanium. Thus the order with respect to chlorine in the chlorination and hydrochlorination of silicon is higher in the presence of copper and impurities, while the activation energy falls by ~10–12 kcal mole^{-1}, i.e. by ~30% (Tables 1 and 2). The activation energy is halved with germanium. Such a relation is observed in hydrobromination (Table 4) and in the synthesis of dimethyldihalogeno-derivatives (Table 5).

(*d*) The nature of the halogen in RX (Cl or Br) has no marked effect on the kinetic parameters of the synthesis of halogenosilanes containing hydrogen or organic groups (Tables 2–4).

The decisive factor can be regarded[27,131] as the strength of the M–M bond on the surface of the solid reactant M. The higher activation energies with silicon can be explained by a more stable bond between silicon atoms, on the assumption that the same fraction of the energy of silicon–silicon and germanium–germanium bonds in the surface and adjacent layers enters as components of the activation energy[28,131]. In the hydrohalogenation of technical samples of silicon, as well as of silicon–copper and germanium–copper contact masses, the impurities and the additions of copper probably influence the energy of the M–M bond, promoting both easier rupture in the transition state and strong deformation of the H–X bond until the latter dissociates.

The effect of copper is not universal. Specimens of technical silicon even in the absence of copper are sufficiently reactive in some processes (chlorination[26], hydrochlorination[45], and hydrobromination[48] of silicon, synthesis of methyl-[68] and ethyl-dichlorosilanes[18] from mixtures of the alkyl and hydrogen chlorides). Nevertheless, specimens of high-purity silicon become considerably more active on the introduction of copper, and react at a lower temperature.

Various surface compounds of copper, regarded in several cases as independent phases, have been postulated as intermediates to explain the specific effect of copper on direct syntheses (CuR,[92] CuCl, RCuCl,[94] $HCuCl_2$,[136] Cu_3Si,[78] etc.). The role of copper is mainly to transfer chlorine atoms or R or RCl groups to the silicon atom. The regenerated copper again takes part in forming the intermediate compound.

Published mechanisms of direct synthesis do not reveal sufficiently clearly the functions of copper as a catalyst, and existing views are in some cases directly contradictory. In the first paper Hurd and Rochow[92] suggested that an indispensable condition for effective synthesis was close contact between silicon and copper phases, since rapid consumption of silicon occurred precisely at the interface. Essentially the same attitude was adopted by Bažant et al.[56,137] and also by Rossmy[138]. At the same time, beginning with the work of Klebanskii[78] and Trambouze[37] followed by the investigations of Voorhoeve[88] and of Kolster[139], silicon present as an intermetallic compound was assumed to be reactive. Andrianov, Golubtsov, et al.[140] and also Krylov and Efremov[81,82] showed that the intermediate compound acts as a donor of catalytically active copper, for contact masses not containing Cu_3Si are also catalytically active[141,142]. The functions of the copper catalyst formed by breakdown of the intermetallic compound are not clear from this work.

Such contradictory views are probably due to the absence in the above investigations of direct examination of the surface and adjacent layers of the contact masses. The reaction of hydrogen chloride, hydrogen bromide, and methyl bromide with silicon (formation of trichlorosilane[43], tribromosilane[34], methyldichlorosilane[18], and methylbromosilanes[127]) has established that copper(I) chloride, like the bromide[34], is not a catalyst, since synthesis begins only after this compound has been reduced by silicon and free copper and the Cu_3Si phase have separated.

Even a small copper content (10^{17}–10^{19} atoms cm^{-3}) proves extremely effective both for the adsorption of hydrogen chloride[124] and for sharply increasing the reactivity of the silicon[143]. This effect can be explained by a change in the collective electronic properties of the surface silicon atoms. These changes affect also the character of the adjacent layers. Thus additions of copper over the range 10^{17}–10^{20} atoms cm^{-3} lower the microhardness of a single crystal of silicon from 1250 to 700 kg mm^{-2} for a specimen with a 10^{20} atoms cm^{-3} copper content[143]. Data are also available[144,145], though less complete, on the variation of the microhardness of germanium when fairly extensively alloyed with other elements (10^{18}–10^{20} atoms cm^{-3}). A parallelism has been observed[146] between the variation of microhardness and that of specific surface energy of semiconductor crystals with covalent bonds. Such change in the state of the surface atoms should tend to enhance their reactivity, as has been observed e.g. in the synthesis of trichlorosilane. The combined electronic effect of small additions of copper, evident in the effects on the microhardness, the reactivity, and the chemisorptive power of silicon, cannot be regarded as specific to copper. This conclusion is

supported by the high reactivity of technical silicon, without the addition of copper, towards several direct syntheses (chlorination, hydrochlorination, formation of methyl- and ethyl-dichlorosilanes).

However, the change in the combined electronic properties of silicon with the introduction of small quantities of copper is insufficient for reaction with methyl chloride. Thus methyldichlorosilane is formed from a mixture of hydrogen and methyl chlorides on technical and pure silicon alloyed with copper (0.04–0.3%) in the temperature range 210–240°C, [68] which is close to the range (160–210°C) for the synthesis of trichlorosilane. But formation of dimethyldichlorosilane from methyl chloride alone and similar specimens of silicon was not observed up to 400°C. Hence it may be concluded that, in contrast to the synthesis of hydrogen-containing chlorosilanes, the formation dimethyldichlorosilane requires additional electronic changes in silicon, probably connected with the local action of copper on its surface atoms. Such an effect can be achieved only with a comparatively high content of copper in the surface and adjacent layers of silicon.

The presence of the η-phase or other intermetallic compound of silicon and copper is probably not essential for the local action of copper on the surface silicon atoms, i.e. to ensure the synthesis of dimethyldichlorosilane and probably other dialkyldichlorosilanes. In the presence of a highly active and extensive copper surface (taking into account the abnormally high rate of diffusion of copper atoms in the silicon and Cu_3Si crystal) [139], formation of an intermediate surface compound of silicon with copper may be sufficient for development of a local effect. Formation of the η-phase is a limiting case.

The long induction period in the reaction observed in practice when contact masses comprising a mixture of silicon and copper powders are used, as well as with certain alloy masses, is probably caused by formation of an active surface and of layers adjacent to the surface.

The large quantity of experimental data published on the action of impurity elements and promoters in contact masses, and also of gaseous contact poisons, represent mainly assessment of their overall and selective activity in the synthesis of hydrogen-containing halogeno-silanes and -germanes as well as corresponding organic derivatives. No quantitative data have appeared on the effect of impurities and promoters on the kinetics of the process, and therefore this question will not be examined in detail in the present Review.

The total and the selective activity of the contact masses are not significantly affected [147–149] by the usual impurities —aluminium, iron, and calcium—in silicon up to a total content of 2% and 10% of iron. However, these parameters diminish at higher contents of individual elements (1% of titanium, 2% of aluminium, 1.5% of calcium) [148]. The promoting action of individual elements (antimony, zinc, cadmium, bismuth, phosphorus, arsenic, tin, and indium) and of certain combinations (antimony plus zinc, zinc plus cadmium, antimony plus bismuth, etc.) is apparent in a higher yield of dialkyldichlorosilanes. Use of certain of these promoters (zinc, antimony, arsenic) in the synthesis of alkylhalogenogermanes [150] leads to a sharp increase in the yield of the alkyltrichloro-derivative. The yield of ethyldichlorosilane in the synthesis of ethylchlorosilanes is raised by the addition of 1.7% of aluminium, 1% of titanium, or 2% of calcium [151]. Only a certain content of promoters—not exceeding e.g. 0.001–0.005% of antimony and bismith—is optimal for the total and selective activity. Addition of higher contents of zinc and aluminium to the contact mass promotes the formation of trialkylchlorosilanes [153]. More than 0.01% of lead leads to complete deactivation of the contact mass [148,152]. Addition of aluminium and gallium increases the yield of the trimethylchlorogermane in the synthesis of methylchlorogermanes [154].

Contamination of the alkyl chloride with dimethyl ether [155], methylene dichloride [156], and sulphur dioxide [157] diminishes the activity of the contact masses.

The promoting effect of zinc, cadmium, and mercury has been explained [158] by their reaction with the organic halide in the gas phase to form their chlorides followed by transfer of a chlorine atom to copper to form cuprous chloride, which in turn is effective in the synthesis of alkylchlorosilanes by transferring its chlorine atom to silicon. However, the formation of copper(I) chloride was assumed from the content of Cu_3Si in the contact mass, although this silicide might not have been formed in this way.

Studies of the effect of promoting additions of several elements (aluminium, iron, titanium, zinc, antimony, phosphorus, arsenic, bismuth, boron, indium, gallium, tin, etc.) to samples of pure, purified, and technical silicon merit closer attention. It was concluded [159,160] from the results that promoting additives, introduced into the crystal lattice of silicon, may have either a favourable or an unfavourable effect on direct synthesis depending on their ability to react with the organic halide, and thus function as activators or inhibitors of the catalytic process.

The favourable effect of impurities and promoters in silicon has been attributed [161] to facilitation of the penetration of copper into the silicon lattice, or else the formation of silicides of low melting point.

Since the catalyst (copper) is especially sensitive to impurities, both it and surface silicon atoms can be assumed to be influenced both by gaseous impurities in the organic halide and by solid elements added to the contact masses; these effects will be still greater if a donor–acceptor type of bond can be formed on adsorption. The catalytic properties of copper and its ability to form particular compounds with silicon at the interface may be affected by adsorption on it especially of surface-active substances.

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Hydrolysis of Alkyl Halides Induced by Metal Ions: M^+-S_N1 and M^+-S_N2† Reactions

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Investigations of the kinetics, mechanism, and driving forces of hydrolyses of alkyl halides and several inorganic halides, induced by metal ions M^+ in aqueous media, are summarised. Relations between the rate and the Lewis acidity of M^+ are examined, together with models of M^+-S_N1 and M^+-S_N2 reactions. A list of 163 references is included.

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I. INTRODUCTION

The ability of silver(I) and mercury(II) ions and of certain complexes to accelerate substitution in organic and inorganic halides is well known. The early work was briefly surveyed in monographs [1-3]. In 1937 Roberts and Hammett [4] suggested that a correlation, similar to the Brønsted relation [5,6] for general acid catalysis, may exist between the rates of such reactions and the Lewis acidities of the electrophiles. This question was investigated systematically [7-9] during 1967-1972 on the hydrolysis, induced by metal ions M^+, of alkyl halides of Ingold's classic α-series [1]

$$H_2O + RX + M^+ \rightarrow H^+ + ROH + XM \qquad (1)$$

(R = CH_3, C_2H_5, iso-C_3H_7, t-C_4H_9; X = F, Cl, Br, I). As a consequence of the affinity of X for M the entry of RX into the coordination sphere of M^+ promotes heterolysis of the C-X bond (M^+-S_N1 mechanism) and reactions with a nucleophile (M^+-S_N2 mechanism). The Review is concerned mainly with reactions in aqueous media. Water is more convenient than the non-aqueous and anhydrous media generally used: the kinetics is less complicated by ionic association, extrapolation to zero ionic strength is more reliable, and ample information is available on the stability of the MX complexes [10]. The present Review deals with the kinetics and the mechanism of these reactions, the role of the structure of R, X, M^+, and the medium, the validity of correlations of the Brønsted type, and fine distinctions between the correlations for M^+-S_N1 and M^+-S_N2 mechanisms. For generality reactions of inorganic halides which might have an M^+-S_N1 mechanism are also considered.

II. ROLE OF METAL IONS IN THE HYDROLYSIS OF t-BUTYL HALIDES—CORRELATION BETWEEN RATE AND LEWIS ACIDITY OF M^+

The solvolysis of t-butyl chloride is accelerated by silver salts in acetone [11] and by mercury(II)chloride in aqueous ethanol and in acetone [12-14], while hydrogen exchange between the t-butyl group and the solvent in acetic deutero-acid is accelerated by chlorides in the sequence [15]

antimony(V) > iron(III) > tin(IV) > zinc(II) > mercury(II).

Alkali-metal ions are inactive in the hydrolysis of t-butyl chloride [16]. Detailed studies have been made of the effects of other ions in the hydrolysis of t-butyl fluoride, chloride, and bromide in aqueous media [7,17-27] (Table 1). At constant ionic strength μ the kinetics of the hydrolysis is represented by the equation [18]

$$k \equiv \frac{1}{[RX]}\frac{d[RX]}{d\tau} = k_0 + k_1[M^+] \qquad (2)$$

where k_0 corresponds to the reaction with the solvent, and k_1 to that with the M^+ ion.

The activity of the ions corresponds to the concept of "hard" and "soft" acids and bases [28]. The "hard" acids—Zr^{4+}, Th^{4+}, Sc^{3+}, Al^{3+}, etc.—are active with t-butyl fluoride (detachment of the "hard" base F^-). The activity increases with decrease in the atomic number within a subgroup of the Periodic System: e.g. $In^{3+} < Ga^{3+} < Al^{3+}$; $La^{3+} < Y^{3+} < Sc^{3+}$; and $Sr^{2+} < Mg^{2+} < Be^{2+}$. "Soft" Lewis acids are active with t-butyl chloride and bromide, and k_1 increases with increase in atomic number within a subgroup: $Hg^{2+} > Cd^{2+} > Zn^{2+}$; $Tl^{3+} > Ln^{3+} > Ga^{3+} > Al^{3+}$; $Pd^{2+} > Ni^{2+}$.

A clear relation exists between k_1 and the stability constant $K_{MX} = [MX]/[M^+][X^-]$ of the complex MX: [17,20,21]

$$\lg k_1 = A_X + \beta \lg K_{MX} \qquad (3)$$

For each X = F, Cl, Br the activity of M^+ is higher the greater the Lewis acidity of M^+. The activity series of the metals follow the variations in K_{MX}, and are different for X = F from those for X = Cl, Br. Thus Al^{3+} is active with the fluoride and relatively inactive with the chloride. The opposite situation is found for the silver ion. The independent terms A_X in Eqn. (3) are different for X = F, Cl, Br, but all the lines have roughly the same slope β. As was to be expected for reactions of acid–base type, the electronic structure (completeness of the electron shell) of the metal ions does not influence their effectiveness in the hydrolysis of alkyl halides. The acid hydrolysis ($M^+ = H^+$) of t-butyl fluoride has also been studied [21]. The nature of the anion (A = NO_3^- or ClO_4^-) does not affect the value of $k_1 = k/[H^+]$ extrapolated to $\mu = 0$ (for $\lg k_1$ varies

†Usage of the symbol "M^+" in this paper follows that of the original Russian, and does not necessarily imply "unit" positive charge: M^{n+} would have been more explicit (Ed. of Translation).

linearly with [HA])[24]. The same information is conveyed[21] by the Hammett equations: $\lg k = -1.14H_0 - 3.61$ (for perchloric acid) and $\lg k = -1.06H_0 - 3.72$ (for nitric acid), where H_0 is the acidity function. The value of k_1 for H^+ corresponds to the great stability of the complex HF, and is consistent with the general correlation (3).[26] Hydrogen chloride is significantly less stable[10]. Therefore the contribution of H^+ to the hydrolysis of t-butyl chloride becomes appreciable only in concentrated acids, e.g. perchloric acid[29].

Table 1. Stability of complexes MX and rates of M^+–S_N1 hydrolysis of t-C_4H_9X (values of K_{MX} and k_1 extrapolated to $\mu = 0$).

No.	Ion	$\lg(K_{MX}, M^{-1})$	$\lg(k_1, M^{-1}s^{-1})$ expt.	$\lg(k_1, M^{-1}s^{-1})$ calc. from Eqn.(12)
	t-butyl fluoride (aqueous solution at 25°C, effect of M^{+a}, $\lg(k_0, s^{-1}) = -6.50$) (Ref.22)			
1	Zr^{4+}	9.8±0.2	+0.7±0.3 [21]	+1.0
2	Th^{4+}	8.8±0.1	−0.2±0.3 [21]	0.0
3	Sc^{3+}	7.1±0.1	−1.16±0.1 [26]	−1.2
4	Al^{3+}	7.0±0.1	−1.70±0.1 [26]	−1.4
5	Fe^{3+}	6.1±0.1	−1.92±0.2 [26]	−2.2
6	Be^{2+}	5.6±0.1	−2.02±0.1 [26]	−2.2
7	Ga^{3+}	5.6±0.2	−2.4±0.3 [21]	−2.7
8	Cr^{3+}	5.2±0.1	<−5.0 [26]	−3.1
9	Y^{3+}	4.8±0.1	−3.7±0.3 [21]	−3.4
10	In^{3+}	4.6±0.1	−3.4±0.3 [21]	−3.6
11	H^+	3.2±0.1	−3.74±0.1 [24]	−3.9
12	La^{3+}	3.6±0.1	−4.4±0.2 [26]	−4.6
13	Mg^{2+}	1.8±0.1	−5.9±0.2 [22]	−5.9
14	Zn^{2+}	1.3±0.1	−6.1±0.2 [26]	−6.4
15	Cd^{2+}	1.1±0.1	−6.3±0.2 [26]	−6.5
	t-butyl chloride (31.9 wt.% C_2H_5OH–H_2O at 25°C, effect of M^{+b}, $\lg(k_0, s^{-1}) = -2.70$) (Ref.17)			
16	Hg^{2+}	7.6±0.2	>0	+3.7
17	Tl^{3+}	8.5±0.3	>0	+3.9
18	Ag^+	3.5±0.2	0.0±0.2	+0.2
19	Bi^{3+}	3.6±0.3	−1.0±0.1	−0.9
20	Cd^{2+}	2.3±0.2	−1.8±0.1	−1.7
21	In^{3+}	3.2±0.5	−1.5±0.1	−1.4
22	Pb^{2+}	1.8±0.2	−2.2±0.1	−2.1
23	Mn^{2+}	0.9±0.3	−3.1±0.3	−3.1
24	Tl^+	0.8±0.2	−3.0±0.3	−2.5
25	Co^{2+}	0.6±0.2	−3.0±0.2	−3.4
26	Cu^{2+}	0.6±0.4	−3.3±0.3	−3.4
	t-butyl bromide (44.6 wt.% C_2H_5OH–H_2O at 20°C, effect of M^{+c}, $\lg(k_0, s^{-1}) = -2.16$) (Ref.27)			
27	Cd^{2+}	2.7±0.2	−1.2±0.1	−0.9
28	Pb^{2+}	2.5±0.3	−1.4±0.1	−1.0
29	Zn^{2+}	0.4±0.3	−2.5±0.3	−3.2
30	Co^{2+}	0.9±0.3	−2.3±0.3	−2.7
31	Ni^{2+}	0.9±0.3	−2.7±0.3	−2.7
32	Cu^{2+}	0.5±0.2	−2.7±0.3	−3.1

[a]The theoretical equation for this system is $\lg(k_1/k_0K_{MX})_{theor} = -3.1Z_M/(4.5 + r_M)$, where Z_M and r_M are the charge and the radius of M^+ (in Å)(see Section III).
[b]Theoretical equation $\lg(k_1/k_0K_{MX})_{theor} = -4.1Z_M/(5.4 + r_M)$.
[c]Theoretical equation $\lg(k_1/k_0K_{MX})_{theor} = -4.6Z_M/(5.7 + r_M)$.

An important exception to the correlation (3) has been established[26] for the Cr^{3+} ion, which is inert in the hydrolysis of t-butyl fluoride despite the great stability of CrF^{2+}. Since $[Cr(H_2O)_6]^{3+}$ has an abnormally low rate of exchange of the aquo-ligands $k_{exch} = 10^{-6}$ s^{-1},[28,30] this exception indicates inner-sphere coordination in the interaction of RX with M^+, and hindrance to M^+–S_N1 reactions, when the ion is not accessible to direct contact with the substrate. Rates of exchange are high in the case of other metal ions[28,30], and departures from correlations (3) are not observed.

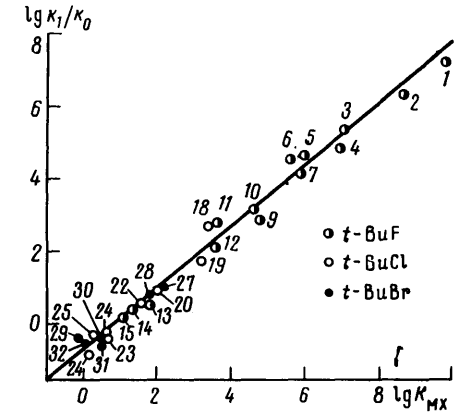


Figure 1. Dependence of $\lg(k_1/k_0)$ on $\lg K_{MX}$ for the hydrolysis of t-butyl halides in the presence of aquo-ions of metals. The numbering and the characteristics of the systems are given in Table 1.

Table 2. Effect of composition of aqueous ethanolic solvent on rate of reaction between t-C_4H_9Cl and Cd^{2+} at 25°C.[8]

C_2H_5OH, wt.%	D	$\lg K_{MX}$	$\lg k_1$, expt.	$\lg k_1$* calc. from Eqn.(12)
30.0	61.1	2.5	−1.7±0.1 [19]	−1.3
35.0	58.1	2.6	−2.0±0.1 [19]	−1.6
40.0	55.0	2.7	−2.2±0.1 [19]	−1.9
49.7	49.2	2.9	−2.4±0.1 [27]	−2.3
64.7	40.9	3.4	−3.0±0.2 [27]	−2.9

*Theoretical equation $\lg(k_1/k_0K_{MX})_{theor} = -76/D$.

Plots of k_1/k_0 against K_{MX}, both taken at zero ionic strength, merge into a single line for different t-butyl halides (Fig. 1). This leads to a correlation of great generality

$$\lg k_1/k_0 = -0.7 + 0.84 \lg K_{MX} \quad , \qquad (4)$$

which allows for the effects of both M^+ and X.[7,23] Equation (4) represents also the effects of the solvent for the reactions of t-butyl chloride with Cd^{2+} in aqueous alcohol (Table 2) and is applicable to the reaction in nitromethane[23]

$$t\text{-}C_4H_9Cl + HCl \rightarrow t\text{-}C_4H_9^+ + HCl_2^-.$$

In the latter case the electrophile is an uncharged hydrogen chloride molecule, and values of k_1, k_0, and $K_{MX} = [HCl_2^-]/[HCl][Cl^-]$ were estimated[23] from published data[31]. Catalysis is clearly developed in aprotic media: the lithium ion accelerates heterolysis of triphenylmethyl chloride in diethyl ether[32] and of diphenylmethyl chloride in 70% dioxan[27].

No detailed study has been made of the reaction products formed from t-butyl halides and metal ions. The yield of isobutene in the hydrolysis of t-butyl fluoride falls[27] in parallel with increase in the contribution of $k_1[M^+]$ to the total rate $k_0 + k_1[M^+]$. Reaction with strong electrophiles M^+, in contrast to reaction with the solvent, is evidently not accompanied by elimination. The proportion of elimination decreases in the reactions of other alkyl halides with the silver ion[33,34].

III. MODELS OF M^+–S_N1 REACTIONS

According to Ingold[1] t-butyl halides (fluoride, chloride, bromide, and iodide) are hydrolysed by an S_N1 mechanism owing to the enhanced stability of $(CH_3)_3C^+$, in comparison with e.g. CH_3^+, $C_2H_5^+$, iso-$C_3H_7^+$, and steric hindrance to nucleophilic attack at the carbonium centre. The above results show that an S_N1 mechanism is maintained even with induced reactions. The M^+–S_N1 and S_N1 mechanisms differ in the replacement of a solvent molecule in the solvate sheath of the transition state by an M^+ ion having a higher affinity for X^-, and in the quantitative characterisation of the participation of the electrophile in the M^+–S_N1 reaction by the order and the rate constant of the reaction with M^+.

The fundamental model of an M^+–S_N1 reaction[20] is represented by the scheme

$$\begin{array}{lcccccc} & (a) & & (b) & & (c) & \\ \mathrm{A} & RX & \xrightarrow{K_0^{\neq}} & R^{\delta+} \ldots X^{\delta-} \ldots S & \xrightarrow{kT/h} & R^+ + X^- & \\ & M^+\downarrow\uparrow K_{gr.} & & \downarrow\uparrow K_{tr.} & & & \\ \mathrm{B} & RX \ldots M^+ & \xrightarrow{K^{\neq}} & R^{\delta+} \ldots X^{\delta-} \ldots M^+ & \xrightarrow{kT/h} & R^+ + XM. & (5) \\ & (d) & & (e) & & (f) & \end{array}$$

Route A comprises a slow stage of S_N1 solvolysis of RX by the solvent S, involving an activation equilibrium $(a \rightarrow b)$ and breakdown of the transition state $(b \rightarrow c)$ at a rate kT/h.[35] Formation of the complex (d) gives rise to an induced reaction (route B). The activation equilibrium constants are denoted by $K_0^{\neq}$ and $K^{\neq}$, and the equilibrium constant of formation of the complex in the ground state is

$$K_{gr.} = [RX \ldots M^+]/[RX][M^+] \quad . \qquad (6)$$

This mechanism leads to the equation

$$k = \frac{k_0 + k_1[M^+]}{1 + K_{gr.}[M^+]} \quad , \qquad (7)$$

which is well known for such reactions[19,20]; it simplifies to (2) when $Kgr[M^+] \ll 1$.

Formulation of the principle of equilibrium solvation of the transition state in S_N1 reactions[36] led to the concept of the equilibrium constant of transition states for M^+–S_N1 and S_N1 reactions. From the chain of equilibria $(b) \rightleftharpoons (a) \rightleftharpoons (d) \rightleftharpoons (e)$ (Eqn. 5) it may be concluded that the transition states (b) and (e) are in equilibrium in the sense that they appear simultaneously and in proportions corresponding to the equilibrium constant (8a)

$$K_{tr.} = \frac{[R^{\delta+}X^{\delta-}M^+]}{[R^{\delta+}X^{\delta-}][M^+]} \quad (8a), \qquad K_{MX} = \frac{[MX]}{[M^+][X^-]} \quad . \qquad (8b)$$

The species $R^{\delta+} \ldots X^{\delta-} \ldots M^+$ can be regarded as the equilibrium solvate (complex) $R^{\delta+} \ldots X^{\delta-}$ together with M^+, where the latter is regarded as a constituent of the medium. The numerical value of K_{tr} is determined directly from kinetic data[19,20].

$$K_{tr.} = K_{gr.}K^{\neq}/K_0^{\neq} = k_1/k_0 \quad . \qquad (9)$$

A quantity similar to K_{tr} has been discussed by other authors[37]. Several consequences follow from a comparison[20] of formulae (8a) and (8b): (i) since the parameters K_{tr} and K_{MX} have the same dimensions (M^{-1}) and are described by similar expressions, the relation between them should be more general than the correlation (3) between k_1 and K_{MX}; furthermore, (ii) K_{tr} and K_{MX} depend differently on the ionic strength, so that values of $K_{tr} = k_1/k_0$ and of K_{MX}, all extrapolated to zero ionic strength, should be used for the correlation. As shown above (Fig. 1) these conclusions agree with experiment. For all the systems studied the numerical values of

$$k_1/k_0 \leq K_{MX} \quad , \qquad (10)$$

which is understandable, since the energy of interaction of M^+ is smaller with the transition state $R^{\delta+} \ldots X^{\delta-}$ than with X^-.

The slope of the Brønsted correlation $\lg k = A + \beta \lg K$ usually indicates[38–41] the position of the transition state on the reaction coordinate: the structure of the transition state resembles either the final or the initial state according as $\beta = 1$ or 0. It is implied that $0 \leq \beta \leq 1$, but there are exceptions[42–47]. Charge separation is nearly complete in S_N1 reactions, so that it is reasonable that the slope of line (4) is close to unity. However, the numerical coincidence[23] of $\beta = 0.84$ and $\delta = 0.8$ [16,48,49] for the transition state in the hydrolysis of t-butyl chloride is probably fortuitous.

A quantitative model has recently been suggested[8] for an M^+–S_N1 reaction. Complete separation of charges $(\delta = 1$, Eqn. 5) is assumed for the transition states—the intimate ion-pair $R^+ \ldots X^-$ for reactions with the solvent, and the trio $R^+ \ldots X^- \ldots M^+$ for those with M^+. Solvation is discussed in terms of a simple coordination model on the assumption that the coordination number of the ion and the energy of local interaction between the ion and a molecule of the medium are the same whether the ion is isolated or present in a pair or in a trio. This applies also to the $M^+ \ldots X^-$ bond energy in the trio and in the complex MX. On these hypotheses the equilibrium constant of disproportionation of the ion-pairs

$$\overset{(b)}{R^+ \ldots X^-} + \overset{(f)}{X^- \ldots M^+} \overset{K}{\rightleftarrows} \overset{(e)}{R^+ \ldots X^- \ldots M^+} + \overset{(c)}{X^-} \quad , \qquad (11)$$

which from Eqns. (8a), (8b), and (9) is given by $K = k_1/k_0k_{MX}$, is independent of solvation interactions and is determined solely by intramolecular Coulombic interactions. The complete equation

$$\lg k_1 = \lg k_0 + \lg K_{MX} - \frac{Ne^2Z_RZ_M}{2.303RTDl_{R-M}} \qquad (12)$$

includes a Coulombic term allowing for destabilisation of the transition state[8] due to repulsion of the outer groups R^+ and M^+ in the trio $(e$, Eqn. 5). The symbol N in Eqn. (12) denotes Avogadro's number, e is the charge on the electron, Z_R and Z_M are the charges on R and M, and

$$l_{R-M} = r_M + 2r_X + r_R -$$

is the distance between R and M defined in terms of the crystallographic radii of the ions r_i. With the complex structure of R and M taken into account the Coulombic term becomes

$$\left(-\frac{Ne^2}{2.303RTD}\sum_{i\neq j}\frac{Z_iZ_j}{l_{ij}}\right) ,$$

where i and j denotes the local charges in R and M respectively.

Several important consequences follow from the theory. According to (12) the parameter k_1 is strictly proportional to k_0 and K_{MX}, and depends also on the parameters of the transition states Z_R, Z_M, and l_{R-M}. This opens up a path for studying the structure of transition states from kinetic and thermodynamic data. It is significant that the effects of reactants and reaction conditions are transmitted to k_1 along many channels: thus change in M^+ influences k_1 through K_{MX}, Z_M, and l_{R-M}; variation in X through k_0, K_{MX}, and l_{R-M}; and changes in the medium through k_0, K_{MX}, and D. It follows from (12) that

$$E_1 = E_0 + \Delta H_{MX} + \frac{Ne^2 Z_R Z_M}{l_{R-M} D}\left(1 + \frac{T}{D}\frac{dD}{dT}\right) \quad , \quad (13)$$

where E_1 and E_0 are the activation energies of the reactions of RX with M^+ and with the solvent, and

$$\Delta H_{MX} = 2.303RT^2 \frac{d \lg K_{MX}}{dT}$$

is the enthalpy of formation of the complex MX. For reactions of uncharged and cationic halides, when $Z_R Z_M \geq 0$, Eqn. (12) leads to the rule (10). With anionic substrates, however, cases are possible in which $K_{tr} > K_{MX}$. Values of $\lg k_1$ found experimentally and calculated by means of Eqn. (12) for several systems are compared in Table 1.[8] The radius of $t\text{-}C_4H_9^+$ was taken[8] to be r_R = 1.8 Å.

The good agreement between calculation and experiment (Tables 1 and 2) throughout the range of variation in conditions—M^+, X, and medium—indicates that the initial model was correct. The use of crystallographic radii instead of actual distances in the calculation is explained by the slight effect of the system of radii adopted on the Coulombic correction: thus an error of ±0.5 Å in the determination of l_{R-M} leads to an error of only ±0.1 in $\lg k_1$. It was found also[8] that formula (4) reproduces the experimental data well (Fig. 1) because of the existence of a secondary correlation between the Coulombic term and $\lg K_{MX}$, the slope of which is −0.16, corresponding to the difference between the theoretical slope of unity and the empirical slope of 0.84.

Few of the activation-energy data required for further testing of the theory are yet available. The reactions of t-butyl fluoride with water and with the ions Be^{2+}, Fe^{3+}, Al^{3+} and Sc^{3+} have the same activation energy: $E_0 = E_1 = 25 \pm 1$ kcal mole^{-1}.[26] These values satisfy Eqn. (13), since $\Delta H_{MX} = -1 \pm 1$ for the fluoride complexes of these ions, while the third term in (13) has the value −0.1 when $(T/D)dD/dT = -1.37$.

The S_N1 and M^+–S_N1 mechanisms of the reactions of t-butyl halides are regarded in the above theory as limiting in the sense that complete separation of charges along the R–X bond is achieved in the transition state. On this view there can be no reaction of greater S_N1 character, and Eqns. (12) and (13) should be satisfied for the S_N1 reactions of other substrates. Discrepancies may indicate that a different mechanism is actually operating[9] (Section V).

Results obtained by Anantaraman and his coworkers[14] illustrate the proportionality between k_0 and k_1 with variation in R for typical S_N1 reactions of aralkyl chlorides with mercury(II) chloride (Table 3). They show that changes in k_0 and k_1 by factors of 10^4 correspond to only a fourfold variation in the quantity $(k - k_0)/k_0 = k_1[M^+]/k_0$. The residual effect can be explained by a decrease in the Coulombic term due to an increase in the effective radius of R^+. The electrophile in this system may be either $HgCl_2$ or $HgCl^+$; the latter is present at a lower concentration, but is more active. To obtain an estimate we make the crude assumption that $HgCl^+$ acts as electrophile. The transition state will then have the form $R^+ \ldots Cl^- \ldots Hg^{2+} \ldots Cl^-$, from which we have

$$\lg \frac{k - k_0}{k_0} = \lg K_{MX} + \lg [HgCl^+] - 8.1\left(\frac{2}{l_{R-Hg}} - \frac{1}{l_{R-Cl}}\right) \quad (14)$$

The terms in brackets allow for the interactions of R^+ with Hg^{2+} and with the terminal Cl^-: $l_{R-Hg} = r_R + 2r_{Cl} + r_{Hg}$ and $l_{R-Cl} = r_R + 3r_{Cl} + 2r_{Hg}$. Application of Eqn. (14) to data for t-butyl chloride yields

$$\lg K_{MX} + \lg [HgCl^+] = 3.39$$

and the radii on other cations R^+ (last column of Table 3). The r_R values obtained increase with the size of the cation, with increasing transfer of positive charge to the periphery of the cation; their order of magnitude appears to be reasonable.

Table 3. Solvolysis (S_N1) of RCl in 0.075 M $HgCl_2$ in 80% aqueous acetone at 20°C.[14]

RCl	$10^7 k^*$, s^{-1}	$\frac{k-k_0}{k_0}$	r_R, Å calc.
t-BuCl	10.4	57	(1.8)
t-AmCl	14.7	70	2.1
Ph(Me)CHCl	4.0	100	2.5
Ph(Et)CHCl	0.93	100	2.4
Ph(*i*-Pr)CHCl	0.24	120	2.7
Ph(*t*-Bu)CHCl	0.02	150	2.9
(*p*-MePh)(Me)CHCl	180	200	3.4
		2500**	

*Values rounded off.
**Maximum value at $r_R = \infty$, calculation based on Eqn. (14).

Winstein and his coworkers[50–53] investigated the "regeneration" of ion-pairs in the M^+–S_N1 reactions of optically active *p*-chlorophenylphenylmethyl and *exo*-norbornyl chlorides with mercury(II) chloride and acetate in 80% aqueous acetone and in formic and acetic acids. The racemisation and solvolysis rate constants k^{rac} and k^t vary linearly with the concentration of mercury(II) chloride over the range 0.001–0.01 M: $k = k_0 + k_1[HgCl_2]$, which corresponds to Eqn. (2). It is assumed that every act of ionisation (k^α) leads to racemisation[53]:

$$d\text{—RCl} + HgCl_2 \xrightarrow{k^\alpha} R^+ \ldots ClHgCl_2^- \begin{cases} \xrightarrow{dl\text{-RCl} + HgCl_2\,(k^{rac})} \text{HOS} \\ \xrightarrow{dl\text{-ROS} + HCl + HgCl_2\,(k^t)} \end{cases} \quad (15)$$

We then have $k^\alpha = k^{rac} + k^t$, and we can estimate the proportions of the intimate ion-pairs which dissociate and which revert k^t/k^α and k^{rac}/k^α‡. Table 4 lists the proportions of dissociating ion-pairs in the reactions of the organic chlorides with the solvent and with mercury(II) chloride and acetate[51–53]. Although the electrophilic effect for mercury(II) chloride reaches $k_1^t/k_0^t = 10^2$–10^3 M^{-1}, the

‡If configuration is partly maintained during the reversion of ion-pairs to the initial substrate, k^α will give a lower limit to the rate of ionisation of RX. Comparison of the rates of racemisation and of the isotopic exchange of chlorine between RCl and $Hg^{36}Cl_2$ shows[51] that *p*-chlorophenylphenylmethyl chloride is regenerated from the ion-pair $R^+[HgCl_3]^-$, in which the three chlorine atoms are equivalent.

proportion of dissociating ion-pairs amounts to 10–50% for various media, and changes little on passing from reaction with the solvent to reaction with the mercury chloride. This shows that the acceleration of S_N1 reactions on the addition of an electrophile is due mainly to increase in the rate of ionisation k^{α}, not to retardation of the reversion of ion-pairs, as is sometimes assumed [54]. A larger fraction of dissociating ion-pairs are present in the reaction of *exo*-norbornyl chloride with mercury(II) acetate in acetic acid. Mercury acetate accelerates the reaction not only as a stronger electrophile than the chloride but also by supplying acetate ions to R^+.

Table 4. Fraction of dissociating ion-pairs k_1^t/k_1^{α} and electrophilic effect of mercury salts k_1^t/k_0^t in the solvolysis of *p*-chlorophenylphenylmethyl and *exo*-norbornyl chlorides.

Chloride	Solvent	Hg salt	k_1^t/k_0^t, M^{-1}	k_1^t/k_1^{α}
exo-Norbornyl	formic acid	—	—	0.25[a]
		$HgCl_2$	$0.93 \cdot 10^2$	0.51
exo-Norbornyl	acetic acid	—	—	0.09[a]
		$HgCl_2$	$0.89 \cdot 10^2$	0.10
		$Hg(OAc)_2$	$1.6 \cdot 10^5$	0.83
p-Chlorophenyl-phenylmethyl	80% aqueous acetone	—	—	0.43[a]
		$HgCl_2$	$2.4 \cdot 10^3$	0.55

[a]Values of k_0^t/k_0^{α}.

IV. M^+–S_N1 HYDROLYSIS OF INORGANIC HALIDES

The hydration of octahedral cobalt(III), chromium(III), etc. complexes is of the greatest interest, and is assumed to take place, in the absence of metal ions, by an S_N1 (or a dissociative) mechanism [28,41]. The hydration of $CrCl_2(H_2O)_4^+$ and $CrCl(H_2O)_5^{2+}$ is accelerated by Ag^+ and Hg^{2+} ions [55,56]. The complex $CrCl_2(H_2O)_4^+$ interacts with Hg^{2+} and $HgCl^+$ considerably more rapidly than with $HgCl_2$ and $HgCl_3^-$. Similarly, the rate of reaction between $FeCl(H_2O)_5^{2+}$ and $TlCl_n^{(3-n)}$ decreases as n increases from 0 to 3. [57] The stability of the resulting halide complexes falls in the same sequences. Variation of X^- and M^+ in $CrX(H_2O)_5^{2+}$ (X = Cl, Br, I) does not affect the distribution of the products of solvolysis in aqueous methanol $[Cr(H_2O)_6^{3+}]/[Cr(H_2O)_5CH_3OH^{3+}]$ catalysed by Tl^{3+}, Hg^{2+}, and Ag^+ ions, which is regarded as proof of an S_N1 mechanism with the slow stage

$$Cr(H_2O)_5X^{2+} + M^+ \rightarrow Cr(H_2O)_6^{3+} + MX \qquad (16)$$

followed by competing rapid reactions of $Cr(H_2O)_5^{3+}$ with water and with methanol [58]. The fractionation of oxygen-18 in the products of the hydrolysis of $CoX(NH_3)_5^{2+}$ (X = Cl, Br, I) has been studied [59] in the presence of Ag^+, Hg^{2+}, and Tl^{3+}. The reaction with Hg^{2+} yields $CoH_2O(NH_3)_5^{3+}$ enriched with the isotope by a factor of 1.012 relative to the oxygen-18 content of the solvent. An S_N1 mechanism was deduced from the fact that the effect was independent of X^-. In the reactions with Ag^+ and Tl^{3+} the fractionation coefficients are smaller and dependent on X, which indicates a possible contribution by an S_N2 mechanism. In the reaction with Tl^{3+} it is assumed that the attacking water molecule arrives from the inner sphere of the thallium ion [59].

At constant ionic strength induced hydrations are usually of the first order with respect both to the substrate and to M^+. [59,60] Detachment of the first chlorine atom from *cis*-$CoCl_2en_2^+$ (but not from the *trans*-isomer) involves a stage of formation of a stable intermediate:

$$cis\text{-}Co(en)_2Cl_2^+ + Hg^{2+} \underset{}{\overset{K}{\rightleftharpoons}} \left[(en)_2Co\begin{matrix}Cl\\ \diagdown\\ \diagup\\ Cl\end{matrix}Hg\right]^{3+} \qquad (17)$$

with $K = 650\ M^{-1}$. [60] Under the same conditions Tl^{3+}, in contrast to Hg^{2+}, does not give such a complex [61]. Replacement of chlorine in $CoClEDTA^{2-}$ by a carboxyl of ethylenediaminetetra-acetic acid is catalysed by metal ions that form stable complexes with the chloride ion [62–64]. A correlation has been noted between the reaction velocity and K_{MX}, [64] and equilibrium constants of formation of the intermediate have been found from kinetic data. However, the reaction is complicated by a protolytic equilibrium involving a complexone carboxyl uncombined with Co^{3+} and by coordination of this ligand with M^+.

Table 5. Aquation of halogeno-complexes induced by metal ions (in aqueous solution of ionic strength μ at 25°C).

Complex	M^+	μ	k_1, $M^{-1}\,s^{-1}$	k_0, s^{-1}	$\lg k_1/k_0$	Refs.[a]
1	2	3	4	5	6	7
$Co(NH_3)_5F^{2+}$	Th^{4+}	2	0.031	$4.7 \cdot 10^{-8}$[b]	5.82	71/28
$Co(NH_3)_5F^{2+}$	H^+	0.11	$1.1 \cdot 10^{-4}$	$8.6 \cdot 10^{-8}$	3.10	65/28
cis-$Co(en)_2F^{2+}$	H^+	0.01	$3.0 \cdot 10^{-3}$	$3.0 \cdot 10^{-6}$	3.00	66/66
trans-$Co(en)_2F_2^+$	H^+	0.1	$8.2 \cdot 10^{-5}$	$1 \cdot 10^{-6}$	1.9	66/66
$Co(H_2O)_5F^{2+}$	H^+	1.0	$1.4 \cdot 10^{-3}$	$6.2 \cdot 10^{-10}$	1.34	68/28
$Cr(tren)F_2^+$	H^+	0.5	$3.5 \cdot 10^{-3}$	$9.0 \cdot 10^{-6}$	2.58	69/69
$Co(NH_3)_5Cl^{2+}$	Hg^{2+}	2.0	0.55[c]	$6.0 \cdot 10^{-6}$[c]	4.96	61/28
$Co(NH_3)_5Cl^{2+}$	$HgCl^+$	2.0	0.59[c]	$6.0 \cdot 10^{-6}$[c]	4.99	61/28
$Co(NH_3)_5Cl^{2+}$	Tl^{3+}	2.0	0.034[c]	$6.0 \cdot 10^{-6}$[c]	3.75	61/28
$Co(NH_3)_5Cl^{2+}$	$TlCl^{2+}$	2.0	0.012[c]	$6.0 \cdot 10^{-6}$[c]	3.30	61/28
cis-$Co(en)_2(NH_3)Cl^{2+}$	Hg^{2+}	1.0	$1.5 \cdot 10^{-2}$	$5 \cdot 10^{-7}$	4.5	60/28
trans-$Co(en)_2(NH_3)Cl^{2+}$	Hg^{2+}	1.0	$4.6 \cdot 10^{-3}$	$3.4 \cdot 10^{-7}$	4.13	60/28
cis-$Co(en)_2(H_2O)Cl^{2+}$	Hg^{2+}	1.0	$4.2 \cdot 10^{-2}$	$1.6 \cdot 10^{-6}$	4.41	60/28
trans-$Co(en)_2(H_2O)Cl^{2+}$	Hg^{2+}	1.0	$1.3 \cdot 10^{-2}$	$2.5 \cdot 10^{-6}$	3.74	60/28
cis-$Co(en)_2Cl_2^+$	Hg^{2+}	1.0	200	$2.4 \cdot 10^{-4}$	5.92	60/28
trans-$Co(en)_2Cl_2^+$	Hg^{2+}	1.0	3.8	$3.5 \cdot 10^{-5}$	5.04	60/28
cis-$Co(en)_2Cl_2^+$	$HgCl^+$	1.0	240	$2.4 \cdot 10^{-4}$	6.00	60/28
cis-$Co(en)_2Cl_2^+$	Tl^{3+}	1.0	17	$2.4 \cdot 10^{-4}$	4.84	61/28
trans-$Co(en)_2Cl_2^+$	Tl^{3+}	1.0	0.45	$3.5 \cdot 10^{-5}$	4.11	61/28
cis-$Co(en)_2(Py)Cl^{2+}$	Hg^{2+}	1.0	$1.5 \cdot 10^{-2}$	$5 \cdot 10^{-7}$	4.5	60/60
trans-$Co(en)_2(N_3)Cl^+$	Hg^{2+}	1.0	19	$2.2 \cdot 10^{-4}$	4.93	60/28
cis-$Co(en)_2(NO_2)Cl^+$	Hg^{2+}	1.0	78	$1.1 \cdot 10^{-4}$	5.85	60/28
trans-$Co(en)_2(NO_2)Cl^+$	Hg^{2+}	1.0	77	$9.8 \cdot 10^{-4}$	4.90	60/28
cis-$Cr(H_2O)_4Cl_2^+$	$HgCl^+$	0.50	50	$4.3 \cdot 10^{-5}$	6.06	80/28
trans-$Cr(H_2O)_4Cl_2^+$	$HgCl^+$	0.50	67	$8.3 \cdot 10^{-5}$	5.91	80/28
trans-$Cr(H_2O)_4Cl_2^+$	Hg^{2+}	0.50	31	$8.3 \cdot 10^{-5}$	5.57	81/28
$Cr(NH_3)_5Cl^{2+}$	Hg^{2+}	2.0	$8.7 \cdot 10^{-2}$	$7.3 \cdot 10^{-6}$	4.08	82/28
$Cr(NH_3)_5Cl^{2+}$	$HgCl^+$	2.0	0.10	$7.3 \cdot 10^{-6}$	4.14	82/28
cis-$Co(en)_2(NH_3)Cl^{2+}$	Hg^{2+}	0.2	$5.7 \cdot 10^{-3}$	$5.5 \cdot 10^{-7}$	4.01	84/83
cis-$Co(en)_2(MeNH_2)Cl^{2+}$	Hg^{2+}	0.2	$1.5 \cdot 10^{-2}$	$4.0 \cdot 10^{-7}$	4.57	84/83
cis-$Co(en)_2(EtNH_2)Cl^{2+}$	Hg^{2+}	0.2	$8.8 \cdot 10^{-3}$	$1.5 \cdot 10^{-7}$	4.77	84/83
cis-$Co(en)_2(n\text{-}PrNH_2)Cl^{2+}$	Hg^{2+}	0.2	$1.0 \cdot 10^{-2}$	$3.2 \cdot 10^{-7}$	4.49	84/83
cis-$Co(en)_2(i\text{-}PrNH_2)Cl^{2+}$	Hg^{2+}	0.2	$5.4 \cdot 10^{-2}$	$1.2 \cdot 10^{-6}$	4.65	84/83
$Fe(H_2O)_5Cl^{2+}$	$HgCl^+$	0.5	$1.7 \cdot 10^7$	12	6.15	85/85
$Fe(H_2O)_5Cl^{2+}$	$HgCl_2$	0.5	$8.5 \cdot 10^8$	12	1.85	85/85
$Cr(H_2O)_4Cl_2^+$	Ag^+	6	$3.7 \cdot 10^{-2}$	$6 \cdot 10^{-5}$	2.8	55/28
$Cr(H_2O)_5Cl^{2+}$	Ag^+	6	$1.1 \cdot 10^{-4}$	$2.8 \cdot 10^{-7}$	2.61	55/28
$Cr(H_2O)_5Cl^{2+}$	Hg^{2+}	1.0	$4.8 \cdot 10^{-2}$	$2.8 \cdot 10^{-7}$	5.23	56/28
$Cr(H_2O)_5Cl^{2+}$	$HgCl^+$	1.0	0.11	$2.8 \cdot 10^{-7}$	5.57	56/28
$Ru(NH_3)_5Cl^{2+}$	Hg^{2+}	0.17	$9.0 \cdot 10^{-4}$	$3.8 \cdot 10^{-8}$	4.37	86/86
$Co(NH_3)_5Br^{2+}$	Hg^{2+}	0.03	12	$6.3 \cdot 10^{-6}$	6.28	87/28

[a]The first reference relates to k_1, and the second to k_0.
[b]At 20.5°C.
[c]At 35°C.

The hydrolysis of inorganic fluorides, like that of organic fluorides, is catalysed by acids ($M^+ = H^+$). Studies have been made of the acid hydrolysis of $CoF(NH_3)_5^{2+}$, [65] *cis*- and *trans*-$CoF_2en_2^+$, [66] *cis*-$CrF_2en_2^+$, [67]

$CrF(H_2O)_5^{2+}$,[68] $CoF_2tren_2^+$,[69] etc. (tren = $N(C_2H_4NH_2)_3$). The reactions are assumed to involve protonation of the fluorine. In the case of $CoF_2tren_2^+$ formation of an intermediate has been detected from kinetic data. A linear dependence of $\lg k$ on H_0 with slope −0.97 has been found[70] for the acid hydrolysis of PF_6^- over the range 2–10 M hydrochloric acid. The hydration of $CoF(NH_3)_5^{2+}$ is accelerated by Th^{4+},[71] and the hydrolysis of XeF_2 by Th^{4+}, Al^{3+}, Be^{2+} and La^{3+} ions[72] in qualitative agreement with the stability sequence of their fluoride complexes. Clark and Jones have found that Zr^{4+}, Th^{4+}, Al^{3+}, Be^{2+}, and Ti^{4+} induce the hydrolysis of BF_4^-, PF_6^-, $AsOHF_5^-$, and AsF_6^- in strongly acid media[73]. Iron(III) complexes induce the hydrolysis of $AsOHF_5^-$.[74] All these reactions are assumed to involve the direct interaction of M^+ with the fluoride ligand[71,73], and they are regarded as similar to the splitting of the Co–Cl bond by the Hg^{2+} ion[74]. Chelate complexes of Cu^{2+}, Th^{4+}, and Zr^{4+} catalyse the hydrolysis of $(iso\text{-}C_3H_7O)_2POF$ and $iso\text{-}C_3H_7P(CH_3)OF$ (Sarin)[75–77]. The mechanism of these reactions is complicated.

The inadequacy of a simple S_N1–S_N2 classification for inorganic complexes has already been stressed[41,78]. Nevertheless, the above results indicate a certain analogy in the kinetics, mechanism, and driving force of the M^+–S_N1 hydrolysis of organic and of inorganic halides. Values of k_1 and k_0 for the hydration of cationic complexes (Table 5) show that the relation between them is close to Eqn. (4) for t-butyl halides[79]. The agreement is improved by introducing an additional term containing the product of the charges Z_1Z_2 to allow for the Coulombic repulsion of the reactants. Sykes et al.[61] had already used Coulombic repulsion to explain the greater activity of Hg^{2+} than of Tl^{3+} contrary to the sequence of K_{MX} for $HgCl^+$ and $TlCl^{2+}$ in the hydrolysis of $CoCl(NH_3)_5^{2+}$ and of *cis*- and *trans*-$CoCl_2en_2^+$. The data compiled in Table 5 satisfy the inequality (10), as would be expected. It is noteworthy that the ratio k_1/k_0 is in all cases larger for *cis*-complexes than for the *trans*-isomers[79].

Table 6. Calculation of rates of M^+–S_N1 hydrolysis of BF_4^- and PF_6^- (aqueous solutions at 25°C; k_1 in M^{-1} s^{-1} and k_0 in s^{-1}).

Ion	BF_4^- $\lg k_0 = -7.0$[68]		PF_6^- $\lg k_0 = -10.9$[68]	
	$\lg k_1$ expt.	$\lg k_1$ calc. from Eqn.(12)	$\lg k_1$ expt.	$\lg k_1$ calc. from Eqn.(12)
H^+	−3.9	−3.7	−6.8	−7.6
Be^{2+}	−1.0	−1.4	−4.3	−5.3
Al^{3+}	−0.8	0.0	−4.0	−3.9
Th^{4+}	+0.2	+1.8	−3.2	−2.1

Equation (12) cannot in general be used to process the results in Table 5: with reactants of like charge the effects of the ionic strength, which differ with different systems, may lead to overestimates of 1–2 units in $\lg k_1$. Nevertheless, several examples have shown[8] that theoretical approaches are applicable to M^+–S_N1 reactions of inorganic halides. The induced hydrolysis of BF_4^- and PF_6^- has been studied[73] in hydrochloric acid (1–2 M) without extrapolation to zero ionic strength. It is difficult to assess the accuracy of the results. An S_N1 mechanism is probable in both cases, since the central atoms in BF_4^- and PF_6^- are shielded from S_N2 attack. Covalent models of the transition states—$F_3B\ldots F^-\ldots M^+$ and $F_5P\ldots F^-\ldots M^+$—were adopted for the calculations. The theoretical equation is $k_1 = k_0K_{MX}$. The results are given in Table 6. Ionic models of the transition states of these reactions—$(F^-)_3B^+\ldots F^-\ldots M^+$ and $(F^-)_5P^{5+}\ldots F^-\ldots M^+$ with $r_F = 1.33$, $r_B = 0.20$, and $r_P = 0.35$ Å—lead to underestimates of k_1 by factors of $10–10^2$. Agreement between calculated and experimental values of k_1 has been shown[8] also for the reactions of $CoBr(NH_3)_5^{2+}$ and $RhCl(NH_3)_5^{2+}$ with Hg^{2+}, which have been studied at a low ionic strength (Table 5). The theoretical equation for the ionic model of the transition state $(NH_3)_5M^{3+}\ldots X^-\ldots Hg^{2+}$ is $(\lg k_1/k_0K_{MX})_{theor} = -27.9/l_{M\text{–}Hg}$.

Data extrapolated to zero ionic strength, as well as information on the actual geometry of the complexes and the delocalisation of charges on the ligands, are required in order to make an extensive test of the theory. It is quite possible that, with accurate values of k_0, k_1, and K_{MX}, the above approach may give valuable information on the structure of transition states.

The above regularities in the detachment of halogens by metal ions can probably be extended to the detachment of other groups. As with halides, the driving force of such reactions is the formation of a stable bond between the metal and the detached group. The hydration of $Fe(CN)_6^{4-}$ is accelerated by mercury(II) and silver(I) salts[90], that of $CrCN^{2+}$,[91] $CrSCN^{2+}$, and $CrNCS^{2+}$[92,93] by mercury(II) salts, and the hydration of $CoCO_3(NH_3)_5^+$ by bivalent mercury, lead, and barium salts[94]. As a consequence of high affinity for the sulphur atom, Ag^+ and Hg^{2+} ions accelerate reactions involving cleavage of phosphorus–sulphur[95] and carbon–sulphur[96–99] bonds. The kinetics and the mechanism of these reactions have not yet been adequately studied.

V. M^+–S_N2 REACTIONS OF PRIMARY AND SECONDARY ALKYL HALIDES

The acceleration of the reactions of primary and secondary alkyl halides by the ions Ag^+[100–108] and Hg^{2+}[4,109–112] (see also Refs. 2 and 3) was originally discussed in terms of Ingold's hypothesis[1] that the mechanism changes from S_N2 to Ag^+–S_N1 (or Hg^{2+}–S_N1) under the influence of M^+. For example, the reaction of benzyl chloride with mercury(II) nitrate in aqueous dioxan was represented by the scheme[4]

$$C_6H_5CH_2Cl + Hg^{2+} \xrightarrow[\text{slow}]{} HgCl^+ + C_6H_5CH_2^+ \longrightarrow \begin{cases} \xrightarrow{NO_3^-} C_6H_5CH_2ONO_2 \\ \xrightarrow{H_2O} C_6H_5CH_2OH + H^+ \end{cases} \quad (18)$$

An M^+–S_N1 mechanism was suggested also for the reactions of primary alkyl bromides with Hg^{2+},[111,112] but the sequence of rates—$C_2H_5Br > n\text{-}C_3H_7Br > iso\text{-}C_4H_9Br$[111]—indicates nucleophilic attack. On the other hand, cases of the rearrangement and racemisation of the alkyl group[1,3,113], indicating intermediate formation of an ion-pair, may be a consequence of a slow reaction with the solvent under the same conditions, but without M^+, also by an S_N1 mechanism. Several later attempts were made[114–121] to prove that a nucleophile was involved in the reactions of primary and secondary alkyl halides with Ag^+, but it was difficult to distinguish the roles of the anion (nitrite, nitrate, perchlorate) as a nucleophile and as a ligand changing the activity of M^+. Furthermore, the reactions were usually studied in anhydrous or nearly anhydrous media, where the effects of ionic association were significant.

The results of detailed kinetic investigations of the hydrolysis of methyl, ethyl, and isopropyl halides in the presence of metal ions in aqueous solution [9,122-130] are summarised in Table 7. These reactions outwardly resemble M^+–S_N1 reactions of t-butyl halides: the kinetics are in most cases represented by Eqn. (2), metal ions that form stable complexes MX—in particular Ag^+, Pb^{2+}, Cd^{2+}, Hg^{2+}, and Tl^{3+}—are active, and the dependence of $\lg(k_1/k_0)$ on $\lg K_{MX}$ is nearly linear for a given alkyl group with electrophiles having the same charge [125,126]. However, significant differences were revealed. Experimental values of $\lg(k_1/k_0)$ are lower than those calculated by means of Eqn. (4) (Fig. 2). The differences increase with enhancement of the S_N2 character of the reactions, i.e. in the sequence isopropyl < ethyl < methyl, and with increase in the charge on the metal ion. The Tl^{3+} ion is less active than Hg^{2+}, although the Lewis acidity of the former is greater (Table 1). Correction for the Coulombic destabilisation of the transition state (Section III) is insufficient to explain the discrepancies, which reach $\Delta \lg(k_1/k_0) = 4-6$ for Hg^{2+} and Tl^{3+}.

Table 7. Rate constants of M^+–S_N2 reactions in aqueous solutions of zero ionic strength at 25°C (k_0 in s^{-1} and k_1 in $M^{-1}\ s^{-1}$).

	Reaction	Ref.	$\lg k_0$ [131,132]	$\lg k_1$ expt.	$\lg k_1$ calc. from Eqn.(19)
1	MeCl+Hg^{2+}	125	−7.62	−5.2	−5.2
2	MeBr+Hg^{2+}	125	−6.39	−2.5	−2.4
3	MeI+Ag^+	127	−7.13	−2.6	−2.6
4	MeI+2Ag^+	127	−7.13	−0.8[a]	−0.8[a]
5	MeI+Hg^{2+}	125	−7.13	+0.1	0.0
6	EtCl+Hg^{2+}	125	−7.70	−4.7	−4.7
7	EtBr+2Ag^+	123	−6.42	−2.7[a]	−3.0[a]
8	EtBr+Pb^{2+}	126	−6.42	−6.6	—
9	EtBr+Cd^{2+}	126	−6.42	−6.5	−6.6
10	EtBr+Hg^{2+}	122,126	−6.42	−1.8	−1.8
11	EtBr+Tl^{3+}	128	−6.42	−3.9	−3.8
12	EtI+Ag^+	129	−6.82	−1.8	−2.0
13	EtI+2Ag^+	129	−6.82	−0.1[a]	0.0[a]
14	EtI+Hg^{2+}	125	−6.82	+1.2	+1.1
15	*i*-PrCl+Hg^{2+}	125	−6.67	−2.2	−2.3
16	*i*-PrCl+Tl^{3+}	128	−6.67	−2.8	−2.7
17	*i*-PrBr+Ag^+	129	−5.42	−2.2	−2.0
18	*i*-PrBr+2Ag^+	129	−5.42	−0.7[a]	−0.8[a]
19	*i*-PrBr+Cd^{2+}	126	−5.42	−5.0	−4.9
20	*i*-PrBr+Hg^{2+}	125	−5.42	+0.9	+0.8
21	*i*-PrBr+Tl^{3+}	128	−5.42	−0.4	−0.5

[a] $\lg(k_2,\ M^{-2}\ s^{-1})$.

The above reactions have therefore been included [9] in the M^+–S_N2 type, their driving force being an electrophilic contribution to heterolysis of the C–X bond with simultaneous attack by the nucleophile on the carbonium centre. Since bonds in the transition state

$$H_2O^{+\delta_B}\cdots\overset{|}{C}{}^{+\delta_C}\cdots X^{-\delta_X}\cdots M^+$$

are partly covalent (it is assumed that $\delta < 1$), the electronic effect may be transmitted by an induction mechanism. Displacement of the electrons towards M^+ lowers the electron density on the $H_2O\ldots C\lessdot$ bond in the transition state, which diminishes the S_N2 character of the reaction. This effect, termed [9] "inductive retardation", should be most intense with methyl halides, when overlapping of the orbitals at this bond is greatest, and with multicharged ions, e.g. Tl^{3+}, having a high electron affinity.

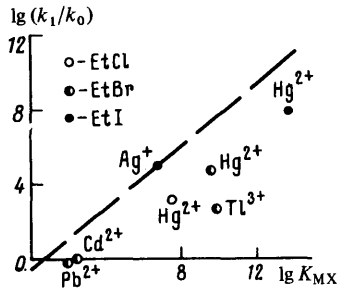


Figure 2. Comparison of values of $\lg(k_1/k_0)$ for the reactions of $C_2H_5X + M^+$ with correlation (4) for t-C_4H_9X (broken lines).

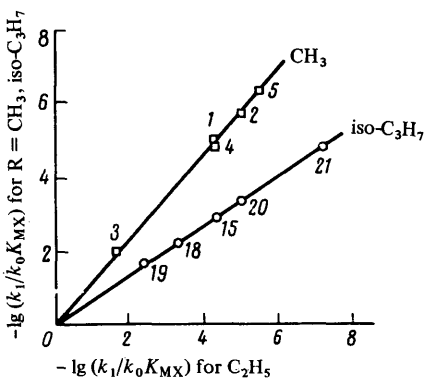


Figure 3. Correlation between values of $\lg(k_1/k_0K_{MX})$ for CH_3X, iso-C_3H_7X, and C_2H_5X with variation in M^+ and X. For the reactions of RX with two silver ions, k_1 and K_{MX} have been replaced by k_2 and K_{Ag_2X}. Numbering as in Table 7.

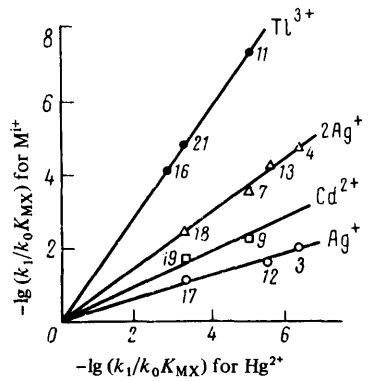


Figure 4. Correlation between values of $\lg(k_1/k_0K_{MX})$ for Tl^{3+}, $2Ag^+$, Cd^{2+}, and Ag^+ and for Hg^{2+}, with variation of R and X.

The effects of R, X, and M^+ in M^+–S_N2 reactions (Table 7) are reproduced by the equation

$$\lg (k_1/k_0) = \lg K_{MX} - P_R \cdot P_X \cdot P_M \quad , \qquad (19)$$

where P_R, P_X, and P_M are positive constants depending on the properties of the respective species. The overall effect of the metal ion is determined by competition between electrophilic bonding of X^-, represented by the term $\lg K_{MX}$, as for t-butyl halides, and inductive retardation ($P_R P_X P_M$). Equation (19) leads to the correlations

$$\left(\lg \frac{k_1}{k_0 K_{MX}}\right)_{R_1} = \frac{P_{R_1}}{P_{R_2}} \left(\lg \frac{k_1}{k_0 K_{MX}}\right)_{R_2} , \text{ varying X, } M^+ \qquad (20)$$

$$\left(\lg \frac{k_1}{k_0 K_{MX}}\right)_{X_1} = \frac{P_{X_1}}{P_{X_2}} \left(\lg \frac{k_1}{k_0 K_{MX}}\right)_{X_2} , \text{ varying R, } M^+ \qquad (21)$$

$$\left(\lg \frac{k_1}{k_0 K_{MX}}\right)_{M_1} = \frac{P_{M_1}}{P_{M_2}} \left(\lg \frac{k_1}{k_0 K_{MX}}\right)_{M_2} , \text{ varying R, X} \qquad (22)$$

which can be verified directly (Figs. 3–5). Table 8 gives values of P_R, P_X, and P_M determined [9] for the standard conditions $P_{Br} \equiv 1$ and $P_{Hg} \equiv 12.8$; Table 7 compares experimental values of k_1 with those calculated by means of Eqn. (19). For M^+–S_N1 reactions of t-butyl halides $P_R = 0$ (if Coulombic repulsion is neglected). The interpretation of P_M as an induction constant of the M^+ ion is confirmed by comparing [9] P_M and the equilibrium constant $K_{MOH} = [MOH][H_2O]/[M^+][OH^-]$, which is determined mainly by charge transfer to the aquo-ion

$$\begin{matrix} H \\ H \end{matrix}\!\!\searrow\!\!\nearrow O \rightarrow M^+ ,$$

and by the correlation of P_M with the electron affinity of the M^+ ions in the gas phase.

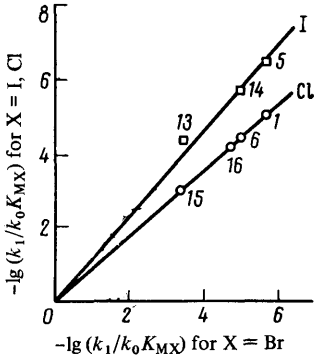


Figure 5. Correlation between values of $\lg (k_1/k_0 K_{MX})$ for I, Cl, and Br with variation of R and M^+.

The above results indicate the occurrence of a broad spectrum of S_N2 reactions depending on the overlap of nucleophile and $R^{\delta+}$ orbitals in the transition state. Here S_N1 reactions correspond to the limit at which the action of the solvent nucleophile is restricted by solvation. The overlap of the orbitals is determined by the nucleophilic character of the medium and the nature of the alkyl group; it depends little on the strength of the electrophile, at least in the range from H_2O to Tl^{3+}. The above slight diminution of S_N2 character of the reaction due to the inductive effect of M^+ is consistent with data on the reactions of alkyl halides with sodium and silver nitrites forming the basis of Kornblum's rule [114,133,134]. Since electrophiles accelerate S_N1 reactions more strongly than S_N2 reactions (Fig. 2), the variations in mechanism indicated in Table 9 are possible under the influence of metal ions.

Table 8. Values of the parameters P_R, P_X, and P_M for M^+–S_N2 reactions [9].

R		*i*-Pr		Et		Me	
P_R		0.261±0.004		0.386±0.005		0.440±0.002	
X		Cl		Br		I	
P_X		0.862±0.004		(1)		1.13±0.04	
M^+	Ag^+	Pb^{2+}	Cd^{2+}	$2Ag^+$	Hg^{2+}	Tl^{3+}
P_M	4.2±0.3	5.7	6.3±0.5	9.5±0.3	(12.8)	18.6±0.2

Table 9.

Reaction with solvent		Reaction with M^+ in same medium
S_N1	I	M^+–S_N1
	III	
S_N2	II	M^+–S_N2

Transition III, corresponding to S_N2 reactions with slight overlap of the orbitals, has not yet been demonstrated, but may occur in the solvolysis of n-propyl bromide in 90% formic acid in the presence of Hg^{2+}, when the formation of propan-2-ol can be explained [113] only by a 1–2 hydride shift in the n-propyl cation. Another approach [135–139], which describes the kinetics of the reactions of primary and secondary alkyl halides with a nucleophile N^- in terms of the general scheme of S_N1 reactions

$$RX \rightleftharpoons R^+ \ldots X^- \xrightarrow{N^-} RN + X^-$$

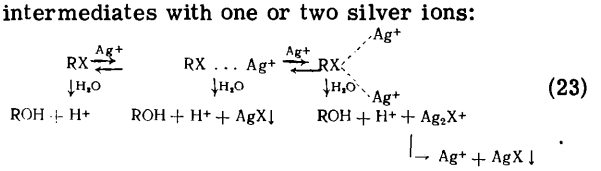
seems less probable, in view of the above differences between M^+–S_N1 and M^+–S_N2 reactions and the fact that the transition state $N^- \ldots R^{\delta+} \ldots X^{\delta-}$ for S_N reactions should be more stable than an intimate ion-pair $R^+ \ldots X^-$. Transition III can be expected also for isopropyl and benzyl halides. Results for the hydrolysis of isopropyl halides in the presence of metal ions (Table 7) are in fact reproduced by Eqns. (4) and (12) for M^+–S_N1 reactions, although less accurately than by Eqn. (19). This can be interpreted as indicating that the mechanism for isopropyl halides is intermediate between M^+–S_N1 and M^+–S_N2. The formation of propene in the hydrolysis of isopropyl bromide in the presence of silver ions [129] is consistent with an M^+–$E2$ mechanism and with elimination from the ion-pair. The electrophilic contribution of metal ions to the hydrolysis of benzyl fluoride [140,141] is conveyed approximately by correlation (4) for M^+–S_N1 reactions [26,27].

The above model of M^+–S_N2 reactions is equivalent to Swain's push–pull mechanism suggested in 1948.[142,143] However, only by the use of aquo-ions of metals has it become possible in principle to study the role of the electrophile with the nucleophile and the medium fixed.

VI. ASPECTS OF THE REACTIONS OF ALKYL HALIDES WITH SILVER IONS

Until recently the mechanism of the reactions of alkyl halides with silver salts[11,54,100–108,114–121,130,144–151] remained obscure owing to the complexity of the kinetics, especially in non-aqueous media, and the unusual reaction orders with respect to silver—from 0 to 2 and higher, including fractional orders. The traditional explanation of these anomalies was based[114,116–121,130,152] on the nucleophilic contribution of anions (nitrate and perchlorate), the influence of the ionic strength, and the effects of ionic association in low-polarity solvents. The hypothesis that these reactions were accelerated significantly by precipitated silver halides[1,3] has not been confirmed[54,123,118–121,130,153].

Detailed kinetic studies of the hydrolysis of t-butyl chloride[25], isopropyl bromide[129], ethyl bromide[123], ethyl iodide[129], and methyl iodide[127] in the presence of silver ions in aqueous media indicate that these complications are due to a special mechanism involving the formation of intermediates with one or two silver ions:

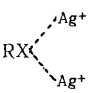


(23)

This mechanism corresponds to the kinetic equation[24,123]

$$k \equiv -\frac{1}{[RX]}\frac{d[RX]}{d\tau} = \frac{k_0 + k_1[Ag^+] + k_2[Ag^+]^2}{1 + K_{gr}[Ag^+]}, \qquad (24)$$

where k_0, k_1, and k_2 are the rate constants of reaction with the solvent and with one and two silver ions, and $K_{gr} = [RX\ldots Ag^+]/[RX][Ag^+]$ is the stability constant of the intermediate $RX\ldots Ag^+$. The concentration of the intermediate



is assumed[123,127,129] to be minute. In M^+–S_N1 reactions ($R = t\text{-}C_4H_9$) intermediates of these types dissociate with the formation of R^+, whereas in M^+–S_N2 reactions ($R = CH_3$, C_2H_5, iso-C_3H_7) they undergo nucleophilic attack by water, but the stepwise scheme (23) is the same in the two cases. Partition kinetic methods have been elaborated[19,24,26] which enable us to determine not only the rate constant but also the solubility of the substrates, which depends on complex formation between the alkyl halide and the silver ion.

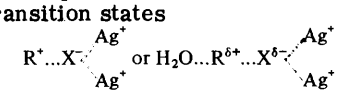
Table 10 gives the values of K_{gr} for the complexes $RX\ldots Ag^+$ together with values, obtained spectrophotometrically in aqueous solution at 25°C, for the kinetically stable $CH_2X_2\ldots Ag^+$ species. The stability of the complexes increases in the sequences Cl < Br < I and $CH_3 < C_2H_5 <$ iso-C_3H_7. Their formation is a consequence of the low hydration energy of the silver ion and its comparatively high affinity for halogen. Complex formation between RX and Hg^{2+} is considerably weaker[122,125], although HgX^+ is more stable than AgX. Mercury(II) chloride forms a complex with benzyl bromide[155]. Many observations have been made in non-aqueous media of complexes of alkyl halides with the silver ion[149,150] and other Lewis acids (see reviews[156,157]).

Values of k_1 and k_2 are given in Table 7. Reactions of the first order with respect to the silver ion do not differ from the reactions of alkyl halides with other metal ions. Reaction paths of the second order ($2Ag^+$, Table 7) occur[9,25,123,127] as a consequence of the great stability of the complexes Ag_2X^+ with the anion as centre of coordination. The composition, stability, and structure of complexes of this type—Ag_2X^+, Ag_3X^{2+}, Hg_2X^{3+}, Cd_2X^{3+}, and several others—have been widely discussed[158–161].

Table 10.

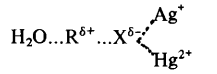
Substrate	MeI[127]	EtI[129]	EtBr[123]	*i*-PrBr[129]	CH_2Cl_2[154]	CH_2Br_2[154]	CH_2I_2[154]
K_{gr}, M^{-1}	15	32	1.6	4.2	0.1	0.5	20.2

Reactions involving two silver ions provide a further example of the generality of the correlation between the rate of the induced detachment of a halide ion and the stability of the complexes formed in the rate-determining stage. The transition states



(for M^+–S_N2 reactions), of which the complex Ag_2X^+ is a fragment in both cases, are advantageous despite the Coulombic repulsion of the two silver ions. The second silver ion acts as a catalyst, promoting detachment of the halide ion and ultimately being regenerated (Eqn. 23). Values of k_2 for the reactions of methyl iodide, ethyl iodide, ethyl bromide, and isopropyl bromide (Table 7) agree with those calculated by means of Eqn. (19), with $P_2Ag \simeq 2PAg$ (Table 8). The additivity of the effects of the two silver ions is consistent with the interpretation of P_M as a measure of the inductive effect of the metal ion. Agreement between k_2 and K_{Ag_2X} has been shown also for t-butyl chloride[25].

Reaction paths of the third order with respect to the silver ion[127] and of the second order with respect to Hg^{2+},[125] corresponding to the complexes Ag_3X^{2+} and Hg_2X^{3+}, have not yet been observed, but the stability constants suggest that such reactions are possible at salt concentrations of 5–10 M. The hydrolysis of ethyl bromide in solutions containing both Ag^+ and Hg^{2+} ions reveals[124] a component rate $k_2[RX][Ag^+][Hg^{2+}]$ of the first order with respect to each ion, which corresponds to the transition state



in which one of the two silver ions has been replaced by an Hg^{2+} ion. A cross route has been found also for silver and cadmium ions[124]. Kinetic data have been used to estimate[124] stability constants of hitherto unknown complexes with an anionic centre of coordination and two different metal ligands—$HgBrAg^{2+}$ ($10^{9.3}$ M^{-2}) and $CdBrAg^{2+}$ (10^7 M^{-2}).

A reaction path involving two silver ions has been found in the hydrolysis of 1-benzoyl-1-methylethyl bromide[162]. Competition between reactions of first and second orders with respect to silver ions has been

observed [95-99] in the cleavage of carbon–sulphur and phosphorus–sulphur bonds. Mechanism (23) can therefore be regarded as general for the reactions of silver ions with substrates having a soft basic centre such as a halogen or sulphur.

Thus the Brønsted relation is widely applicable to the effects of the electrophilic contribution to the detachment of halogens and perhaps other groups in the reactions of organic and inorganic substrates. These reactions can be included among the M^+–S_N1 and M^+–S_N2 types. In order to calculate the rate constant of an M^+–S_N1 reaction in terms of a model of the transition state with complete charge separation along the bond undergoing cleavage, it is sufficient to take into account the Lewis acidity of the electrophile. In an M^+–S_N2 reaction the electrophilic contribution is accompanied by retardation due to the inductive effect of the electrophile. Reaction paths of the second order with respect to silver ions conform to the general rules for M^+–S_N1 and M^+–S_N2 reactions.

NOTE ADDED IN PROOF

The theory of M^+–S_N1 reactions outlined in this Review has recently been generalised [163] to the S_N1 solvolysis of t-butyl halides. Interaction of the transition state with the medium is separated into Coulombic interaction in the ion-pair and actual solvation, which is taken into account on the basis of a coordination model and the solvation energies of the ions. Direct theoretical calculation gave quantitative agreement with experimental rates of solvolysis with the medium varied within wide limits, which provides reliable evidence of the generality of the S_N1 and M^+–S_N1 mechanisms.

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Chemistry in the USSR Academy of Sciences

N.M.Emanuel'

Chemistry as a scientific discipline originated in our country at the time of the first Russian Academician in Chemistry, Mikhail Vasil'evich Lomonosov. As early as 1741 Lomonosov gave a completely modern definition of this science: "Chemistry is the science of the changes occurring in a compound body because it is compound". About 130 years later D. I. Mendeleev, in "The Principles of Chemistry", wrote: "The immediate object of chemistry is to study the homogeneous substances whose combination produces all the bodies in the world, their interconversions, and the phenomena accompanying such transformations". Both definitions are profoundly dialectical, for they regard chemistry as the whole set of manifestations of the chemical form of transformation of matter.

In its usual sense chemistry has always been and remains the science of the substances, products, and materials necessary to man and of the methods for their extraction and manufacture.

However, the ways of studying the composition, structure, and properties of many millions of individual substances, of knowing the detailed mechanism of the immense number of reactions at an elementary, atomic-molecular level, controlling chemical processes, and obtaining end-products with specified properties are so complicated and multifarious that modern chemistry is most intimately linked with mathematics, physics, and biology.

The Soviet period of development in chemistry is characterised by exceptionally high rates of growth of the volume of scientific research and increase in the number of lines of scientific investigation. Chemical laboratories changed radically in appearance, periodically undergoing almost complete material and technical re-equipment owing to the widespread introduction of the experimental methods of modern physics, radioelectronics, computer technology. The present time is characterised both by a process of obliteration of the boundaries between physical, organic, inorganic, and analytical chemistry and by the birth of new branches of chemical science.

Chemical research is conducted in the Soviet Union by large bodies of scientists associated in institutes of the USSR Academy of Sciences and those of the Union Republics, institutions of higher education, industrial institutes, and factory laboratories.

In many fields Soviet chemistry occupies leading positions in world science and has good prospects for further development, thanks to the constant attention of Party and Government, expressed in the resolutions of the Twenty-fourth Congress of the Communist Party of the Soviet Union.

The present paper gives a brief historical sketch of the development of chemistry in our country, mainly in the USSR Academy of Sciences.

PHYSICAL CHEMISTRY

The development of physical chemistry was directly connected with its previous history. It began with M. B. Lomonosov, who proposed the term "physical chemistry" for that branch of science which "uses the principles and experiments of physics to explain what occurs in compound bodies during chemical operations".

In pre-Revolutionary times physical chemistry developed in Russia mainly in the universities (Moscow, St. Petersburg, Kazan, Kiev, etc.). The situation changed substantially during the Soviet period, when physicochemical investigations came to be widely conducted not only

in university centres but also in institutes of the USSR Academy of Sciences, as well as in several branch scientific research establishments.

The first institute having a physicochemical outlook was the Karpov Physicochemical Institute founded in 1918 by A. N. Bakh, who remained its director for three decades.

Chemical physics—the physics of chemical processes—arose during the 1920s in the Leningrad Physicotechnical Institute, directed by A. F. Ioffe. The creation of this branch contributed to the development, in the mid-1920s, of the principles of L. V. Pisarzhevskii's electronic theory of valency and the publication in 1927 of the monograph "Elektronnaya Khimiya [Electronic Chemistry]" by V. N. Kondrat'ev, N. N. Semenov, and Yu. B. Khariton. The USSR Academy of Sciences Institute of Chemical Physics, founded in 1931 and directed by N. N. Semenov, became a most important centre of kinetic investigations. During recent years diverse kinetic researches have been made in the Institute of Kinetics and Combustion of the Siberian Division of the USSR Academy of Sciences, especially on the reactions of combustion and also the study of the structure of coordinated metal complexes.

In 1945 the Laboratory of Colloidal Electrochemistry (founded in 1930 by V. A. Kistyakovskii) formed the basis for establishing the Institute of Physical Chemistry of the USSR Academy of Sciences, where work has been done on the problems of surface phenomena, the theory of chromatography, problems of corrosion, radiochemistry, thermodynamics, and colloid chemistry.

The study of the theory of electrochemical processes, in particular the electrochemistry of organic compounds, and problems of radiation and quantum chemistry and of hydrodynamics provide the subject-matter for the Academy's Institute of Electrochemistry, founded in 1958 by A. N. Frumkin.

The Institute of Catalysis of the Siberian Division occupies a leading position in the field of heterogeneous catalysis.

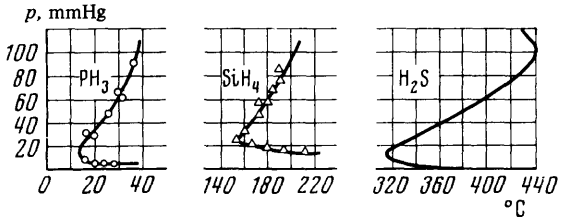


Figure 1. Regions of chain ignition of phosphine, silane, and hydrogen sulphide.

At the present time hardly any branch of chemistry and biochemistry is conceivable without the use of physicochemical methods for analysing and investigating chemical substances, their structure, and properties. Physicochemical investigations are therefore undertaken in almost all chemical institutes. Examples are the Institute of Organoelementary Compounds, in which the structures and reactivities of organic compounds are studied by infrared, nuclear magnetic resonance, and electron spin resonance spectroscopy, and the Institute of Organic Chemistry, where N. D. Zelinskii founded the theory of organic catalysis, later developed by his students, and where A. A. Balandin made his investigations on heterogeneous catalysis.

The Institute of Petroleum-chemical Synthesis, founded by A. V. Topchiev in 1958, studies the mechanism of many petrochemical and polymerisation processes, the physical chemistry of polymers, and in particular the rheology of polymers.

The Institute of General and Inorganic Chemistry (founded by N. S. Kurnakov) has become a centre for developing physicochemical methods of analysis.

Physicochemical methods of studying chemical reactions are widely used in the institutes of the Siberian Division of the USSR Academy of Sciences (Institute of Organic Chemistry), as well as in the Arbuzov Institute of Organic and Physical Chemistry (Kazan), in the Institute of Chemistry in Gorky, and in many other institutes of the USSR Academy of Sciences.

The oldest of the physicochemical institutes of the academies of Union Republics is the Pisarzhevskii Institute of Physical Chemistry of the Ukrainian SSR Academy of Sciences, which is concerned with investigating radical reactions, polymerisation processes, and heterogeneous catalysis.

Chain Reactions and Elementary Chemical Processes

One of the greatest achievements of Soviet physical chemistry is the theory of branched chain reactions. At the end of the 1920s N. N. Semenov, Yu. B. Khariton, and Z. F. Val'ta discovered that phosphorus vapour ignited only when a certain critical oxygen pressure had been reached. Addition of an inert gas (argon) enabled ignition to be observed at oxygen pressures below the critical value. The existence of a "critical" diameter of the reaction vessel was also discovered. Semenov put forward the idea of branched chain reactions to explain the new facts. The reaction was assumed to be a chain process, with an increase in the number of free radicals occurring in elementary steps which were termed chain branchings. The progressive growth in the concentration of free radicals, under conditions such that the rate of chain branching exceeded the rate of chain termination, led to chain self-ignition (Fig. 1).

Chain ignition is an isothermal explosion. The evolution of heat in this process is insignificant, since the explosion is due to a progressive growth of the number of active centres. In subsequent years the work of many scientists has demonstrated the widespread occurrence of branched-chain reactions. It was Semenov who inferred that high concentrations of free radicals are formed in branched-chain processes.

In this connection a large number of determinations were made of the concentrations of free radicals in chain reactions. After several years V. N. Kondrat'ev had developed methods enabling free atoms and radicals to be studied while reaction was proceeding (line absorption and catalytic recombination methods). Hydrogen atoms and hydroxyl radicals were detected by these methods in the combustion of molecular hydrogen, and carbonyl sulphide in that of carbon disulphide. It was also discovered that SO free radicals were formed in the slow oxidation of hydrogen sulphide. The concentrations observed exceeded by many orders of magnitude the thermodynamic equilibrium concentrations under the experimental conditions.

In 1944 E. K. Zavoiskii discovered the remarkable phenomenon of electron spin resonance (e.s.r.). Research on its extensive use in chemistry was undertaken by V. V. Voevodskii and his students and coworkers. At the end of the 1950–1960s the latter worker collaborated with A. V. Nalbandyan in recording by e.s.r. the formation of hydrogen and oxygen atoms in the combustion of hydrogen, together with other free radicals (Fig. 3).

Figure 2. Institute of Chemical Physics of the USSR Academy of Sciences, main building.

Kondrat'ev used electron bombardment to examine the dissociation of species, and was the first to apply mass spectrometry to the investigation of chemical reactions. The mass-spectrometric method was later developed by V. L. Talroze, who also developed the method of the diffusion flame in a flow system for studying the gas-phase reactions of atoms with molecules in order to determine their rate constants. This method enables reactions to be studied in the absence of the wall effect of the reaction vessel.

The possibility of heterogeneous chain initiation was suggested in 1927 by M. V. Polyakov, and experimental proof of the occurrence of this important process was given in 1948 by A. A. Koval'skii using his method of separate calorimetry.

The next stage in the development of the theory of branched-chain reactions was the concept of degenerate branching (Semenov). Such slowly evolving branched reactions were assumed to involve formation of a comparatively labile intermediate, which had a certain probability of breaking down into free radicals. Examples of products causing degenerate chain branching are formaldehyde in the high-temperature oxidation of methane and hydroperoxides in the oxidation of organic compounds at 100–150°C.

Semenov put forward the hypothesis that free radicals may be formed in bimolecular interactions between saturated molecules. Experimental evidence was given by A. E. Shilov and F. S. D'yachkovskii for the interaction of triphenylmethyl chloride and ethyl-lithium: triphenylmethyl radicals, formed by the reaction

$$EtLi + Ph_3CCl \rightarrow LiCl + Ph_3C^{\cdot} + Et^{\cdot}$$

were recorded by electron spin resonance. Subsequently the possibility of occurrence of the reactions

$$RH + O_2 \rightarrow R^{\cdot} + HO_2,\ 2RH + O_2 \rightarrow R^{\cdot} + RO^{\cdot} + H_2O,\ ROOH + RH \rightarrow RO^{\cdot} + R^{\cdot} + H_2O$$

was established.

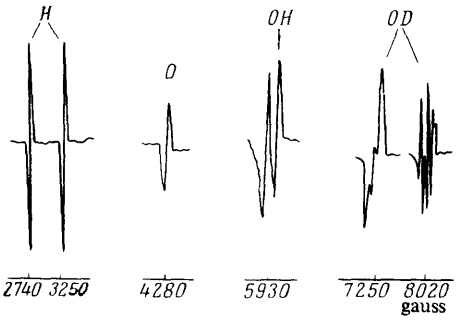


Figure 3. Electron spin resonance spectra of H and O atoms and OH and OD free radicals in the oxidation of H_2 and D_2.

Processes of this type proved to be especially characteristic of reactions involving molecular fluorine. Strong chemiluminescence in the visible region of the spectrum was observed by A. E. Shilov, L. Yu. Rusin, and A. M. Chaikin in the reaction

$$F_2 + HI \rightarrow F + HF + I$$

and this could be due only to formation of an electronically excited IF* molecule. Superequilibrium concentrations of atomic iodine were recorded by e.s.r. in this reaction. The method of diffusion flames was used to determine the rate constant both here and in the reaction of fluorine with hydrogen bromide.

Investigation of the chain reactions involved in the gas-phase fluorination of hydrogen, methyl iodide, methylene dichloride, etc. led Semenov and Shilov to the concept of energy branching—a new type of branched-chain reactions—in which excited molecules, capable of breaking down to form free radicals, were formed in chain propagation.

The reaction between hydrogen and fluorine is accompanied not only by the usual emission $HF^* \rightarrow HF + h\nu$ but also by stimulated emission, which reaches 1–2% of the energy of the chemical reaction. The duration of the flash of stimulated emission is 5×10^{-6} s, whereas that of chemiluminescence is 5×10^{-2} s (Fig. 4).

A recently developed laser, which uses the slow oxidation of hydrogen sulphide, is the first example of a chemical laser whose functioning is determined entirely by a set of elementary chemical reactions, and there is hardly time for the "leakage" of vibrational energy as a consequence of collisions during the emission.

Shock tubes began to be widely used during the 1960s. They were essentially ideal pulsed reaction vessels in which a rapid change of pressure heated the gas almost instantaneously to temperatures of the order of 1000° and even 10 000°C. A temperature pulse lasted for $(1–50) \times 10^{-4}$ s, and any surface effect was almost completely absent.

Studies were made of the elementary processes of the vibrational excitation and the dissociation of diatomic molecules—halogens, oxygen, nitrogen, and carbon monoxide (S. A. Losev)—and polyatomic molecules—hydrocarbons and nitro-compounds (A. A. Borisov, V. G. Knorre)—as well as electronic excitation and ionisation involving atoms and radicals (S. M. Kogarko and I. S. Zaslonko). Examination of the decomposition of ammonia and nitrous oxide showed directly the occurrence and the main features of "energy" chain processes, as well as the presence of critical conditions for autocatalysis due to the non-equilibrium distribution of the internal energy of the reactants. Vibrationally excited molecules N_2^V act as chain-transfer agents in the decomposition of hydrogen azide: their collisions with the initial molecules transfer vibrational energy to the latter by resonance, thereby increasing the rate of decomposition. Fig. 5 illustrates the shock tube with which G. B. Manelis and A. P. Genich studied the decomposition of ammonia.

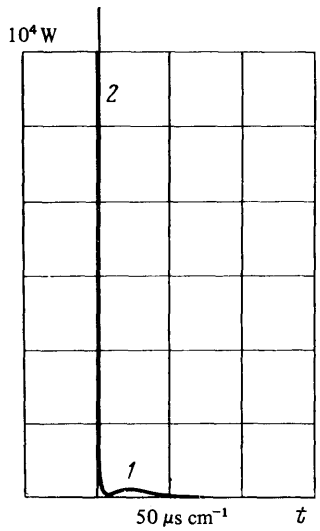


Figure 4. Intensity of chemiluminescence: 1) spontaneous; 2) induced (laser).

The development of ideas on a chain mechanism of the cracking of hydrocarbons and investigation of the kinetics and the mechanism of the elementary stages can be attributed to the work of V. V. Voevodskii and A. D. Stepukhovich.

The theory of the activated complex has been used to interpret the mechanism of a large number of elementary chemical reactions. Stepukhovich calculated the steric factors of many bimolecular reactions. E. A. Shilov and Ya. K. Syrkin introduced the concept of the formation of cyclic (four- and six-membered) transition complexes in bimolecular reactions.

V. I. Gol'danskii has recently made a detailed examination of the general theory of tunnel transitions in the kinetics of chemical reactions with a Maxwellian energy distribution of the interacting molecules. He obtained a criterion characterising the temperature below which tunnel transitions predominate over barrier transitions. A negative temperature coefficient of reaction velocity is shown to be possible because of quantum effects in barrierless transitions like inverse spontaneous predissociation. The recently discovered low-temperature quantum limit to the rate of chemical reaction in the radiation-induced solid-phase polymerisation of formaldehyde can be regarded as experimental confirmation of the possibility of sub-barrier transitions. The rate of growth of the polymer chain, induced by cobalt-60 γ-rays, was found to obey the Arrhenius law at 80–150°K, but strongly diverged from this law when the temperature fell further. At 10°K the experimental rate of addition of one monomer unit to the chain exceeded the extrapolated value by many powers of ten. It thus appeared that, instead of complete freezing of processes at temperatures close to the absolute zero, there was a measurable limiting rate of exothermic reaction, perhaps resulting from the increasing importance of tunnel transitions at extremely low temperatures.

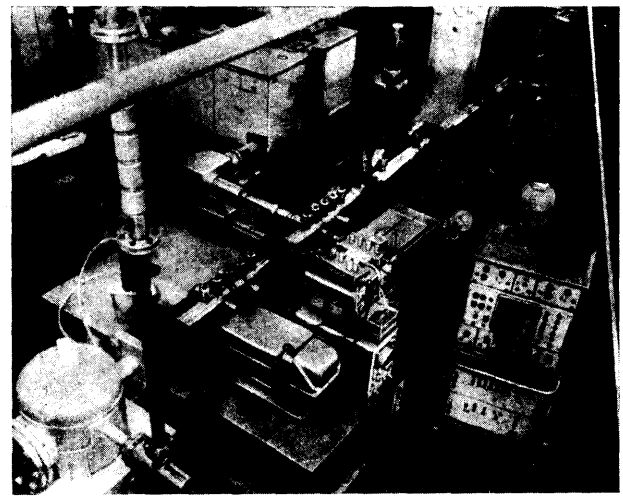


Figure 5. Equipment for investigating elementary chemical processes in a shock tube.

During recent years E. E. Nikitin has further developed the theory of the elementary acts of chemical reactions to describe the kinetics of non-equilibrium processes, which are important at high temperatures and under high vacua (e.g. in the upper layers of the atmosphere). His theory of the non-equilibrium decomposition of diatomic molecules takes into account the dependence of the probability of vibrational transitions on the vibrational quantum number. A general statistical theory of unimolecular reactions starts from the postulate that the total energy of an active molecule is redistributed statistically among active degrees of freedom, and it includes as a particular case all other theories of unimolecular reactions. N. M. Kuznetsov made theoretical calculations of vibrational temperatures and rate constants for the dissociation of certain small molecules under conditions of a non-equilibrium energy distribution. New experimental methods were proposed for studying the elementary acts of chemical reaction.

A widely used method for studying the mechanism of chemical reactions is to conduct them under ultra-high pressures, comparable with the internal pressure, when change of pressure leads to a change of the effective volume of the reaction. This enables hypothetical models of the activated complex to be tested. M. G. Gonikberg studied the effect of pressure on sterically hindered reactions and on polymerisation processes. Kinetic measurements in various solvents under high pressures have enabled the solvation of the activated complex to be studied.

Yu. N. Ryabinin suggested that the adiabatic expansion and compression of gases could be used to investigate the kinetics of fast non-isothermal reactions. Later this method was applied to the quantitative study of processes (the rate of cooling of the gaseous mixture reached 10^6–10^7 deg s^{-1}).

The rate constants of elementary reactions have been measured by means of a hydrogen maser. The method is based on measuring the reaction velocity from the change in the spin state of hydrogen on interaction of its atoms with non-paramagnetic molecules (Tal'roze).

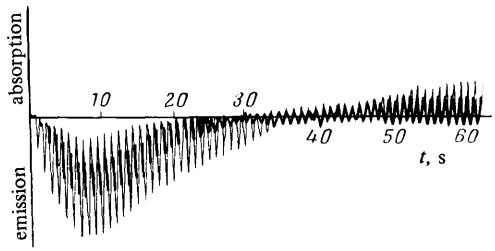


Figure 6. Kinetics of polarisation of the protons in nitrobenzene.

The mechanism of radical reactions can be investigated by studying the chemically induced dynamic polarisation of the product nuclei in a magnetic field. The basis of the method is that preferential orientation of the nuclear spins in the molecules of the products results from the occurrence of radical reactions in a magnetic field (chemically induced dynamic polarisation of the nuclei), and the nuclear magnetic resonance spectrum exhibits either abnormally large absorption or the emission of radio-frequency energy. Fig. 6 illustrates the kinetics of the variation of the n.m.r. signal (i.e. the kinetics of nuclear polarisation) obtained by A. L. Buchachenko and E. T. Lipmaa for the protons of nitrobenzene formed in the reaction of *p*-nitrobenzenediazonium tetrafluoroborate with sodium methoxide. A quantitative theory of dynamic nuclear polarisation was developed.

An interesting phenomenon was observed in the effect of a magnetic field on the proportions of the products of free-radical reactions. Thus the ratio of the yields of products obtained from the reaction of fluorobenzoyl fluoride with n-butyl-lithium changes by 37% on passing from the Earth's magnetic field of 0.5 to fields up to 25 000 oersteds (U. N. Molin).

Gol'danskii established a new "positronium" method for studying the kinetics of fast chemical reactions in gas and condensed phases. Rate constants of the formation of positronium atoms, as well as those of the excitation of electronic levels of the molecules, are determined by observing the lifetime of positronium and the intensity of the long-lived component in the annihilation.

The resolving power of a new method of microwave spectroscopy—the spin echo resulting from the action of modulated ultra high-frequency power (a series of short-lived pulses) on the specimen—exceeds that of the e.s.r. method by factors of 10–10^2 in the investigation of hyperfine interactions (Yu. D. Tsvetkov, D. G. Semenov).

Gol'danskii developed the application of γ-resonance spectroscopy to the investigation of chemical reactions. The use of Mössbauer spectroscopy enabled the rate of intramolecular electron transfer to be measured. The time of transfer in the radioactive transmutation of cobalt-57 in the compounds $^{57}Co^{II}_m[Fe^{III}(CN)_6]_n$ and $Fe^{II}_m[^{57}Co^{III}(CN)_6]_n$ was $(1-2)\times 10^{-8}$ s.

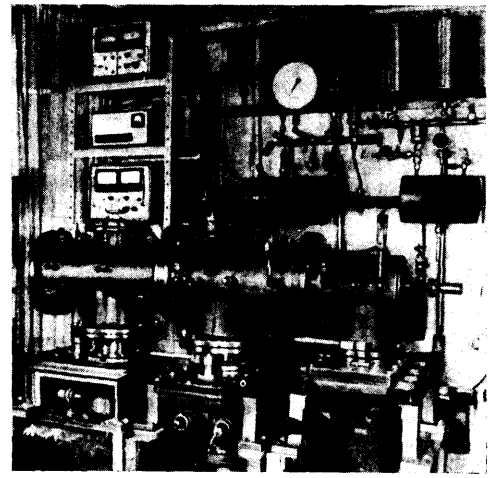


Figure 7. Equipment for studying elementary chemical reactions by the molecular beam method.

In connection with the practical importance of non-equilibrium processes the need arose for the experimental investigation of elementary reactions under conditions such that the chemical interaction of two species is an isolated process, unaccompanied by deactivation of the molecules or secondary chemical reactions, due to collisions with other molecules. Such conditions also provide new opportunities for examining the dynamics of the elementary act. Elaboration of such methods led to the design of apparatus with crossed molecular beams. Pressures of 10^{-6}–10^{-7} torr in the scattering vessel eliminate "background" collision of particles, since under these conditions any particle undergoes at most one collision in the scattering zone. The vacuum in the detector entered by the reaction products is maintained at 10^{-9}–10^{-10} torr. Fig. 7 illustrates equipment for the investigation of elementary processes in molecular beams.

Yu. B. Khariton and Ya. B. Zel'dovich worked out a chain theory of the fission of uranium.

Chain Reactions in the Liquid Phase

At the end of the nineteenth century A. N. Bakh put forward the peroxide theory of slow oxidation processes. This theory has been repeatedly confirmed in practice. During recent years kinetic methods have made it possible to extend ideas on the chemical mechanism of the liquid-phase oxidation of organic compounds. New types of elementary reactions have been discovered (in particular, new types of reactions of chain branching and chain initiation have been suggested), rate constants for various elementary stages have been measured, and processes of catalytic and inhibited oxidation have been studied quantitatively (N. M. Emanuel', I. V. Berezin, D. G. Knorre, E. T. Denisov, Z. K. Maizus, E. A. Blyumberg, V. Ya. Shlyapintokh, G. E. Zaikov, N. I. Mitskevich, R. V. Kucher, B. K. Zeinalov, and others). Heterogeneous reactions have been shown to play an important part in liquid-phase oxidations, just as in the gas-phase reactions. The effect of the solvent on individual elementary reactions has been established, and the roles of specific and non-specific solvation of the reactants in homolytic reactions have been established. Ideas on the catalysis of slow chain oxidations have been put forward and developed, and a procedure for gaseous initiation by "weak" radicals (ozone, nitrogen dioxide, etc.) is suggested.

V. Ya. Shlyapintokh and R. F. Vasil'ev studied the chemiluminescence accompanying oxidation. They showed that the chemiluminescence of hydrocarbon oxidations arises in the act of recombination of free peroxy-radicals. Measurements of chemiluminescence enable the radical-recombination rate constants to be determined (under non-stationary conditions), as well as the rate constants for the reactions of the radicals with molecules and with inhibitors of radical reactions.

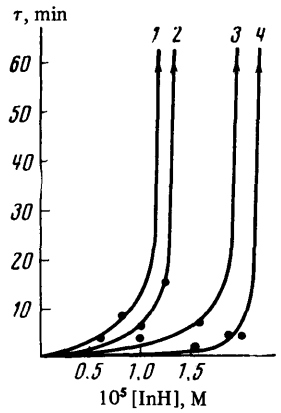


Figure 8. Dependence of induction period in the oxidation of ethylbenzene on the concentration of the inhibitors: 1) diphenylamine; 2) *N*-phenyl-2-naphthylamine; 3) 2-naphthol; 4) 1-naphthol.

The action of inhibitors on slow oxidations exhibited critical phenomena, indicating the branched-chain character of these processes (A. B. Gagarina) (Fig. 8). Study of the synergism appearing on the introduction of a mixture of inhibitors into an oxidisable medium suggested radical interaction of the inhibitors resulting in regeneration of the more effective inhibitor (G. V. Karpukhina).

The laws of liquid-phase oxidation in open systems were investigated as the scientific foundation for continuous processes in chemical technology (I. P. Skibida).

At the beginning of the present century N. A. Shilov put forward a theory of chemical induction. In his monograph on coupled oxidations he introduced the idea that chemical induction (the acceleration of a chemical reaction by another reaction taking place spontaneously in the system) is due to the formation of intermediates involved in both stages of the process. Shilov was in effect the first to draw attention to the fact that redox reactions are complicated multistage processes involving the formation of intermediate products.

The method suggested recently for the preparation of methyloxiran by oxidising a mixture of propene and acetaldehyde is based on the principles of simultaneous oxidation applied to slow chain reactions. The hydroperoxy-radical formed by oxidation of the acetaldehyde serves as epoxidising agent for propene.

A fertile application of kinetic methods has been to describe the development with time of several biological processes, such as malignant growth, aging, radiation sickness, and the action of chemical and physical factors in the environment on living organisms. Kinetic parameters have been revealed which permit the efficiencies of different methods for the therapy of malignant diseases to be evaluated quantitatively.

It has been discovered that the content of free radicals in tumour tissue increases during the initial period of growth. This relation is extremal: a maximum content of free radicals is observed before the tumour attains its maximum rate of growth. A group of compounds has been found which have an anticancer effect, which are able to diminish the scale of harmful effects of chemical contamination of the environment on the organism, which extend the life of experimental animals, and which possess radiation-protective properties. All these substances are inhibitors of free-radical processes.

Homogeneous Catalysis

One of the first investigators of homogeneous catalysis in Russia was E. I. Shpital'skii, who as early as the beginning of the present century developed the main theoretical concept of homogeneous catalysis—the formation of active intermediate products—and, in contrast to van't Hoff and Arrhenius, suggested that not one but several intermediate catalyst–substrate complexes were formed, differing in composition, stability constant, and reactivity (down to complexes that deactivate the catalyst). This theory later received convincing experimental support: intermediate products in the decomposition of hydrogen peroxide by molybdates and by tungstates (permolybdates and pertungstates respectively), etc. were isolated.

The formation of molecular complexes of compounds of metals of variable valency with hydroperoxides (in catalytic decompositions) and their role in catalysis have been confirmed quantitatively by S. K. Maizus and I. P. Skibida using kinetic and spectroscopic methods.

E. A. Shilov established that π-complexes have a decisive role as intermediate species in various reactions involving alkenes. In a study of acid catalysis (in particular by the Lewis acids—boron trifluoride, aluminium trichloride, etc.) N. M. Chirkov concluded that reactive intermediate

π-complexes of alkenes with hydrogen ions were formed. Ya. K. Syrkin and I. I. Moiseev examined the formation of π-complexes of palladium(II) chloride with alkenes in the preparation of aldehydes. These workers used phenomena such as synergism occurring in mixtures of several catalysts for the oxidation of ethylene to acetaldehyde in the presence of the palladium(II) chloride–copper(II) chloride catalytic system.

A. I. Shatenshtein proposed a new kinetic method for determining the strengths of very weak acids and bases (e.g. hydrocarbons), and traditional views on acids and bases were revised.

The study of metal-complex catalysis, which is closely connected with enzymic catalysis, began to acquire great importance during the 1950s. Organometallic (especially π-allylic) complexes are used as catalysts for stereospecific polymerisation (B. A. Dolgoplosk). Papers by L. A. Nikolaev and A. P. Purmal' reported studies of the mechanism of enzymic catalysis, investigation of the roles of ligand and metal in various types of reactions (the oxidation of ascorbic acid, the decomposition of hydrogen peroxide, etc.), and elucidation of the detailed chemical mechanism of catalysis.

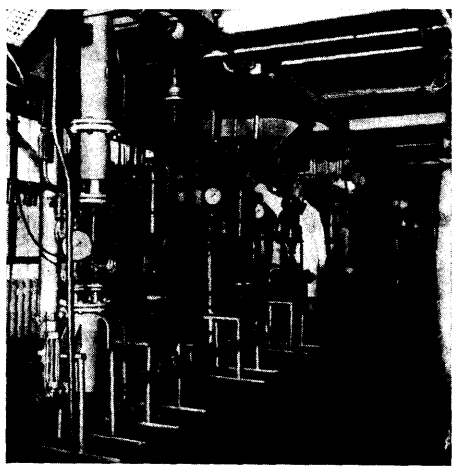


Figure 9. Pilot plant for synthesis of hydrazine from molecular nitrogen and water.

The problem of the catalytic fixation of small molecules—the activation of oxygen, nitrogen, carbon dioxide, and carbon monoxide by catalytic systems—has aroused interest recently. During the 1960s M. E. Vol'pin and A. E. Shilov discovered the catalytic fixation of nitrogen with the formation of hydrazine and ammonia (Fig. 9). Compounds of bivalent vanadium in the presence of magnesium salts form an effective catalytic system in alkaline and alcoholic aqueous media. The yield of ammonia and hydrazine increases with the ratio of magnesium to vanadium. The fixation of carbon dioxide by complexes of Group VIII transition metals has been studied.

When hydrocarbons and compounds of metals are oxidised together in organic solvents, conversion of the hydrocarbons (cyclohexane, alkanes) to alcohols is accompanied by a change in the valency of the metal.

A nevel type of catalysis—micellar catalysis—was discovered by I. V. Berezin. It consists in a marked change (by several powers of ten) in the rate of organic reactions in aqueous solutions under the influence of surface-active substances, as a consequence of solubilisation of the reactants by micelles of the surface-active compounds (Fig. 11).

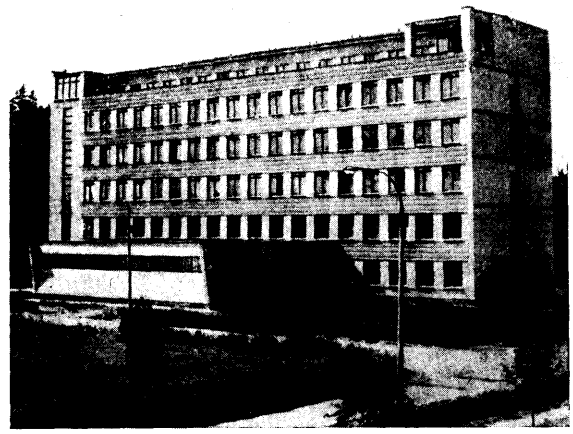


Figure 10. Laboratory building of the Department of Kinetics and Catalysis of the Institute of Chemical Physics of the USSR Academy of Sciences.

A paper by D. G. Knorre, L. G. Chuchukina, and N. M. Emanuel' established that a catalyst has a "dual function": at sufficiently high concentrations salts of metals of variable valency cease to exhibit catalytic properties, and the "catalysts" begin to inhibit the process. The dependence of the inhibiting properties on the composition of the chelate group, the redox potential, and the electron density on the central atom of the chelate has been studied, and the conversion products of the metal complexes have been isolated and examined.

Heterogeneous Catalysis

In the field of heterogeneous catalysis numerous papers have appeared on the selection of effective new catalytic systems. At the start of the 1920–1930s V. N. Ipat'ev began a comprehensive investigation of metal oxides as heterogeneous catalysts. N. D. Zelinskii discovered general-purpose hydrogenation and dehydrogenation catalysts such as nickel on alumina and platinum on carbon. In 1928 S. V. Lebedev proposed a mixed zinc–aluminium catalyst for the synthesis of butadiene from ethanol. The action of catalytic semiconductors, in particular germanium, was investigated (S. Z. Roginskii, O. V. Krylov).

Investigations of adsorption and chemisorption were very important in connection with the study of heterogeneous catalytic reactions. A theory of catalysis and chemisorption on non-uniform surfaces was elaborated (S. Z. Roginskii, O. M. Todes). A correlation between activation energy and heat of adsorption was established by M. I. Temkin. The principles of physical sorption on porous materials were studied by M. M. Dubinin.

Various methods were suggested for investigating the structure, properties, and activity of catalysts. Besides the usual X-ray diffraction, electron diffraction, magnetic methods, sedimentation analysis, and microweighing were introduced into practical heterogeneous catalysis.

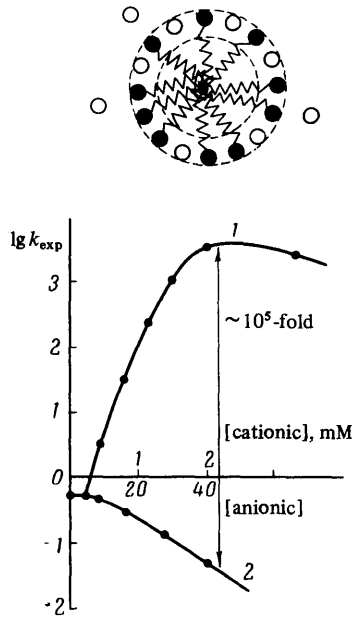


Figure 11. Formation of micelles (upper diagram) in micellar catalysis. Variation of acylation rate constant with concentration of surface-active agents: 1) cationic; 2) anionic.

A. M. Rubinshtein suggested determining specific surface from the adsorption isotherms of benzene or carbon tetrachloride vapour determined under dynamic conditions. The displacement of characteristic curves for a sorbed gas and measurement of the work of sorption of the gas (vapour) have been used to measure the specific surface of a catalyst (M. M. Dubinin and A. V. Kiselev). Various physicochemical methods (electrochemical and chromatographic) were used by A. A. Balandin and Kh. M. Minachev.

Kiselev calculated theoretically the energies of adsorption of complicated molecules on crystalline surfaces. A. N. Frumkin and A. I. Shlygin proposed to study the mechanism of hydrogenation from the charging curves for the catalytic electrodes. This made it possible to examine quantitatively the adsorption of hydrogen on the surfaces of metals (platinum).

Investigation of the properties of species adsorbed on a catalyst surface has been approached in earnest with the development of the most recent physicochemical methods. V. V. Voevodskii used electron spin resonance to study the structure of the active centres (radicals and ions), and showed their non-uniform distribution on solid surfaces. The O_2^- radical-ion adsorbed on a surface has recently been detected by γ-resonance (Mössbauer) spectroscopy (Fig. 12).

Kinetic isotope methods opened up great possibilities for investigating the mechanism of heterogeneous chemical reactions (S. Z. Roginskii, M. B. Neiman).

Balandin's multiplet theory of catalysis presupposes structural and energetic conformity between the crystal lattice of the catalyst and the molecule of the reactant. The formation of surface complexes involving active centres of catalysis (multiplets) is significant for catalysis. Physical adsorption on the catalyst surface is followed by movement of the molecule along the surface and formation of a multiplet complex at a certain orientation of reactant molecules and active centres. Bond redistribution in such a complex results in formation of the final products. Multiplet schemes, based on a large quantity of experimental information, explain almost all routes of catalytic conversion of hydrocarbons.

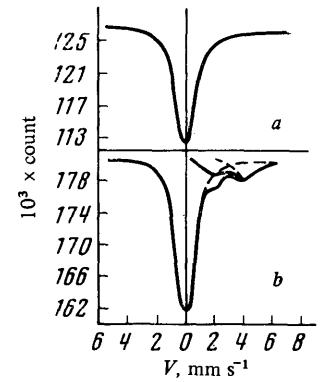


Figure 12. γ-Resonance spectra of tin–molybdenum catalyst (V = relative rate of movement of source): *a*) initial specimen; *b*) specimen after adsorption of oxygen and propene at 200 °C.

N. I. Kobozev applied a theory of active ensembles to deposited catalysts. It was based on the assumption that a certain number of catalyst atoms—not a single atom—was involved in catalysis. Such groups may be formed by the migration of atoms along the catalyst surface.

A large number of publications on aspects of the chemistry of heterogeneous catalytic reactions have appeared from G. K. Boreskov, K. V. Topchieva, V. A. Roiter, and others. Boreskov suggested that the activity of a heterogeneous catalyst should be measured by the rate of chemical conversion per unit active surface of the catalyst: i.e. he introduced the concept of specific catalytic activity. He examined the mutual influence of catalyst and substrate on the properties of the catalytic system, which may lead to a strong dependence of catalytic activity not only on the degree of conversion of the reactants but also on their initial concentration.

Roginskii proposed a new classification of catalysts linking the activity of a catalyst with the character of the interaction between catalyst and substrate. Catalysts were divided into two groups—electrical conductors (metals and semiconductors) and non-conductors (ionic crystals, gels). This classification has been tested on

many oxidation processes (S. Yu. Elovich, L. Ya. Margolis, G. M. Zhabrova).

L. V. Pisarzhevskii's electronic theory played an important part in establishing the theory of the elementary act of heterogeneous catalysis. It assumed that electrons of the catalyst took part in redox reactions. The modern form of the electronic theory of catalysis was formulated by F. F. Vol'kenshtein. Free electrons and holes of the semiconductor, acting as free valencies, are supposed to take part in chemisorption processes. The reactivity of a chemisorbed molecule depends on the form of the chemisorption (valency-saturated, radical, or radical-ionic form).

N. N. Semenov, V. V. Voevodskii, and F. F. Vol'kenshtein put forward a chain theory of heterogeneous catalysis based on the electronic theory and on their view of the role of heterogeneous factors in the formation and destruction of radicals. This theory assumes that reaction may occur on the surface of a heterogeneous catalyst by a chain mechanism. O. M. Poltorak has recently developed the concept of chains of redistribution of bonds, and used it for a theoretical analysis of diverse catalytic processes. It permits a unified approach to the mechanism of homogeneous, heterogeneous, and enzymic catalyses.

The work of A. A. Balandin, D. A. Frank-Kamenetskii, G. K. Boreskov, Ya. B. Zel'dovich, M. G. Slin'ko, O. M. Todes, D. V. Sokol'skii, G. I. Panchenkov, M. F. Nagiev, I. I. Ioffe, S. L. Kiperman introduced into practical heterogeneous catalysis methods for calculating the reaction order, rate constants, and activation energy of heterogeneous reactions in vessels with ideal mixing and displacement, examined the macrokinetics of reactions in a fluidised bed, and applied statistical methods to investigating the kinetics of heterogeneous reactions. The gradient-free methods of conducting chemical reactions (under conditions of ideal mixing) proposed by M. I. Temkin have been applied to such kinetic studies.

Various processes—dehydrogenation, dehydrocyclisation, hydrogenation, etc.—can be combined in the same apparatus as a consequence of the development of original membrane catalysts (V. M. Gryaznov, V. S. Smirnov).

The role of heterogeneous catalysts and the mechanism of their action in liquid-phase processes have been investigated in the oxidation and decomposition of hydroperoxides (E. A. Blyumberg, Yu. D. Norikov, Ya. B. Gorokhovatskii). The heterogeneous catalyst is shown to be involved in initiation, branching, and termination of the oxidation chain, and also to influence the way in which the hydroperoxide breaks down.

The catalytic properties of heterogeneous catalysts can be varied by donor–acceptor modification by means of gaseous additives.

Thermal Explosion, Combustion, Detonation

The theory of thermal ignition in exothermic reactions, formulated by N. N. Semenov and subsequently developed by his school, has been exceptionally important, both theoretically and practically. The nature of thermal ignition, resulting from the predomination of the evolution of heat over its removal from the system, is apparent in an exponential increase in reaction velocity with rise in temperature in the vessel and a corresponding temperature rise. The theory of thermal explosion was developed and refined by O. M. Todes and D. A. Frank-Kamenetskii. Conditions of ignition were determined for vessels of various geometrical shapes taking into account the thermal conductivity equation. These conditions enable flash points of various substances to be calculated with good accuracy.

The theories of flame propagation, detonation, and explosion limits were developed by Ya. B. Zel'dovich. Specific régimes of combustion were investigated by K. I. Shelkin, Ya. K. Troshin, et al., who showed that the rate of flame propagation was affected by the movement of the gas caused by expansion of the products of combustion. Investigations were made of the burning of light fuel in engines. On the basis of this work A. S. Sokolik and A. I. Voinov proposed a new mode of organisation of combustion in motors—fuel injection—which has been further developed by L. A. Gusak.

Kinetic studies of the decomposition of condensed explosives were begun in 1929 by S. Z. Roginskii. Together with Todes he elaborated a statistical theory of the kinetics of topochemical and crystallisation processes. Yu. B. Khariton and also A. F. Belyaev studied the kinetics of the breakdown of explosives. They revealed the mechanism of explosion after impact, and formulated the principle defining the conditions of persistent explosion. Belyaev's discovery that the combustion of explosives takes place in the gas phase, after they have vaporised, became widely known.

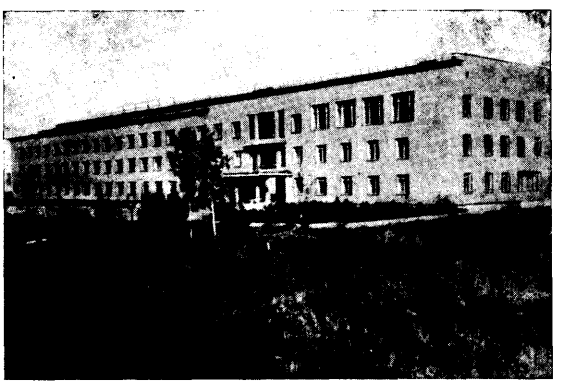


Figure 13. Institute of Chemical Kinetics and Combustion of the Siberian Division of the USSR Academy of Sciences.

P. F. Pokhil, A. Ya. Apin, A. A. Andreev, F. I. Dubovitskii, V. K. Bobolev, B. P. Zhukov, A. G. Merzhanov made many investigations of the mechanism of thermal explosion. M. A. Sadovskii studied the structure, mechanism of formation, and propagation of shock waves. The mechanical action of a shock wave in air was examined, and the dependence of the maximum pressure in the wave on the weight of the charge and the distance from the site of explosion was determined. Spherical detonation, which has found application in seismic exploration, was studied by S. M. Kogarko.

Merzhanov worked out a new method for obtaining refractory compounds (nitrides, carbides of Groups III–VI metals)—"self-propagating high-temperature synthesis"—and a new form of propagation of the seat of chemical reaction—a kind of spiral motion of the focus of combustion on the surface of the specimen—was studied. Reaction vessels have already been constructed which enable

considerable quantities of titanium carbide and molybdenum disulphide to be obtained (Fig. 14). A. N. Dremin showed that new crystalline modifications can be obtained by the action of powerful shock waves on various substances.

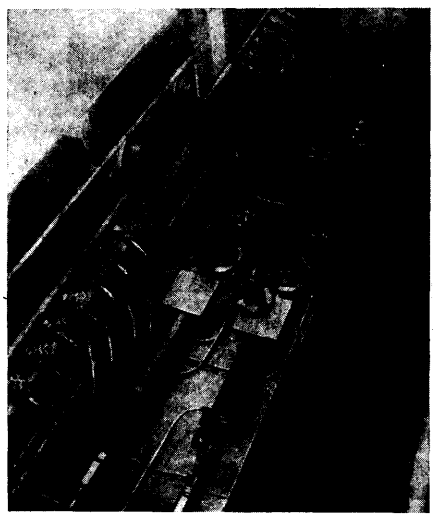


Figure 14. Equipment for the production of refractory inorganic compounds by "spontaneously propagated high-temperature synthesis".

High-energy Chemistry

This field of science is concerned with the kinetics, mechanism, and practical application of reactions in which the energies of individual atoms, molecules, and radicals exceed the energies of thermal motion and frequently the energies of chemical bonds. These result in peculiar new mechanisms of chemical reaction, which are improbable in equilibrium systems at ordinary temperatures.

Research on radiation chemistry began with the work of V. A. Kargin, V. V. Voevodskii, S. S. Medvedev, N. A. Bakh, and others. The theoretical principles of radiation chemistry are now being worked out: studies are being made of elementary processes in gas and condensed phases, of the nature and properties of short-lived intermediate products of radiolysis (solvated electrons, ions, free radicals, excited molecules), the kinetics and mechanism of radiation-chemical reactions in homogeneous systems, aspects of radiation polymerisation, problems of the radiation modification and radiation-chemical protection of various materials, etc.

Ion–molecule reactions of organic compounds have been discovered (V. L. Tal'roze), methods have been suggested and developed for the radiation cross-linking of polyalkenes and the modification of polymeric, porous, and other materials (V. L. Karpov, Kh. U. Usmanov, A. M. Kabakchi, E. E. Finkel', V. L. Tsetlin), and theories have been elaborated for the radiation-chemical oxidation of organic compounds (Bakh), gaseous and heterogeneous radiation-chemical reactions (S. Ya. Pshezhetskii), radiation polymerisation (A. D. Abkin, V. I. Gol'danskii, V. L. Tal'roze), and the radiolysis of water and aqueous solutions (P. I. Dolin, M. A. Proskurnin, B. V. Ershler, A. K. Pikaev, L. T. Bugaenko). Stabilisation of the hydrated electron has been detected in frozen aqueous solutions (Pikaev), and principles have been worked out for the chemical dosimetry of ionising radiations (S. V. Starodubtsev, A. M. Kabakchi).

The theoretical investigations have served as a basis for the development of applied radiation chemistry. Processes have already been worked out for obtaining a biodegradable sulphonate (R. V. Dzhagatspanyan), synthesising telomers of ethylene with carbon tetrachloride (A. A. Beer), and making polyheterosiloxane insulating tape and rubber–glass cloth (I. Ya. Poddubnyi et al.).

The unique phenomenon has been observed that the coefficient of dry friction is reduced by several powers of ten when non-metallic rubbing surfaces are exposed to a slight flux of short-range radiation (V. L. Tal'roze, A. N. Ponomarev, A. A. Silin, E. M. Dukhovskoi).

Experimental and theoretical research on low-temperature plasma constitutes a new sector of high-energy chemistry. General principles of non-equilibrium kinetics have been formulated, and its fundamental equations given (L. S. Polak, D. I. Slovetskii, Yu. A. Kolbanovskii). The scientific foundations of plasmachemical technology have been laid, its characteristic features being short reaction time (10^{-5}–10^{-3} s), high degree of conversion, pure products, and in several cases the accomplishment of difficultly realisable processes. Plasmachemical methods are used to prepare acetylene, pigment titanium dioxide, materials for microelectronics, and other products.

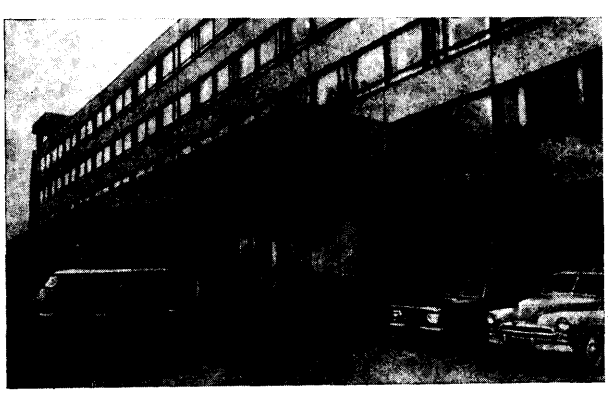


Figure 15. Radiochemical building of the Institute of Physical Chemistry of the USSR Academy of Sciences.

A shock wave provides a new method for stimulating and accomplishing chemical conversions: the chemistry of shock waves constitutes a new branch that studies the transformations of condensed substances resulting from percussive compression. These researches, started by Yu. N. Ryabinin, were developed by V. I. Gol'danskii, A. N. Dremin, P. A. Yampol'skii, S. S. Bogdanov, G. A. Adadurov, O. N. Breusov. High-pressure phases—diamond and wurtzite-like boron nitride (B–BN)—have been obtained by percussive compression. The latter has yielded especially durable polycrystals, suitable for the

production of high-quality cutting tools with the best available characteristics. Polymerisation has been observed, and the possibility shown of cross-linking macromolecules by the action of shock waves to form a three-dimensional network.

Figure 16. Linear electron accelerator of the Institute of Physical Chemistry of the USSR Academy of Sciences.

An important sector of high-energy chemistry is nuclear chemistry—investigation of the chemical consequences of nuclear processes (nuclear reactions, radioactive disintegration) and research on the chemistry of new atoms and the peculiar systems produced by the action of positrons and various mesons on matter. The high and specific reactivity of the hot species resulting from nuclear processes has been the subject of research by An. N. Nesmeyanov, A. N. Murin, V. D. Nefedov, B. G. Dzantiev, T. V. Tsetskhladze, and others. Methods have been found for the chemical stabilisation of hot atoms of tritium, carbon, nitrogen, sulphur, halogens, and certain metals in organic and inorganic media, in gas and condensed phases. The results open up new paths for the preparation of labelled compounds and for the concentration of radioisotopes.

Various types of chemical reactions of positronium have been studied, and the physical chemistry of the positron and of positronium has been established (V. I. Gol'danskii, V. P. Shantorovich). The foundations of the physical chemistry of muonium have been laid down in the works of V. G. Firsov, I. I. Gurevich, V. G. Nosov. Research has started on the chemistry of mesoatoms and mesomolecules (Yu. D. Prokoshkin, L. I. Ponomarev).

Photochemistry

The study of chemical reactions occurring under the influence of light is very important for the theory of chemical processes and for solving problems of photosynthesis, photoreception, photography, the photostabilisation of polymeric materials, etc.

P. P. Lazarev investigated the fading of dyes for the first time.

Fundamental photochemical researches were carried out by A. N. Terenin. His hypothesis of the triplet nature of the metastable states of organic molecules which are responsible for their phosphorescence has received much experimental confirmation. The properties of triplet states have been studied, and their role in various photochemical and photophysical processes has been revealed. The phenomenon of triplet–triplet energy transfer has been established (A. N. Terenin, V. L. Ermolaev). Flash photolysis was used by A. V. Karyakin and A. K. Chibisov to show the important role of the triplet state in photochemical redox reactions involving pigment and dye molecules.

Figure 17. Apparatus for studying radiation copolymerisation in the Institute of Physical Chemistry of the USSR Academy of Sciences.

The work of V. N. Kondrat'ev gave rise to study of the elementary act of interaction between light and matter. The mechanism of induced predissociation and energy-transfer processes was investigated. A. B. Nalbandyan studied the mechanism of the photochemical oxidation of hydrocarbons sensitised by mercury vapour and by chlorine. Mass spectrometry yielded several results on photoionisation in the gas phase (F. I. Vilesov).

Two-quantum reactions involving triplet states of organic molecules form a special class of photochemical processes. Kh. S. Bagdasar'yan examined the kinetics of the sensitised dehydrogenation of alcohols, which has a two-quantum mechanism, and made the first measurements of the absolute efficiencies of the two-quantum photoionisation of organic compounds in a condensed phase. N. V. Fok, M. V. Alfimov, V. E. Kholmogorov also investigated two-quantum processes.

The discovery and manufacture of laser sources of radiation led to promising new lines of research in photochemistry. It was established that infrared rays were photochemically active, ensuring the selective occurrence of a reaction whose activation energy was substantially larger than the energy of an infrared quantum (N. G. Basov, A. N. Oraevskii, A. V. Pankratov).

The development of modern pulse methods has permitted the study of extraordinarily fast photoprocesses (down to

10^{-9} s), which is of fundamental importance for investigation of the mechanism of elementary reactions. A flash fluorometer has been used to study heterolytic dissociation and the phototransfer of an electron and a proton (M. G. Kuz'min). A kinetic study has been made of the protonation of excited acridine molecules (Fig. 18). In the course of an investigation of intermediate products in the flash photolysis of solutions of various phenols in the presence of compounds of transition metals (V. A. Kuz'min and I. V. Khudyakov) complex formation was established between the *o*-methylphenoxyl radical and cobalt acetylacetonate (Fig. 19).

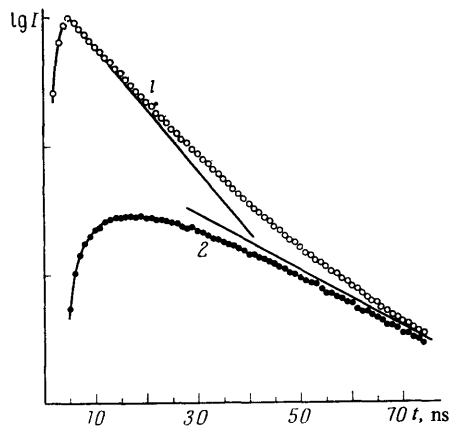


Figure 18. Kinetics of the fluorescence in aqueous solution of: 1) acridine; 2) the acridinium ion.

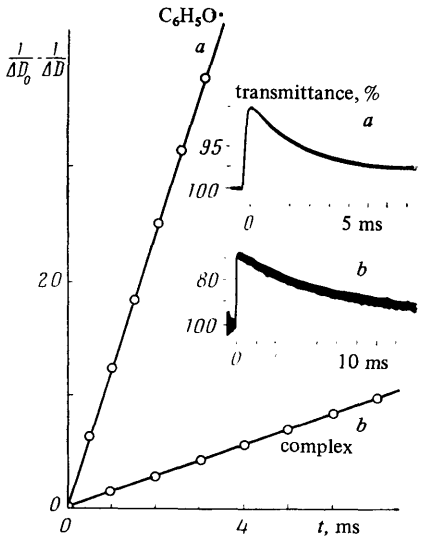


Figure 19. Kinetic curves of the decay of: *a*) *o*-methylphenoxyl radical; *b*) complex of *o*-methylphenoxyl radical with cobalt acetylacetonate.

The widespread application of photochromic compounds in technology led to an intense investigation of their properties and of the mechanism of photochromism (V. A. Krongauz, K. G. Dzhaparidze, M. A. Gal'bershtam). Work is being undertaken on the synthesis of new photochromic compounds based on spiropyrans, which absorb visible light (E. R. Zakhs, L. S. Efros).

One problem of present-day science and technology of photographic materials is to obtain emulsions that possess high sensitivity over a wide spectral range. I. I. Levkoev and A. I. Kiprianov prepared efficient new spectral sensitisers for various photographic materials, and introduced these polymethine dyes into industry.

K. V. Chibisov investigated the photochemistry of photographic processes. He discovered the nature of photographic sensitivity, and examined the mechanism of the chemical sensitisation of photographic emulsions.

Photochemical methods have proved effective in the chemistry and technology of polymers. Monolithic glasses of any thickness have been obtained by photopolymerisation for the first time on an industrial scale (S. R. Rafikov, G. P. Gladyshev).

An important sector is preparative organic photochemistry. V. F. Kucherov has studied the photoinduced *C*-addition of alcohols, acetals, ethers, and esters to acetylene and its monosubstituted derivatives. Alkene systems substituted by various functional groups have been obtained by means of this reaction.

In order to prepare materials possessing superconducting and semiconducting properties, K. N. Anisimov and N. E. Kolobova investigated the photochemical reaction of tetracarbonyl-π-cyclopentadienylniobium with silicon, germanium, and tin acetylides.

Photosubstitution in aromatic compounds and the photoreduction of aromatic nitro-compounds have been investigated (A. V. El'tsov).

S. Ya. Pshezhetskii examined the effect of the medium on the mechanism of the photoconversion of free radicals in solutions of ethers and anhydrides of monocarboxylic acids. The formation of hydrogen bonds between radicals and molecules in alcohols and acids plays an important part in such processes.

The modelling of various photobiological processes and the investigation of the photochemical reactions of biologically important molecules constitute an actively developing line of research. A. A. Krasnovskii and V. B. Evstigneev have made a series of studies of the redox photoreactions of chlorophyll and related compounds in various systems. Elementary photochemical processes involving photosynthetic pigments and other metal-containing porphyrin compounds have been investigated by A. K. Chibisov, G. P. Gurinovich, A. N. Sevchenko, K. N. Solov'ev, I. I. Dilung. Artificial photosynthetic systems are being examined by G. G. Komissarov.

Reversible photochemical changes undergone by the visual pigment rhodopsin are being investigated (M. A. Ostrovskii, V. A. Krongauz).

I. V. Berezin, K. Martinek, and N. F. Kazanskaya have proposed a new chemical system for intensifying a light signal by means of enzymic reactions. The high quantum yield (10^{10}–10^{12}) can be utilised for the production of new supersensitive materials.

Photoinduced free-radical processes involving proteins are being studied (L. P. Kayushin).

Electrochemistry

Although the first electrochemical investigations in Russia were made as early as the nineteenth century by V. V. Petrov, F. F. Grotgus, B. S. Yakobi, E. Kh. Lents, A. S. Savel'ev, A. P. Sokolov, only the applied aspects of this important branch of physical chemistry were largely developed right up to post-Revolutionary times. The Soviet period is characterised by intense activity on the problems of electrochemistry. Many investigations have been made on the structure of the electrical double layer, the effect of adsorption on the kinetics of electrode processes, the role of diffusion factors, the theory of hydrogen overpotential, the quantum-mechanical theory of electrode processes, the electrochemical theory of corrosion and passivity, the mechanism of metal electrodeposition, and the electrochemistry of melts.

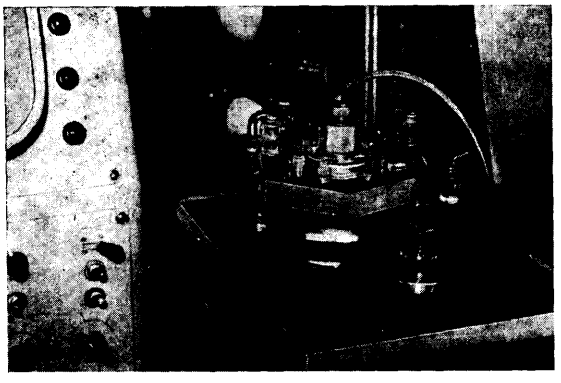


Figure 20. Apparatus for determining dependence of solid–liquid interfacial tension on surface charge (Institute of Electrochemistry of the USSR Academy of Sciences).

The most eminent electrochemical school in our country is that of A. N. Frumkin. As early as the 1930s he established the relation between the rate of reaction and the structure of the electrical double layer. The rate of discharge of ions was shown to be determined by their concentration at the electrode surface and to depend on the potential drop in the dense region of the double layer acting directly on the ions. Frumkin introduced the concept of the zero-charge potential as an individual characteristic of metals, which led to a solution of one of the problems of the theory of voltaic cells—the relation between their electromotive force and the contact potential difference between the two metals in a vacuum (the so called Volta problem). This work laid the foundations of quantitative electrochemical kinetics. Frumkin's school developed and perfected methods for investigating the metal—solution interface, measuring the capacitance of electrodes by means of alternating currents, determining charging curves and the adsorption of labelled atoms, and applying the isoelectric displacement method (P. I. Dolin, B. V. Ershler, N. A. Balashova, V. E. Kazarinov, O. A. Petrii). A quantitative theory of the double layer and a theory of adsorption at charged interfaces were elaborated (B. B. Damaskin).

During recent years advances have been made in the quantum-chemical interpretation and experimental investigation of the mechanism of the elementary step in electrode reactions and processes in the bulk solution which accompany electron transfer (R. R. Dogonadze, A. M. Kuznetsov, L. I. Krishtalik). A new electrochemical field—the electrochemistry of solvated electrons—was developed. Krishtalik has established the laws of dark emission, and A. M. Brodskii, Yu. V. Pleskov, et al. those of the photoemission of electrons from a metal into a solution. The theory of convective diffusion (V. G. Levich) helps to solve the problems of the transport of material to the electrode surface.

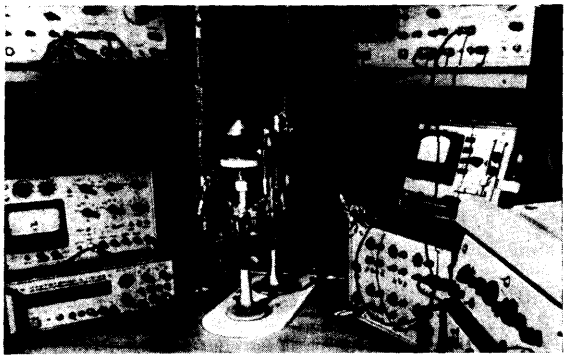


Figure 21. Apparatus for potentiometric investigation of state of surface and kinetics of electrochemical reactions using a rotating disc electrode with a ring (Institute of Electrochemistry of the USSR Academy of Sciences).

A. N. Frumkin and L. N. Nekrasov have proposed a disc electrode with a ring (Fig. 21) for investigating intermediate products of electrochemical processes.

A theory of the establishment of a potential on ion-selective membranes has appeared in papers by B. P. Nikol'skii, M. M. Shult's, and their coworkers; new types of glass and other ion-selective electrodes have also been developed.

The theory of corrosion processes and the struggle against corrosion have been widely researched, beginning with the investigations of V. A. Kistyakovskii and N. A. Izgaryshev. This work has been developed by G. V. Akimov, who put forward a theory of multicomponent systems containing metal–solution microsystems differing in structure and properties, and by Frumkin (the theory of coupled reactions). Ya. M. Kolotyrkin obtained important results on the theory of corrosion and on methods of corrosion protection. He revealed the role of complex formation and established experimentally for the first time the direct involvement of water molecules in the electrochemical stages of the dissolution of active metals (nickel, manganese). He showed that a purely chemical mechanism of dissolution of metals was possible in addition to the electrochemical mechanism. N. D. Tomashov suggested a novel method for producing corrosion-resistant alloys by cathodic alloying, i.e. by introducing into the alloy small quantities of such components as palladium, platinum, ruthenium, etc., which accelerate the cathodic evolution of hydrogen.

K. M. Gorbunova and P. D. Dankov studied the mechanism of crystal growth and nucleation during electrolysis; they worked out the theory and a technology of chemical nickel plating. Yu. Yu. Matulis is undertaking comprehensive investigations on the electrodeposition of metals and the production of the bright coatings used in industry. G. S. Vozdvizhenskii has studied the electrolytic polishing of metals.

The Ural school has made a great contribution to the development of high-temperature electrochemistry. Data have been obtained on electrochemical kinetics in molten salts and on the structure of the electrical double layer at the boundary between molten metals and electrolytes (S. V. Karpachev, O. A. Esin, M. V. Smirnov, V. A. Kuznetsov, E. A. Ukshe). Diffusion kinetics in molten salts has been investigated by Yu. K. Delimarskii. The possibility has been established of using solid electrodes for polarographic purposes and of applying polarography to the study of complex formation in melts.

The development of fuel cells—devices in which the chemical energy of the fuel is converted directly into electrical energy—has stimulated a number of theoretical investigations. The mechanism of processes occurring in fuel cells (the ionisation of hydrogen and the electrochemical reduction of oxygen) has been examined, the phenomena of electrocatalysis have been studied, model systems have been analysed, and a theory of mass transfer in porous electrodes has been developed which permits more efficient utilisation of their surface (V. S. Bagotskii, A. G. Pshenichnikov, R. Kh. Burshtein). Most of the work in this field has been undertaken by industrial institutes. The experience accumulated in work on the hydrogen—oxygen fuel cell has been used to lower the voltage in the electrolysis of water. The development of high-temperature fuel cells has led to a theory of conduction by solid electrolytes in equilibrium with the gas phase (S. F. Pal'guev).

The Institute of Electrochemistry of the USSR Academy of Sciences has recently developed electrochemical transformers (memory cells, integrators, pressure and acceleration transducers, etc.), which materially supplement semiconductor devices at low frequencies and in control by weak signals (P. D. Dukovtsev, B. M. Grafov).

Chemical Thermodynamics

The foundations of thermochemistry as a science were laid by the work of G. I. Gess [Hess]. The law which he discovered, that the total heat of a chemical reaction is independent of the intermediate states of the system, is a particular formulation of the first law of thermodynamics. Systematic and accurate thermochemical investigations have been made by B. F. Luginin, M. M. Popov, S. M. Skuratov, and others.

Generalisation and systematisation of experimental thermochemical results led to the discovery of several regularities. D. P. Konovalov (1924) proposed the well known relation for determining heats of combustion of organic compounds from their composition and their membership of a known homologous series. A. M. Berkengeim (1925) established that heats of formation of inorganic compounds can be calculated as the arithmetic means of the values for the corresponding compounds of the adjacent elements (in a series or a group of the Periodic System). A. F. Kapustinskii showed that the heats of formation of many crystalline compounds of the same type vary linearly with the logarithm of the atomic number of the elements, and suggested a formula for calculating the entropies of ions (in crystal lattices) from the atomic weights of the elements, their valencies, and the ionic radii. V. A. Kireev demonstrated the existence of a simple approximation enabling entropies of formation of crystalline compounds to be computed from their composition.

N. N. Beketov's studies of the reversibility of chemical processes—the dependence of the direction of chemical changes in a system on the concentrations (pressures) of the reactants—played an important part in the development of chemical thermodynamics. This work led to the discovery of the law of mass action—a thermodynamic relation of the greatest importance for chemistry.

Equations of state of gases play a large part in thermodynamics. The Mendeleev–Clapeyron equation of state of ideal gases is widely used. New lines of investigation appeared in the post-Revolutionary period. A general theory of thermodynamic potentials was based by S. A. Boguslavskii on statistical mechanics. The fundamental concepts of thermodynamics have been refined and its theory has been presented more rigorously, the irreversibility of processes has been studied, and the second law of thermodynamics has been analysed (G. A. Afanas'eva-Erenfest, K. A. Putilov), geometrical thermodynamics has been developed (A. B. Mlodzievskii), the thermodynamics of intermolecular interaction investigated (E. S. Rudakov), the thermodynamics of irreversible processes developed (A. I. Veinik), and interaction in multicomponent systems with a variable number of degrees of freedom examined (L. S. Palatnik, A. I. Landau). The requirements of technology for numerical thermodynamic characteristics with wide variation in physical conditions stimulated experimental lines of attack on thermodynamics and promoted the development of methods for the statistical calculation of thermodynamic data. Ya. B. Zel'dovich, A. N. Gurvich, and Yu. M. Shaulov worked out methods for the thermodynamic calculation of combustion processes and explosions. Systematic statistical calculations of thermodynamic data at high temperatures were made by A. V. Frost and I. N. Godnev.

Study of the thermodynamic properties of individual groups of substances used in the new technology (new fuels, semiconducting materials, compounds of rare metals, strong alloys, durable coatings, etc.) is most important for the national economy of the USSR. Ya. I. Gerasimov has devoted his efforts to an important branch of experimental thermodynamics—determination of the free energies of compounds used in non-ferrous metallurgy and the study of heat-resistant alloys, oxides, and semiconductors.

M. Kh. Karapet'yants has elaborated a set of methods for the comparative calculation of several physicochemical properties of various chemical compounds.

Among theoretical investigations mention must be made of the work of L. D. Landau and V. K. Semenchenko on phase transitions of the second kind and on the theory of the thermodynamic stability of systems. D. S. Korzhinskii has applied to geological processes the concept of heterogeneous equilibria in open multiphase and multicomponent systems.

Thermodynamic functions for individual inorganic compounds, groups of compounds, solutions, and alloys have been investigated by many workers in connection with theoretical generalisations and practical problems (E. V. Britske, G. V. Kurdyumov, A. F. Kapustinskii, V. A. Sokolov, N. K. Voskresenskaya, A. I. Vol'skii, A. A. Zhukhovitskii, K. P. Mishchenko, M. M. Popov, K. G. Khomyakov, A. V. Rakovskii, S. M. Skuratov, A. M. Samarin, N. V. Ageev, S. A. Shchukarev).

Liquids and Solutions

Study of the properties of pure liquids and solutions is closely related both to thermodynamics and to aspects of the theory of the structure of matter. However, thermodynamic methods for describing the properties of solutions are the most important at present, because of inadequate development of a molecular—statistical theory of liquids.

The first systematic investigations of the miscibility of liquids were made by V. F. Alekseev during 1878–1884, and played an important role in establishing a thermodynamic theory of solutions. Alekseev also enunciated the "law of the rectilinear diameters" used to estimate the parameters of the critical points of two-phase systems. He visualised dissolution as resulting from two opposing tendencies—thermal motion of the molecules and "chemical" intermolecular interaction. In his general views he was an adherent rather of the physical theory of solutions, although he acknowledged its limited character.

D. I. Mendeleev was one of the authors of the "chemical" theory of solutions. He recognised the role of "physical" factors, but did not regard them as uniquely important in the theory of solutions, especially for solutions of finite concentration. The correctness of this general view has already been quite definitely confirmed in the unification of the general ideas and methods of the physical and chemical theories. In this connection an important role was played by the views of I. A. Kablukov, who regarded solvation as the main cause of the formation of ions in solution.

D. P. Konovalov worked on the thermodynamics of solutions. His study of the vapour pressure of various binary mixtures was crowned by the formulation of his well known laws. Konovalov's laws on the one hand provided a basis for a systematic thermodynamic analysis of the properties of solutions, and on the other hand are widely used in the practical rectification of liquids and in the theory of the distillation of liquid mixtures.

D. K. Chernov made the first investigations on solid solutions and phase diagrams. His "critical points", which have an important role in practical ferrous metallurgy, are actually transition temperatures of solid phases in the iron–carbon system.

Gaseous solutions have been studied. I. R. Krichevskii, P. E. Bol'shakov, and D. S. Tsiklis discovered the limited miscibility of gases in the case of the ammonia–nitrogen system. Similar properties have since been observed in several other systems.

N. S. Kurnakov's investigations on phase equilibria in solution are closely related to the theory of solutions. They led to the foundation of physicochemical analysis on the principles of continuity and congruence, later supplemented by the concept of singular points on phase diagrams. Physicochemical analysis not only was a method for the general description of phase diagrams but also acquired great practical value in the exploitation of salt deposits in the USSR.

Ya. I. Frenkel' was the first to attempt a consistent phenomenological theory of the liquid state based on the special character of molecular motion in a liquid. The movement of a given molecule is determined by the molecular field due to its environment and by its own kinetic energy. This motion is intermittent and is governed by the mean lifetime in temporary equilibrium positions. These ideas served as a basis for much subsequent work.

A more rigorous statistical theory of liquids and solutions, using the concept of correlative distribution functions of groups of particles, was elaborated by N. N. Bogolyubov. A statistically consistent method of calculating the thermodynamic properties of solutions of strong electrolytes, based on the method of correlation functions and variational derivatives, is widely used for solving stochastic problems. This method was developed further by I. Z. Fisher, who applied it in particular to solving the problem of the structure of liquids.

S. A. Shchukarev investigated the periodicity of the properties of chemical compounds in solutions, as well as aspects of chemical hydrology.

Thermodynamic methods of describing binary and multicomponent systems, by means of which possible types of phase equilibrium curves were established in heterogeneous multicomponent systems, were examined by A. V. Storonkin. A series of investigations of phase transitions in solutions of non-electrolytes at high pressures provided a better understanding of the relation between intermolecular interactions and thermodynamic properties (Krichevskii). Thermodynamic methods of calculating phase equilibria in liquid binary and multicomponent systems were evolved by V. B. Kogan for processes of azeotropic and extractive fractionation, from which technical schemes for the separation of mixtures were worked out. V. A. Mikhailov worked on thermodynamic processes of extraction. He suggested an extraction method for determining activity coefficients of electrolytes in aqueous solution.

V. K. Semenchenko demonstrated the effect of ion-pairs on the properties of electrolyte solutions, showed the physical pattern of this phenomenon, and gave its mathematical description. He introduced the concept of the generalised moment as a parameter representing a force constant (charge, dipole and quadrupole moments) per unit dimensions of the molecule. He based a general classification of solutions on a survey of the effective forces of interaction between particles. M. I. Shakhparonov investigated the structure of liquid systems with hydrogen bonds and thermal motion of the molecules.

A. I. Brodskii carried out series of experimental and theoretical investigations on strong electrolytes in non-aqueous media. A. N. Frumkin examined liquid solutions in terms of the energetics of solvation. K. B. Yatsimirskii considered regularities in the energies of formation of ions, together with aspects of proton affinity and ionic hydration.

The only quantitative theory of the dissociation of electrolytes and the theoretical principles of acid—base titration in non-aqueous media are due to N. A. Izmailov. Heats of dissolution in aqueous solutions of electrolytes (in contrast to non-aqueous solutions) become more strongly exothermic with rise in temperature, which indicates that the specific structure of water is a decisive factor in the energetics of the solutions. The idea of a limit of complete solvation has proved extremely useful in the discussion of salting out, acid catalysis, oxygen exchange between anions and water, and many other phenomena (A. M. Sukhotin, K. P. Mishchenko). The effect of the structure of water on the properties of solutions and its variation under the influence of ions have been examined by O. Ya. Samoilov.

Nuclear magnetic resonance, electron spin resonance, and non-resonant paramagnetic absorption have recently found wide application for investigating the structure of liquid solutions. A. I. Rivkind established that the relaxation of protons in solutions of paramagnetic salts takes place mainly in the solvation spheres of the paramagnetic particles, not in the bulk of the free solvent. Study of the relaxation of the solvent nuclei can be used as a method for examining the structure of paramagnetic solutions.

Magnetic resonance has been used to investigate the mobility of water molecules in the vicinity of ions and has confirmed the negative hydration of iodide and bromide ions. Negative and positive hydration of ions has been confirmed also by determining the translational diffusion coefficients of water in electrolyte solutions by the spin echo method (K. A. Valiev).

V. I. Danilov has used X-ray diffraction to investigate liquids and solutions. Analysis of the curves for scattering intensity reveals that liquids near the melting points are characterised by short-range order of the particles resembling their arrangement in the corresponding crystals.

Adsorption and Chromatography

The first work in Russia on adsorption was done as early as in 1785 by T. E. Lovits, who studied the adsorption of dyes on activated charcoal. Fundamental investigations on the adsorption of gases were made at the end of the nineteenth century and the beginning of the twentieth century. Classic studies in this field are those by A. A. Titov on the adsorption of gases on activated carbon and by N. A. Shilov on the dynamics of such adsorption.

During the First World War N. D. Zelinskii used the adsorptive power of carbon to produce a gas mask. The analytical possibilities of adsorption phenomena, and methods for separating mixtures based on differences in the adsorption of the components, were realised in 1903 by M. S. Tsvet. This worker used adsorbents to separate dyes and termed his method "chromatography". This method has found wide practical application only in our times, some fifty years after its creation.

The scope of work on adsorption became especially wide after the Bolshevik Revolution. Shilov and his pupils (S. A. Voskresenskii, L. K. Lepin', A. P. Ivanitskii, I. A. Tserevitinov) investigated the adsorption of solutes on carbon, and revealed the characteristic features of the adsorption of non-electrolytes and strong and weak electrolytes.

Soviet scientists have conducted a long series of investigations on the theory of adsorption phenomena. B. V. Il'in studied the role of intermolecular interactions in adsorption. A. N. Frumkin was the first to obtain an equation to the adsorption isotherm allowing for the mutual attraction of the molecules in the adsorbed layer. This equation was subsequently confirmed by more rigorous molecular–statistical calculation.

M. M. Dubinin evolved a theory that the space in pores became filled during adsorption, which enabled the adsorption isotherms of various vapours to be calculated from the known affinity coefficient and a characteristic curve obtained from the adsorption isotherm of one substance. Together with L. V. Radushkevich he established a relation between the form of the characteristic curve and the porosity of the carbon. The same methods have recently been used to study adsorption on zeolites. Methods have been worked out for obtaining many adsorbents of specified porosity. Dubinin's work on the dynamics of sorption gave rise to the chromatography of vapour mixtures.

A. V. Kiselev studied the adsorption of various classes of compounds on modified and unmodified silica gels, zeolites, and graphitised carbon black. Methods of adsorption, gas chromatography, and molecular spectroscopy were used in this work to investigate intermolecular interactions in general. Views were evolved on specific and non-specific adsorption, with the use of spectroscopy to study the former. Molecular–statistical calculations were employed to compute the main adsorption and gas-chromatographic characteristics of several hydrocarbons and other compounds on graphitised carbon black and on zeolites. A relation was found between the energy of adsorption and the properties of the sorbable molecules. Not only heats of adsorption but also heat capacities of various compounds in adsorbed layers were determined. The improvement of gas-chromatographic methods enabled hundreds of adsorbate–adsorbent systems to be investigated for extremely complicated organic and organoelementary compounds. Molecular liquid chromatography and adsorption from solutions were used to study the intermolecular interactions of simple organic molecules, polymers, biopolymers, and viruses.

In connection with the study of catalytic processes many theoretical and experimental investigations were made on the chemisorption of active gases on energetically non-uniform surfaces. The logarithmic adsorption isotherm first found experimentally (A. I. Shlygin, A. N. Frumkin) was explained theoretically both by the concept of energetic non-uniformity (L. D. Landau, Ya. B. Zel'dovich, S. Z. Roginskii) and by the action of intermolecular forces of repulsion (M. I. Temkin). Zel'dovich was able to show how the distribution function of heats of adsorption could be determined from the experimental equation for the adsorption isotherm, which gave rise to a long series of studies in this field (Roginskii, Temkin).

V. K. Semenchenko studied adsorption phenomena in metallic systems, and discovered several specific effects attributable to the high surface activity of individual components of the alloy. The effect of surface-active metals on the brittleness of metals and alloys was discovered by P. A. Rebinder, Yu. V. Goryunov, and E. D. Shchukin ("Rebinder effect").

K. V. Chmutov is investigating the separation of rare-earth metals, the role of complex formation, and the simulation and intensification of chromatographic processes. V. A. Malyusov has been concerned with the theoretical principles of separation processes (chromatography, fractionation, crystallisation).

G. M. Panchenkov is concerned with ion-exchange equilibria on zeolites and the thermodynamics of heterogeneous equilibria. A. A. Zhukhovitskii has used the theory of mass transfer to describe the dynamics of sorption. The principles of mass transfer and the problems of the automation and optimisation of chemical processes are being dealt with by V. V. Kafarov. Sorption in a fluidised bed has been investigated by D. G. Romankov, who has generalised the equations of sorption dynamics.

The work of E. V. Alekseevskii and his students is widely known in the field of non-carbon adsorbents. They have developed methods for the preparation of active metal oxides and have studied the recovery of various solvents. I. V. Grebenshchikov discovered siliceous adsorbents having a spongy structure–porous glasses.

The laws of the sorption of ions by activated charcoals and silica gels, the mechanism of the adsorption of various complex compounds, and the role of electrochemical factors in these phenomena were studied by D. N. Strazhesko and his coworkers.

Colloid Chemistry

Colloid chemistry began to develop as a physicochemical discipline in the second half of the nineteenth century.

Before that time, however, there were investigations which played a significant role in the establishment of colloid chemistry and its methods. These include the discovery of electrokinetic phenomena—electrophoresis and electro-osmosis (F. F. Reiss)—the first quantitative studies of the formation of jellies and gels (F. N. Shvedov), cryoscopic measurements of the effective molecular weights of various substances in colloidal solution (N. N. Lyubavin, A. N. Sabaneev), and work on the theory of capillarity (A. Yu. Davidov, I. S. Gromeka).

Modern ideas on the nature and properties of the colloidal state are due to P. A. Rebinder and his school (A. B. Taubman, V. I. Likhtman, E. D. Shchukin, et al.). Several fundamental principles of the physical chemistry of surface phenomena in disperse systems were established (evolution and stability of structures, control of their properties by the introduction of surface-active agents). These investigations provided a scientific basis for the application of flotation agents, stabilisers, detergents, demulsifiers, etc.

A. V. Dumanskii has revealed the role of complex formation in the production of colloidal particles, and of the bonding of water in the drying and denaturation of colloids. N. P. Peskov has examined the role of kinetics and state of aggregation in the stability of colloids as functions of their degree of dispersion and their kinetic and adsorption properties. Specific features of adsorption on swollen colloids have been studied by A. V. Rakovskii.

B. V. Deryagin investigated surface phenomena in terms of the action of surface forces. A quantitative theory of the coagulation of disperse systems by electrolytes was formulated that took into account the relative molecular attraction. Direct measurement of the forces acting between surfaces at distances of the order of a micrometre provided experimental verification of the present-day physical theory of long-range molecular action. Cross-linked colloidal systems have been investigated by M. P. Volarovich, A. A. Trapeznikov, K. F. Zhigach, G. V. Vinogradov, and others.

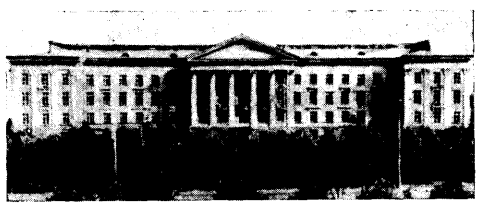


Figure 22. Zelinskii Institute of Organic Chemistry of the USSR Academy of Sciences.

Electrochemical methods are widely used in the study of colloids (A. I. Rabinovich, V. A. Kargin, N. I. Zhukov, and others). An effective method for purifying colloidal systems by high-voltage electrodialysis has been developed from this work. Electron microscopy has revealed the mechanism of the formation of colloidal particles.

The properties of solutions of polymers and the aging and syneresis of jellies have been investigated by S. M. Lipatov and S. A. Glikman. The colloidal properties of proteins were studied by A. G. Pasynskii, V. A. Pchelin.

Numerous applications of aerodisperse systems have been examined. An effective procedure for preventing the formation by radiation of mists of water droplets, based on blocking the hygroscopic condensation centres by adsorbed monolayers of higher alcohols, has been evaluated (B. V. Deryagin, P. S. Prokhorov, V. A. Fedoseev, N. N. Tunitskii, Ya. I. Kagan, A. G. Amelin, I. V. Petryanov-Sokolov).

Work has progressed on applications of colloid chemistry to the food industry (A. V. Dumanskii, N. F. Ermolenko) the rubber and synthetic rubber industry (B. A. Dogadkin, S. S. Voyutskii, A. I. Yurzhenko), dyes (N. P. Peskov, L. I. Belen'kii), cellulose (S. M. Lipatov), etc.

Trapeznikov has developed methods and apparatus for investigating the rheology of cross-linked systems and the mechanical properties of monolayers and soap films.

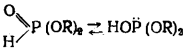
ORGANIC CHEMISTRY

Research on organic chemistry became widespread after the middle of the past century. Fundamental work was done by A. M. Butlerov—author of the theory of the structure of organic compounds—A. E. Favorskii, S. V. Lebedev, N. N. Zinin, N. D. Zelinskii, V. V. Markovnikov. The first institute of the Academy of Sciences to specialise in research on organic compounds was established at Moscow in 1934, and is now the Zelinskii Institute of Organic Chemistry [Fig. 22].

Modern organic chemistry, which already deals with millions of compounds, has been transformed, in the words of A. N. Nesmeyanov, into the structural architecture of molecules.

Theoretical Foundations of Organic Chemistry

A. M. Butlerov's theory of the chemical structure of organic compounds blazed a trail, in the "dense forest" (Wöhler's expression) of organic chemistry, to an understanding of the nature of quadrivalent carbon compounds. Butlerov noted the decisive importance of the interaction of atoms and groups in the molecule, explained the isomerism of the hydrocarbon residues, and was the first to direct attention to the possibility of isomeric conversion (cyanic acid, urea). In 1877 Butlerov pointed out that isodibutylene [2,4,4-trimethylpent-2-ene] was able to react according to two structural formulae or, in the modern idiom, it had dual reactivity. This was the first example of equilibrium isomerism (tautomerism), an understanding of which has been greatly assisted by the work of A. E. Favorskii and A. E. Porai-Koshits. Milestones on the road to a theory of tautomerism and dual reactivity were the discovery of a new type of dyad tautomerism in dialkyl phosphites (A. E. Arbuzov)



and investigation of the reactions of the tautomeric 2-aminopyridine and methylpyridine systems (A. E. Chichibabin). The concept of intramolecular valency tautomerism was first applied in dye chemistry.

Investigations showing the possibility of dual reactivity in the absence of tautomerism constituted a definite stage of development in theoretical organic chemistry. A. N. Nesmeyanov and M. I. Kabachnik drew a sharp distinction between equilibrium dynamic isomerism (tautomerism) and dual reactivity, and worked out a strict classification of various cases of the latter with and without migration of the reaction centre along the chain of conjugated

bonds. The influence of various factors was considered, and quantitative relations were established between the kinetic parameters of the reactions and the solvent, the temperature, and the nature of the reactants. Several general rules were formulated, the application of correlation equations was worked out, and new methods were found for investigating diverse tautomeric systems. It was shown that, in cases of strongly displaced equilibrium, the reaction product corresponding to the tautomer present in low concentration is formed from the other tautomer with transference of the reaction centre. The factors determining the conditions of such transfer have been examined.

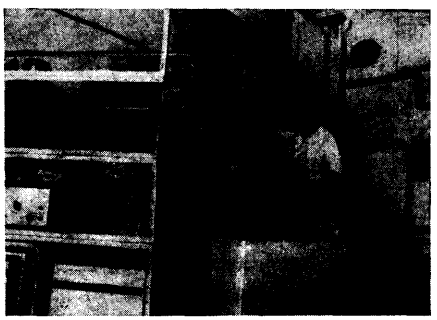
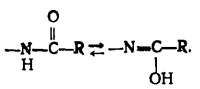
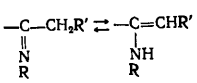


Figure 23. Radiation installation for investigating the mechanism of catalytic reactions during exposure to γ-rays (Institute of Organic Chemistry of the USSR Academy of Sciences).

The tautomerism of many nitrogen-containing heterocyclic systems have been studied by infrared and ultraviolet spectroscopy, and the conditions of displacement of the tautomeric equilibrium have been revealed as functions of the nature of the substituent and the solvent (I. Ya. Postovskii, Yu. N. Sheinker, I. I. Grandberg). The structure of tautomeric and potentially tautomeric nitrogen-containing open-chain systems has been investigated. Thus the application of spectropolarimetry to optically active compounds has revealed amide–imidol tautomerism



It has been used to investigate the tautomeric equilibrium of the ketimide–enamine system



(V. M. Potapov, A. P. Terent'ev), previously detected from the infrared spectra (N. K. Kochetkov, Ya. V. Dombrovskii). M. M. Shemyakin discovered a variety of ring–chain tautomerism involving the amide group, and proposed an isotope method for discriminating between tautomerism and dual reactivity. This method was able to record, for example, the high rate of tautomerisation of diazoaminobenzene, which explains the specific behaviour of the triazen system.

S. S. Novikov published a series of papers on the tautomerism, structure, kinetics, and reaction mechanism of nitroalkanes and their salts. To elucidate the nature of keto–enol tautomerism use has been made of infrared and Raman spectroscopy (D. N. Shigorin, V. A. Mironov, Yu. A. Pentin), as well as high-resolution proton magnetic resonance spectroscopy (E. I. Fedin).

New types of tautomerism—metallotropy, acylotropy, and aroylotropy—have been discovered and studied in several organophosphorus compounds.

The investigation of *O*- and *C*-hetero-substituted derivatives of monocarbonyl and β-dicarbonyl compounds has revealed many examples of dual reactivity. Isomerisation has been observed with migration of the heteroatom (silicon, phosphorus, arsenic, etc.) from carbon to oxygen and from oxygen to carbon in the keto-enol. Heterotropic tautomerisations have been studied in acetone derivatives containing germanium, tin, and antimony (I. F. Lutsenko). It has thus been shown that the well known prototropic tautomeric equilibria represent a particular—though evidently most important—case of the general phenomenon of heterotropic equilibria.

The study of molecular rearrangements is of great value for understanding reaction mechanisms and in the search for paths for the controlled synthesis of compounds of definite structure. Various conversions resulting from molecular rearrangements have been investigated by E. E. Vagner, S. S. Nametkin, A. E. Arbuzov, A. E. Favorskii, N. Ya. Dem'yanov.

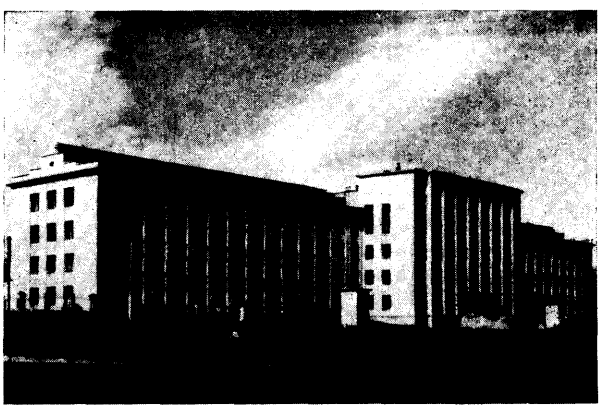


Figure 24. Arbuzov Institute of Organic and Physical Chemistry of the USSR Academy of Sciences.

B. A. Kazanskii's conversion of isopropenylcyclobutane into 1,2- and 3,3-dimethylcyclopentenes was an interesting example of the Vagner–Nametkin rearrangement. I. N. Nazarov extended the concepts of the Favorskii rearrangement to secondary and tertiary polyene alcohols. V. F. Kucherov and M. I. Ushakov discovered the rearrangement of furan derivatives involving multiple bonds. T. A. Favorskaya has found acetylene—allene and allene–diene rearrangements with acetylenic carbinols and halides. The reverse isomerisation (allene–acetylene) was described by A. A. Petrov. Favorskii's mechanism of the acyloin rearrangement of α-hydroxy-ketones was confirmed

by T. I. Temnikova. The rearrangement of α-hydroxy-aldehydes into hydroxy-ketones and α-glycols was studied by S. N. Danilov and E. D. Venus-Danilova. A mechanism was suggested for the aldehyde–ketone rearrangement by T. E. Zalesskaya. The Dem'yanov rearrangement was developed by N. I. Putokhin for the interconversion of five- and six-membered heterocycles. I. L. Knunyants found that polyfluorinated azides underwent a peculiar rearrangement into hydroxamic acids.

A. N. Nesmeyanov and R. Kh. Freidlina studied many examples of the rearrangement of radicals with 1,2-migration of chlorine and thiyl groups. The telomerisation and rearrangements of radicals in the reaction of ethylene with carboxylic acids and their derivatives were investigated, and used to develop an industrial method of producing α-branched monocarboxylic acids. The chemical behaviour of free radicals in the liquid phase was examined by G. A. Razuvaev. A study was made of chain reactions initiated by free radicals generated by irradiation or by the thermal decomposition of organometallic compounds.

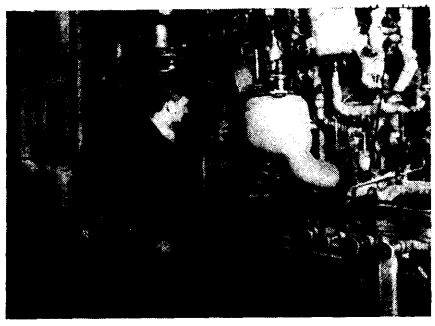
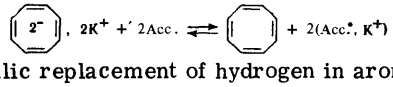


Figure 25. In the Technological Laboratory of the Institute of Organic Chemistry of the USSR Academy of Sciences.

The mechanisms of various organic reactions are being investigated by modern physicochemical methods. A procedure has been worked out for studying electron-transfer reactions in homogeneous media. The cyclo-octatetraene dianion is used as electron-donor, and the extent of reaction is assessed from the yield of neutral cyclo-octatetraene:

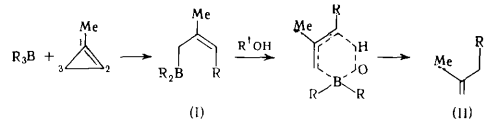


Nucleophilic replacement of hydrogen in aromatic compounds has been accomplished by abstraction of a hydride ion from anionic complexes. σ-Complexes of trinitrobenzene with acetone are oxidised by a wide range of oxidants—halogens, hypohalites, salts of metals of variable valency, peroxides, quinones, tropylium salts, etc.—to give high yields of trinitroacetone. Anionic σ-complexes of trinitrobenzene with compounds of transition metals have been obtained for the first time.

It has been suggested that double bonds can be selectively hydrogenated by silanes in acid solutions in the absence of a catalyst (ionic hydrogenation). The hydrogenation of thiophens under mild conditions gives high yields of the normally difficultly accessible thiophans, which are of great interest for their physiological (e.g. biotin) and antioxidant properties (D. N. Kursanov, Z. N. Parnes, V. N. Setkina, Z. V. Todres).

The mechanism of the oxidation of polymethylated aromatic compounds on reaction with electrophilic reagents in strongly acid media has been elucidated. The formation of intermediate species can be observed by proton magnetic resonance if the reactants are mixed at $-80°$ to $-100°$C and the system is gradually "unfrozen". Voluminous information has been obtained on the mechanisms of these reactions, and convenient methods have been found for obtaining a series of compounds of practical interest (e.g. *p*-methoxytetramethylphenol and its derivatives, which have been tried as stabilisers for certain types of polymer systems (V. A. Koptyug)).

Investigation of the action of organoboranes on the highly strained cyclopropene system showed that 1-methylcyclopropene reacts with trialkylboranes under mild conditions with cleavage of the cyclic $C_{(2)}-C_{(3)}$ single bond:



The resulting boranes of type (I) react with alcohols to give (after allylic rearrangement) the alk-1-ene (II). Conducting this reaction in alcohol will give in a single stage 60–90% yields of alkenes containing a terminal methylallyl group (B. A. Kazanskii, B. M. Mikhailov).

The mechanism of the spontaneous redox reaction of aldehydes in alkaline media (in Cannizzaro reaction) has been investigated. The kinetic data were analysed by means of the alkalinity function, which is a measure of the ability of the medium to ionise a molecule of a weak acid. This approach enabled M. I. Vinnik to establish the composition of the reactive complexes in the Cannizzaro reactions of *m*-nitrobenzaldehyde and *p*-methoxybenzaldehyde.

A systematic investigation is being made of the reactivity of complexes of transition metals with π- and σ-aromatic ligands in electrophilic and protophilic isotope exchanges of hydrogen (Kursanov).

The conformational state in solutions of simple model polyhalogenated alkanes, obtained by telomerisation and containing three- or four-spin molecular fragments, has been investigated. The complicated proton magnetic resonance spectra have been analysed by the use of double homonuclear and heteronuclear resonance, a computer, and the preparation of deuterated analogues. Methods that have been developed for evaluating the conformational composition and the fine structure of chiral molecules are required to solve stereochemical problems of the telomerisation stages—addition and substitution involving aliphatic radicals.

A. N. Nesmeyanov and A. E. Borisov investigated substitution at an alkene carbon atom in 2-chlorovinyl derivatives of various metals, and formulated the rule that geometrical configuration is conserved during substitution at an olefinic carbon. O. A. Reutov and I. P. Beletskaya studied the kinetics, mechanism, and stereochemistry of substitution at a saturated carbon atom. Their investigations led to the well known rule that configuration is preserved in S_E2 reactions.

The dissociative resonance capture of electrons by molecules of various types of organic compound has been investigated by the mass spectrometry of negative ions (S. R. Rafikov, V. I. Khvostenko, R. G. Kostyanovskii).

Many investigations have involved the use of correlation equations, a method which has been widely accepted in the study of reactivity and reaction mechanisms (V. A. Pal'm, Yu. A. Zhdanov, V. I. Minkin).

Quantum-chemical methods have been used to calculate the geometry and the electronic state of organic molecules. This work began with Ya. K. Syrkin and M. E. Dyatkina's application of the Hückel method to the properties of organic compounds having conjugated bonds. A. A. Bochvar calculated the properties of organic molecules with alternating bond lengths. A. B. Bolotin and Yu. A. Kruglyak started the use of rapid electronic computers for molecular calculations. Programs were set up for evaluating molecular integrals (Bolotin). An original density matrix method was elaborated, and successfully applied to the calculation of certain physical properties of conjugated organic compounds (M. M. Mestechkin). A consistent theory was worked out for the interaction of electrons in conjugated systems, and their spectroscopic properties were explained (A. A. Ovchinnikov). A model was suggested for the elementary act of substitution in certain simple hydrocarbons (M. V. Bazilevskii).

Chemistry of Hydrocarbons

A systematic study of the structure and properties of hydrocarbons dates from the mid-nineteenth century, when many investigations were made by A. M. Butlerov and his school. The principles of the chemistry of petroleum hydrocarbons developed in the work of V. V. Markovnikov and N. D. Zelinskii, who were the first to direct attention to the importance of synthesising model compounds. The most reliable results will usually be obtained by comparing petroleum hydrocarbons with known standard (model) substances.

Methods for the synthesis of hydrocarbon standards were developed by B. A. Kazanskii, A. F. Plate, A. L. Liberman, who prepared various substituted cycloalkanes, isolated their geometric isomers, and synthesised several new bicyclic systems. R. Ya. Levina obtained previously unknown homologues of cyclohexane, isoalkanes, alkenes, alkynes, and compounds containing a tertiary carbon atom. V. N. Ipat'ev suggested methods for the preparation of alkenes from readily available oxygen-containing compounds, based on the example of the catalytic dehydration of alcohols. S. V. Lebedev converted ethanol into butadiene, and the mechanism of this reaction was studied by Yu. A. Gorin. The mode of preparation of isoprene from acetone and acetylene discovered by A. E. Favorskii formed the basis of V. F. Kucherov's method for the continuous synthesis of pure isoprene suitable for stereospecific polymerisation. At the beginning of the 1940s N. D. Zelinskii and A. L. Klebanskii accomplished the synthesis of butenyne and later hexa-1,5-dien-3-yne and its homologues.

At the beginning of the present century Ipat'ev and Zelinskii found ways of interconverting hydrocarbons, and were the first to study the hydrogenation of the benzene ring in aromatic compounds. This discovery initiated the development of catalytic organic synthesis. Numerous catalysts, widely employed for the hydrogenation and dehydrogenation of organic compounds, were evolved, and their mode of action was studied (N. I. Shuikin, Kh. M. Minachev, A. V. Frost, L. Kh. Freidlin, D. V. Sokol'skii, Yu. S. Zal'kind, A. M. Rubinshtein, B. L. Moldavskii). The hydrogenation of substituted ethylenes on platinum and palladium catalysts, as well as the hydrogenation of conjugated, vinylacetylenic, and acetylenic hydrocarbons, was studied by S. V. Lebedev, G. G. Koblyanskii, and A. I. Yakubchik. The results of this work were generalised as "Lebedev's rules". The dependence of the rate and order of hydrogenation on the substituents and structure of the isomers and on the free energy of the reaction was investigated. During the 1920–1940s Zelinskii and his pupils carried out a series of studies of the catalytic dehydrogenation of hydrocarbons: they determined methods and conditions for the dehydrogenation of various cyclohexanes, the efficiency of diverse catalysts, and the mechanism and kinetics of the catalytic processes. The results formed the basis for A. A. Balandin's multiplet theory of catalysis. Zelinskii's catalysed dehydrogenation was transformed into the chief method for studying natural petroleum hydrocarbons and became the principal industrial method of obtaining aromatic hydrocarbons. N. D. Zelinskii and N. L. Glinka discovered the catalytic conversion of cyclohexene into cyclohexane and benzene. This reaction, termed "irreversible catalysis", became the subject of numerous investigations, during which it was found to be common to all unsaturated cyclic hydrocarbons.

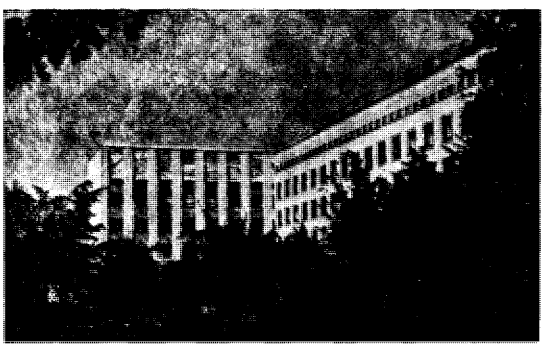


Figure 26. Institute of Organoelementary Compounds of the USSR Academy of Sciences.

Fresh results on the conversion of cyclohexane and cyclohexadiene on platinum and palladium have recently been obtained by V. M. Gryaznov and V. S. Smirnov, who show that the redistribution of hydrogen comprises a set of dehydrogenation and hydrogenation reactions. This discovery has been called membrane catalysis from the practical procedures adopted.

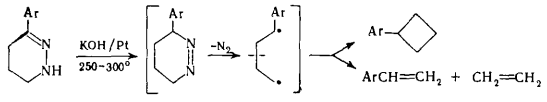
A simple transition from accessible alkanes to valuable aromatic hydrocarbons by means of dehydrogenating catalysts was achieved by three groups of investigators—B. L. Moldavskii and G. D. Kamusher, B. A. Kazanskii and A. F. Plate, and V. I. Karzhev—who studied various questions connected with the mechanism and the practical application of the dehydrogenation of alkanes. The hydrogenation of cyclopentanes—a new direct route to alkanes from the C_5 cycloalkanes widely distributed in petroleum—was discovered and studied, as well as isomeric changes in cyclic hydrocarbons.

Study of the alkylation of aromatic and aliphatic hydrocarbons, resulting from the need to synthesise high-octane components of motor fuel, was begun in the 1920s by

V. N. Ipat'ev, N. A. Orlov, and G. A. Razuvaev, after which it was developed simultaneously in many scientific establishments. Aspects of the synthesis of benzene homologues by means of various catalysts were considered by A. V. Topchiev, Yu. G. Mamedaliev, M. A. Dalin, Ya. M. Paushkin, and others. The catalytic alkylation of alkanes was studied in several investigations.

Work was done on the cracking of heavy petroleum products with the aim of obtaining motor fuel. Thermocatalytic conversions of individual hydrocarbons became one of the main subjects of investigation. M. G. Gonikberg, A. E. Gavrilova, and B. A. Kazanskii examined the effect of high pressure on the rate of thermal and catalytic cracking of alkanes. A. D. Stepukhovich suggested a reaction mechanism of cracking and a theory of the chain decomposition of alkanes. The kinetics, thermodynamics, and technology of the high-temperature processing of saturated hydrocarbon gases were studied systematically by A. M. Brodskii and K. P. Lavrovskii.

The chemistry of hydrocarbons having small rings is a comparatively young branch of organic chemistry. The publications of V. V. Markovnikov, G. G. Gustavson, N. D. Zelinskii, A. E. Favorskii, N. Ya. Dem'yanov, S. V. Lebedev, and N. M. Kizhner planned syntheses and described interesting isomerisations involving small rings, the mechanism of which has only now become clear. An explanation of the electronic structure of small rings was first given by M. E. Dyatkina and Ya. K. Syrkin. A series of studies on the mechanism of the formation of small rings from dibromides was made by Ya. M. Slobodin. Simple cyclic compounds and their isomerisation were investigated by Dem'yanov. The decomposition of pyrazolines, discovered by Kizhner, formed the basis for studies of various cyclopropanes (B. A. Kazanskii, M. Yu. Lukina, A. P. Meshcheryakov, L. V. Petrova). An interesting method of obtaining arylcyclobutanes was discovered in the 1960s by R. Ya. Levina, M. K. Kuz'min, Yu. S. Shabarov, who were studying the chemical and physical properties of arylcycloalkanes:



The stability of three- and four-membered rings was investigated (T. A. Favorskaya), as well as the dehydration and isomerisation of cycloalkylmethanols (Freidlin). The chemistry of small rings has been developed by I. A. D'yakonov, a pupil of Favorskii. This was one of the first researches on the use of carbenes for the synthesis of cyclopropane derivatives. A series of studies was made on the properties, mechanism of catalytic reactions, and spectral characteristics of three-membered rings with unsaturated and aryl substituents, together with the reactivity of cyclopropanes and halogenocyclopropanes.

The first investigations on the chemistry of acetylenic and conjugated systems were made by Favorskii and his students, who established methods of interconversion among acetylenes, allenes, and diene hydrocarbons, ways of passing from acetylenic compounds to terpenes, mechanisms of polymerisation, and various reactions of acetylenic hydrocarbons. This work opened up new fields of organic chemistry, in particular the chemistry of ethynylvinylmethanols (I. N. Nazarov, I. V. Torgov), butenyne (A. L. Klebanskii, A. A. Petrov, T. A. Favorskaya), and butadiyne (Yu. S. Zal'kind, A. D. Petrov, M. F. Shostakovskii). Research on the chemistry of acetylenic and conjugated compounds has immense value for the development of theoretical organic chemistry. Furthermore, these investigations have made available several new classes of unsaturated compounds which are important for the manufacture of synthetic materials.

The chemistry of terpene hydrocarbons has developed in our country by syntheses and studies of the structure and reactions of terpenes, investigations of the composition of native wood-chemical products such as essential oils, turpentines, and vegetable resins, as well as by industrial exploitation of the results. The chemistry of terpene hydrocarbons was studied by A. M. Butlerov, F. R. Vreden, F. M. Flavitskii, E. E. Vagner, L. A. Chugaev, and developed during the Soviet period by V. E. Tishchenko, A. E. Arbuzov, S. S. Nametkin, N. Ya. Dem'yanov, G. V. Pigulevskii, I. I. Bardyshev, V. N. Belov, V. I. Isagulyants, L. Ya. Bryusova, and many other investigators.

The oxidation, halogenation, and nitration of hydrocarbons were investigated because of the requirement by industrial developments to obtain valuable chemical raw material based on hydrocarbons of petroleum origin. The oxidation of organic compounds was studied by N. I. Chernozhukov, K. I. Ivanov, A. N. Bashkirov, V. V. Kamzolkin, V. K. Tsyskovskii, and many others. Researches on oxidising processes became especially interesting in connection with the study of their radical–chain mechanism, work which has been surveyed in the Physical Chemistry Section. Investigation of the halogenation of hydrocarbons was begun by V. V. Markovnikov and continued by A. V. Topchiev, B. A. Krentsel, N. I. Shuikin, who made many innovations both in the development of theoretical ideas in organic chemistry and in improving the technology of organic synthesis. Study of the nitration of hydrocarbons led to A. I. Titov's theoretical views, which are widely applied at the present time.

Aromatic and Heterocyclic Compounds

Aromatic compounds were already under investigation at the beginning of the nineteenth century. A. A. Voskresenskii discovered benzoquinone in 1838, and N. N. Zinin the reduction of aromatic nitro-compounds in 1842. Much work was done on the synthesis and various reactions of aromatic compounds (N. Ya. Dem'yanov, N. D. Zelinskii, N. M. Kizhner, A. E. Chichibabin, P. P. Alekseev, M. G. Kucherov), the nitration, chlorination, and sulphonation of benzene derivatives (N. N. Sokolov, F. F. Beil'shtein [Beilstein]), and the chemistry and technology of anthraquinone (M. A. Il'inskii).

Development of the chemistry of aromatic compounds during the Soviet period has promoted the establishment of a native industry of organic synthesis.

During the 1930s the mechanism of electrophilic substitution in the benzene ring was elucidated, and the dependence of sulphonation on various factors (concentration of sulphuric acid, temperature, presence of impurities) was determined (E. A. Shilov, V. A. Izmail'skii, A. M. Lukin, B. P. Fedorov, I. S. Ioffe). A kinetic study was made of the sulphonation of benzenes, the composition of the products was determined, and methods for the analysis of isomeric sulphonic acids were worked out (A. A. Spryskov). Study of the sulphonation of aromatic compounds occupied an important position in the work of N. N. Vorozhtsov, who investigated the sulphonation of naphthalene and the nature of its sulphonated derivatives, together with the effect of various catalysts on the reaction. Industrial methods were developed for the sulphonation of 2-naphthol (I. I. Vorontsov) and 2-chloronaphthalene (N. N. Vorozhtsov

Jr), as well as an effective method for sulphonating benzene in the vapour phase (R. K. Eikhman, M. I. Bogdanov, V. N. Ufimtsev).

The nitration of aromatic compounds began to be studied in the 1920s, when A. V. Kartashev detected the formation of nitrosophenols when phenol was treated with nitric acid. A. I. Titov carried out his classical work on the theory of nitration, and his suggested mechanisms and views on the nature of the nitrating agents became generally accepted. Many researches were devoted to a comprehensive study of the nitration of various aromatic molecules. The effect of boron trifluoride on the orientation of the nitro-group was determined, and a study made of the steric effect of nuclear substituents on the direction of reaction and the proportions of isomeric nitro-derivatives. Novel methods were worked out for obtaining aromatic nitro-compounds—by the batch and continuous nitration of ethylbenzene with a nitrating mixture, and simple methods for preparing *o*- and *p*-nitrobiphenyl, for obtaining chlorofluoronitrobenzenes, and for the simultaneous introduction of an iodine atom and a nitro-group into *p*-polyphenyl compounds. The nitration of anthraquinones, phenanthrene, acenaphthenes and fluorene, carbazole, dibenzopyrenes, and onium compounds has been investigated.

Vorozhtsov studied the effect of the nature of the catalyst on the kinetics of the chlorination of benzene, explained the mechanism of the catalytic action of iron(II) chloride, and worked out a continuous method of multiple chlorination. The kinetics and the mechanism of the halogenation of aromatic compounds in aqueous medium were examined by Shilov, who proposed an activity sequence of halogenating agents. He determined kinetic isotope effects in the halogenation of aromatic amines and amino- and hydroxy-sulphonic acids. The bromination of sterically hindered phenols was studied by V. V. Ershov and A. A. Volod'kin. The halogenation of more complex aromatic compounds—biphenyl, naphthalene, anthracene, anthraquinones, naphthacene, etc.—was investigated. Several new halogenating agents were suggested, e.g. *N*-chloroamides, *N*-chlorodiethylamine, *N*-bromophthalimide, and dioxan dibromide.

Considerable attention was paid to elucidating the mechanism of the alkylation of aromatic compounds in the presence of aluminium halides, in particular the chloride, whose first use in organic synthesis dates from G. G. Gustavson. The reactivity of alkylating agents towards aromatic hydrocarbons was studied, and schemes suitable for industrial use were proposed for the alkylation of benzenes by alkenes in the presence of aluminium chloride (N. N. Lebedev) and of sulphuric acid (Yu. G. Mamedaliev, M. A. Dalin).

During the 1920s V. M. Rodionov and V. K. Matveev discovered a new method for obtaining aromatic diazo-compounds from phenols and nitrous acid in a mineral medium, and this found industrial application. Azo-coupling, which with diazotisation is the principal reaction in the synthesis of azo-dyes, was studied in detail (A. E. Porai-Koshits).

Nucleophilic substitutions in the aromatic series were studied by A. N. Engel'gardt and P. A. Lachinov, N. N. Vorozhtsov Jr, D. V. Tishchenko, L. Kh. Freidlin, A. I. Kiprianov, E. Yu. Orlov, S. S. Gitis, B. I. Stepanov.

In the mid-1930s P. P. Shorygin and A. V. Topchiev began a systematic study of radical substitution in aromatic compounds. The mechanism and the chief laws of homolytic arylation were established by A. N. Nesmeyanov, Kh. S. Bagdasar'yan. Radical arylation by organometallic compounds was studied by G. A. Razuvaev. Many data on isomerisation in the aromatic series were summarised by V. A. Koptyug.

The chemistry of non-benzenoid aromatic systems has been vigorously developed during the past decades. Diphenylcyclopropenone, the cyclopentadienyl anion, cyclopentodienylides, and the tropylium and ditropylium cations have been investigated (D. N. Kursanov, M. E. Vol'pin, Yu. D. Koreshkov, Z. N. Parnes, I. S. Akhrem). Dipole moments have been measured (Ya. K. Syrkin, A. N. Shidlovskaya), and calculations made on the π-electron systems of certain compounds by the molecular orbital method (A. A. Bochvar).

The first investigations of heterocyclic compounds were made by Chichibabin, and their chemistry was developed by Rodionov's syntheses from β-amino-acids, A. I. Kiprianov and I. I. Levkoev's work on cyanine dyes, investigations of β-lactams and azalactones by I. L. Knunyants, studies by M. M. Shemyakin and V. K. Antonov on oxacyclic compounds, M. G. Voronkov on the chemistry of atran systems, B. A. Arbuzov on the diene synthesis of heterocyclic compounds, M. V. Rubtsov on azabicyclic compounds, and by many others. An original method of synthesising heterocyclic systems of diverse structure from substituted 2-chlorovinyl ketones was described by A. N. Nesmeyanov and N. K. Kochetkov. A general method for obtaining five-membered heterocycles from acetylenic α-oxides was worked out by F. Ya. Perveev.

A series of researches were made on furan derivatives. The reactions of chloromethylfurans, the preparation of nitrogen-containing heterocycles including a furan ring, diene synthesis and substitutive additions, and the reactivity of the furan ring were investigated by Yu. K. Yur'ev, K. Yu. Novitskii, N. S. Zefirov. Interconversion of five-membered heterocycles under conditions of vapour-phase catalysis by aluminium oxide was discovered to be a general reaction. Difficultly accessible 3-substituted furans were obtained, and Ya. L. Gol'dfarb elaborated a method for preparing ketones by acylating furan. A group of researches on the preparation, reactions, and practical application of furan derivatives is being conducted under the direction of S. A. Giller. Methods have been worked out for obtaining various functional derivatives of furan, and their pharmacological activity has been examined (A. L. Mndzhoyan). New methods for preparing furan derivatives —by sulphonation with pyridine—sulphur trioxide, formation of benzofurans from quinones, and production of amines of the furan series, whose oxidation yields amino-acids, some of which may be optically active—were proposed by A. P. Terent'ev. The hydrogenation and hydrogenolysis of furan compounds, as well as thermal and catalytic conversions of dihydrofurans, were studied by N. I. Shuikin.

New methods have been elaborated for the synthesis of pyrones, and their reactions have been studied (R. Ya. Levina, N. P. Shusherina, L. I. Zakharkin). Pyrylium salts, fused with a furan or a thiophen ring, have been investigated (G. N. Dorofeenko, Yu. A. Zhdanov).

The alkylation and acylation of thiophen in the presence of tin(IV) chloride has become generally accepted. A comparative study has been made of the direct metallation of the thiophen, furan, and benzene rings. A simple and effective method has been found for obtaining sulphides and thiols of the thiophen series, together with ways of preparing various functional derivatives.

Knunyants prepared propiothialactones, in which a new type of sulphur-containing four-membered ring has been formed. He also worked out original methods for alkylating 2-aminopyridine, as well as the principles for the industrial

production of quinacrine hydrochloride. N. N. Suvorov synthesised indol-3'-ylbutyric acid and found a new method of obtaining serotonin.

A. N. Kost investigated various nitrogen-containing heterocycles. Extensive investigations of diazaindenes and quinuclidines were made by L. N. Yakhontov in the search for physiologically active compounds. The chemistry of azines and azoles containing another heterocyclic atom (quinazolines, quinoxalines, phenoxazines, acridines, tetrazoles, benzimidazoles, etc.) is being investigated. New reactions non-activated heterocyclic substrates have been detected as well as the dealkylation of sterically hindered tertiary arylamines. The effects of a heterocycle and of other substituents on the amine–imine tautomerism and the conformation of formazans have been established (I. Ya. Postovskii).

Discovery of a new reaction of chlorinated aromatic and heterocyclic derivatives with hydrogen sulphide has been used to work out methods, suitable for industry, of obtaining aromatic and heterocyclic thiols and sulphides (M. G. Voronkov, A. S. Nakhmanovich, E. P. Deryagina). Aromatic and heterocyclic compounds and their fluorinated derivatives react with polyfluoroalkenes to give polyfluorobenzocycloalkenes (V. P. Mamaev).

The investigations of various classes of heterocyclic compounds have largely contributed to the development of theoretical ideas in organic chemistry and helped to solve the problems of producing novel compounds of practical value—pharmacological preparations, dyes, and intermediates for the synthesis of organic fine chemicals.

Chemistry of Organoelementary Compounds

A. N. Nesmeyanov defined organoelementary chemistry as organic chemistry extended to all elements. It has thus become an immense boundary region between organic and inorganic chemistry. Nesmeyanov notes that such boundary regions provide especially favourable soil for "growth points" of science.

Study of the first organometallic compounds was begun in the 1860s by A. M. Butlerov, A. M. Zaitsev, and E. Frankland with the development of organozinc synthesis. After Grignard had shown in 1900 the advantages of replacing zinc by magnesium, A. E. Arbuzov, N. D. Zelinskii, Zh. I. Iotsich, L. A. Chugaev, V. V. Chelintsev, V. S. Yavorskii, A. E. Chichibabin, and others conducted broad theoretical, experimental, and practical investigations on organomagnesium synthesis. In 1920 V. N. Krestinskii prepared isocrotylmagnesium bromide, and thus filled the gap in the sequence of magnesium derivatives differing in the degree of saturation of the carbon atom adjacent to the metal:

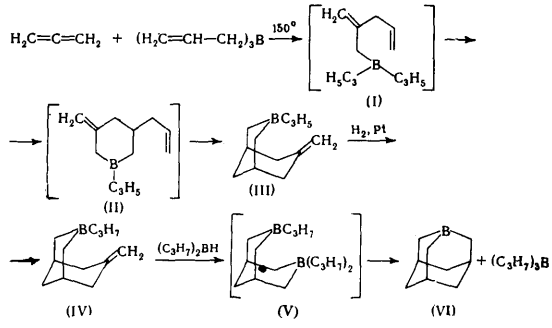
CH_3—MgX, RCH_2—MgX (Grignard) $R_2C{=}CH$—MgX (Krestinskii) $RC{\equiv}C$—MgX (Iotsich)

Theoretical work has developed since the 1920s, and questions have been posed for the first time on the structure and chemical nature of Grignard reagents (N. V. Kondyrev, A. P. Terent'ev) and on the structure of the intermediate products and the mechanism of organomagnesium reactions (A. E. Arbuzov, B. A. Arbuzov, M. I. Konovalov, A. D. Petrov, T. I. Temnikova, A. N. Pudovik). Universal methods of quantitative analysis using organic derivatives of magnesium were elaborated by L. A. Chugaev and F. V. Tserevitinov.

A new field—the chemistry of organic compounds of the alkali metals—grew from P. P. Shorygin's discovery of the formation of sodium alkyls. Methods of preparation, structure, and reactions of organolithium compounds have been studied systematically by K. A. Kocheshkov. This worker elaborated methods for obtaining organocalcium compounds, which are of interest as components of catalysts for the polymerisation of unsaturated hydrocarbons and oxiran derivatives.

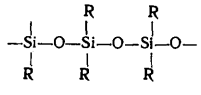
Nesmeyanov's discovery in 1929 of the diazo-method for preparing organomercury compounds started development of the chemistry of organic compounds of heavy metals (G. A. Razuvaev, M. M. Koton, O. A. Reutov, E. A. Shilov, I. P. Beletskaya, I. F. Lutsenko, Yu. K. Yur'ev, N. S. Zefirov).

Investigation of organic compounds of tervalent elements began with the preparation of aluminium and thallium derivatives by Nesmeyanov and Kocheshkov during the 1930s. The organic chemistry of aluminium and especially of boron has recently been intensively developed. New methods of synthesis and various reactions of organoboron compounds are being investigated by B. M. Mikhailov, L. I. Zakharkin, and O. Yu. Okhlobystin. Carborane derivatives are especially interesting as a promising basis for obtaining thermostable polymers. Spontaneous allylic rearrangement has been discovered in allylboron compounds. Condensation of acetylenic and allenic compounds with allylboranes is a new and effective method for the stereospecific synthesis of alicyclic compounds. The unique compound 1-boradamantane has been obtained, in which the boron atom is tetrahedral, in contrast to the usual boron trialkyls:



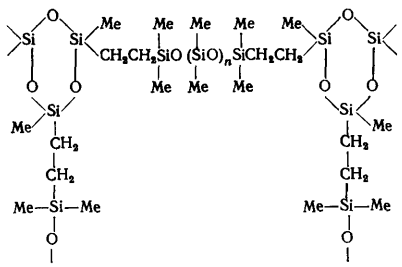
1-Boradamantane possesses several specific chemical and physical properties, in particular high complexing power with respect to various ligands, even those towards which boron trialkyls are inert. A new class of boron hydrides has been obtained—the borines—in which BH_3 is a functional group attached to a metal cation (V. S. Shpak).

The chemistry of silicon compounds had already attracted the attention of D. I. Mendeleev and A. M. Butlerov, the first to note the polymeric character of silicic acid. The ability to form polymers was a distinguishing feature of organosilicon compounds also. During the 1930s K. A. Andrianov first synthesised organosilicon polymers of the type

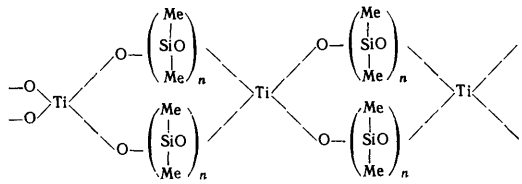


The interesting physicochemical properties of polyorganosiloxanes gave rise to numerous investigations in this

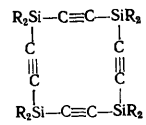
field. Hundreds of promising new compounds were obtained, e.g.



Recently efforts have been directed mainly at developing the preparation of new monomers of interest for obtaining polymers having specified properties—polysiloxanes of spirocyclic, spiral-staircase, and spirolinear structure, carbosilazanes, substituted vinylsilanes, organosilicon compounds containing other heteroatoms, e.g.

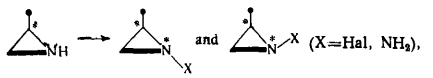


acetylenic silicon derivatives of the type



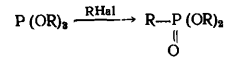
etc. The electronic interactions and special features of the silicon–heteroatom bond are being investigated, as well as the mechanisms and the kinetics of the reactions of organosilicon compounds and their biological activity (M. G. Voronkov). The chemistry of organic derivatives of the silicon analogues—germanium, tin, lead—is being explored.

Derivatives of Group V elements are being actively investigated. The long-standing stereochemical problem of synthesising systems with a non-inverting tervalent nitrogen pyramid has been solved in principle by the isolation of individual diastereomers of 2-substituted *N*-halogeno- and *N*-amino-aziridines (R. G. Kostyanovskii, Z. E. Samoilova, S. A. Giller):



Nitrogen in such compounds is comparable with the phosphorus atom in configurational stability.

The foundations of the chemistry of organic derivatives of phosphorus were laid by A. E. Arbuzov, who detected the rearrangement



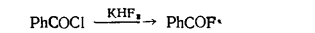
This became one of the chief methods for obtaining some classes of organophosphorus compounds. A new class of aromatic compounds containing a two-coordinated phosphorus atom has been discovered—the phosphadiazoles (A. I. Shvetsov-Shilovskii).

The biological activity of organophosphorus compounds is being studied, many of them finding application as medicinals and insecticides. The possibility of practical use as lubricants, plasticisers, and non-flammable polymers stimulates fresh synthetic exploration in this extremely important field of chemical science and practice.

The complex-forming properties of organophosphorus molecules are of great value, in particular enabling lead and beryllium to be removed from organisms. New principles have now been developed for enhancing the selectivity of organophosphorus complexing agents towards metal cations. Introduction into the molecule of fragments that fix sterically the orientation of donor atoms and the size of chelate rings yields highly efficient and selective new extractants, several of which are produced industrially and used in technical processes. Conditions have been worked out for introducing methylphosphonic groups at the nitrogen in triethylenetetramine and polyethylenimine to yield polymeric complexing agents.

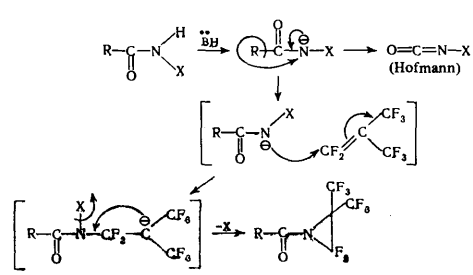
Organophosphorus ion-exchange resins have been synthesised. Methods are being sought for the directed synthesis of insecticides—derivatives of dithioic acids of phosphorus with peptide residues in the side-chain—which are relatively non-toxic to humans and animals, and do not leave toxic residues in the environment. New medicinals (diphenizide, hexaphosphamide, etc.) are being produced and introduced into clinical practice.

A young but vigorously developing field is the chemistry of organofluorine compounds, whose growth is due mainly to the work of I. L. Knunyants and his school (B. L. Dyatkin, L. S. German, Yu. A. Cheburkov, N. P. Gambaryan), N. N. Vorozhtsov, L. M. Yagupol'skii, A. Ya. Yakubovich, A. V. Fokin. In 1868 A. P. Borodin obtained the first fluorinated organic compound—benzoyl fluoride:



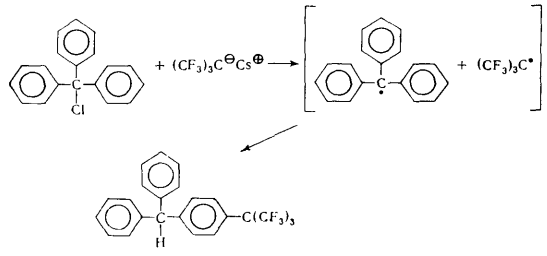
One of the chief general methods for introducing fluorine into an organic molecule—replacing a chlorine atom by fluorine by the action of a metal fluoride—was thus discovered. Fluorinated derivatives have now been obtained for almost all classes of organic compounds. Investigation of the structure, properties, and reactions of fluorinated organic compounds has introduced much that is new, often unexpected, into theoretical ideas in chemistry, and has had a widespread effect in experimental chemistry. Study of the nature of the π-bond in fluorinated alkenes, ketones, ketens, allenes, heterocumulenes, and aromatic compounds has led to the discovery of several unusual new rearrangements and reactions and to the synthesis of new types of compounds of practical importance.

The electronically amphoteric character of the double bond in fluoroalkenes is especially interesting, being responsible in several cases for reversal of the mechanism of addition of electrophilic and nucleophilic reactants. For example, the ability of fluoroalkenes to form anions under the influence of nucleophiles is used to intercept the hypothetical *N*-anion formed in the Hogmann, Curtius, etc. reactions:



The exceptionally strong basicity of the fluoride anion (e.g. in potassium and tetraethylammonium fluorides) in aprotic media has been observed for the first time. It greatly extends the opportunities for preparing various types of fluorinated organic compounds.

Great interest is taken in the chemistry of perfluorocarbanions, for whose study modern physicochemical methods are widely used. Thus the mechanism of the reaction of triphenylmethyl chloride with perfluoro-2-methylpropene in the presence of caesium fluoride, involving migration of the reaction centre, has been established from the variation in the concentration of the intermediate trityl radical measured by electron spin resonance:



Several new methods have been worked out for obtaining fluoro-organic compounds—concerted electrophilic addition to unsaturated systems in strong acids, anodic fluorination of aromatic compounds in organic solvents, and an industrial process for the direct fluorination of uracil to obtain 5-fluorouracil, an anti-tumour preparation —and hexafluorobenzene can be obtained from the more readily available hexachlorobenzene and potassium fluoride. A method has also been found for obtaining partly and completely fluorinated aromatic and heterocyclic compounds.

Processes have been developed for preparing compounds of types $Ar-ElF_n$ and $Ar-ElR_n^f$ (where El = Si, Ge, N, P, O, S, Se, I, Hg). In particular, compounds containing a pentacovalent iodine atom—aryl tetrafluoriodides—have been obtained for the first time.

The discovery and study of carbonyls of the metals—iron, nickel, and cobalt—preceded development of the chemistry of organic derivatives of transition metals. The discovery of ferrocene (dicyclopentadienyliron) began a new stage in organometallic chemistry—the study of sandwich compounds—for which the usual concepts of valency and coordination number have disappeared: here the atom of the transition metal is located between two rings, to which it is attached by a π-bond (Nesmeyanov and Razuvaev schools). Within a comparatively short time a detailed study of the reactivity of ferrocene had indicated its superaromatic character. Numerous substitutions in the cyclopentadienyl ring and reactions involving the iron atom gave rise to new classes of ferrocene compounds. Polymers based on ferrocene derivatives were obtained, including those containing silicon (A. D. Petrov, N. S. Nametkin, V. V. Korshak).

Physicochemical investigations of metallocenes were made by A. I. Kitaigorodskii, Yu. N. Sheinker, L. A. Kazitsyna, and the electronic structures of ferrocene and several other sandwich compounds were calculated by M. E. Dyatkina and E. M. Shustorovich. Cyclopentadienyl and cyclopentadienyl-carbonyl derivatives of manganese, rhenium, titanium, and other transition elements have been investigated. The chemistry of olefinic and acetylenic π-complexes of transition metals is represented by the work of Ya. K. Syrkin, B. A. Dolgoplosk, and I. I. Moiseev.

Complexes of transition metals find wide application in catalysis. Thus the compounds of graphite with low-valency palladium first obtained by M. E. Vol'pin proved to be promising catalysts for several organic reactions. A catalyst has been developed from allyl, acetate, and acetylacetonate complexes of palladium for chemical copper-plating in the manufacture of a self-cleaning foliated resin-impregnated laminated cloth for the printed circuits of high-speed electronic computers. Compounds of transition metals are used as catalysts for several novel reactions (synthesis of ammonia under mild conditions, synthesis of aromatic amines from hydrocarbons and molecular nitrogen, etc.). Lamellar compounds of graphite with several Group VIII transition metals, which are effective catalysts for the fixation of nitrogen and for the hydrogenation and isomerisation of alkenes and alkynes, have been obtained for the first time.

At the present time the chemistry of organoelementary compounds is developing along the lines of the synthesis of new compounds and fundamental research on their structure and reactivity as well as the mechanisms and the kinetics of the reactions.

Theoretical concepts are being shaped in the chemistry of organoelementary compounds. Thus the properties of organic compounds of Group V elements can be understood and predicted from the determination and calculation of the inversion barriers of the elements. In particular, a pyramidal configuration of nitrogen, phosphorus, and arsenic has been demonstrated in ethylenamines, acylphosphines, and acylarsines respectively, which disproves the long held view that they are completely analogous to ordinary amides (Kostyanovskii). During recent years a single system has been constructed for the $\sigma-\rho$ analysis of organophosphorus compounds, the electronic effects of substituents containing Groups IV–VI elements in the three-coordinated state have been studied, and quantum-chemical calculations have been made of certain specific molecules. A rebound mechanism has been suggested for the electrophilic isotope exchange of hydrogen in π-aromatic complexes of chromium and manganese. The structure of new types of compounds has been established by X-ray diffraction. Examination of the e.s.r. spectra of a number of organophosphorus radical-anions has proved unambiguously that the unpaired electron is delocalised over the substituents, and hence that the phosphorus atom is not an "insulating bridge" in the chain of conjugation (A. V. Il'yasov, Ya. A. Levin, I. D. Morozova).

E. I. Fedin developed research on the nuclear magnetic resonance spectra of organoelementary compounds under pulsed conditions (Fourier spectroscopy), which enabled spectra to be recorded not only at extremely low concentrations in solution but also for isotopes having a very small natural content (carbon-13, nitrogen-15, etc.) (Fig. 27). This produced a sharp increase in the information content of n.m.r. measurements in structural investigations and in study of the electronic characteristics of substituents. The SCAD phenomenon—statistically controlled association-complex diastereomerism—has been detected by Fourier $^{31}P-\{^1H\}$ n.m.r. spectroscopy. Thus a solution of unequal concentrations of enantiomeric phosphorus-containing depsipeptides exhibited a doublet of the phosphorus-31 signal with an intensity ratio equal to the concentration ratio of the enantiomers (Fig. 28) (M. I. Kabachnik, T. A. Mastryukova, E. I. Fedin). This unexpected phenomenon opens up, in particular, prospects of investigating the detailed causes of stereospecificity in the action of biologically active substances.

Bio-organic Chemistry

Research on peptides and proteins began with the work of N. D. Zelinskii and his school. Effective methods were found for resolving and analysing such materials, while α-amino acids were obtained by the amination of halogenated acids and by the cyanohydrin reaction. The further development of the chemistry of proteins and peptides in the USSR, as throughout the world, has become increasingly closely interwoven with physicochemical and biochemical investigations.

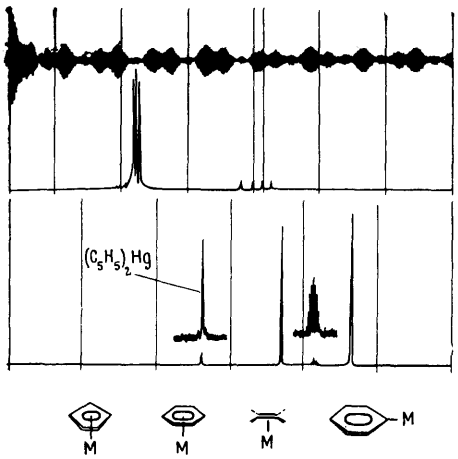


Figure 27. Fourier spectrum of ^{13}C n.m.r. with the natural content (1.1%) of the isotope.

Work on the chemical characteristics of complicated biopolymers has been directed at establishing the structure of glycoproteins (N. K. Kochetkov, V. A. Derevitskaya, E. D. Kaverzneva) and the primary structure of pepsin (V. M. Stepanov) as well as studying the biological role of enzymes (A. E. Braunshtein, V. N. Orekhovich, S. R. Mardashev, V. A. Belitser). Research is being undertaken with the aim of establishing effective new methods for analysing the primary structure of proteins and the sequence of amino-acid residues in peptides. The application of structural mass spectrometry (M. M. Shemyakin, Yu. A. Ovchinnikov, N. S. Vul'fson) has proved especially promising in this respect. Chromatographic procedures have been elaborated for separating and analysing complicated mixtures of amino-acids and methods for determining their optical purity (V. M. Belikov).

An important achievement has been the industrial production of the difficultly accessible hormone, insulin. A combined method has been worked out for separating the pituitary hormones (A. S. Khokhlov, F. Yu. Ryshka), and a technical synthesis of oxytocin and angiotensin (S. A. Giller, G. I. Chipen).

Methodical investigations are being made on the synthesis of amino-acids and peptides. A rapid new method has been suggested for obtaining polypeptides in aqueous medium without the isolation of intermediate products (D. G. Knorre), and also a new method of synthesising peptides on a polymeric carrier in solution (L. A. Shchukina). Priority is due to Soviet investigators in developing the chemistry of biologically important atypical peptides, in particular depsipeptides (M. M. Shemyakin, Yu. A. Ovchinnikov, E. I. Vinogradova). A new method has been discovered for synthesising linear and cyclic peptides and depsipeptides by the insertion of amino- and hydroxy-acyl groups into peptide systems (V. K. Antonov, A. M. Shkrob). The accumulation of empirical data deepens our understanding of the relation between the chemical structure and the biological character of peptides, which makes possible the directed synthesis of compounds having specified properties. During recent years extensive use has been made of physical methods in investigating polypeptides and proteins. Conformational analysis owes its progress to nuclear magnetic resonance (V. F. Bystrov), infrared spectroscopy (Yu. N. Chirgadze), optical rotatory dispersion, (V. T. Ivanov), X-ray diffraction (I. S. Andreeva, B. K. Vainshtein), and the combination of physicochemical methods with theoretical calculations (M. V. Vol'kenshtein, O. B. Ptitsyn).

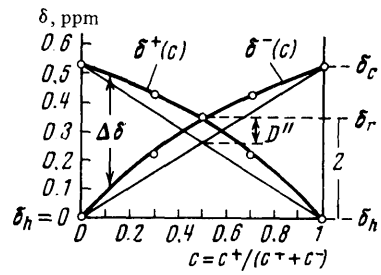
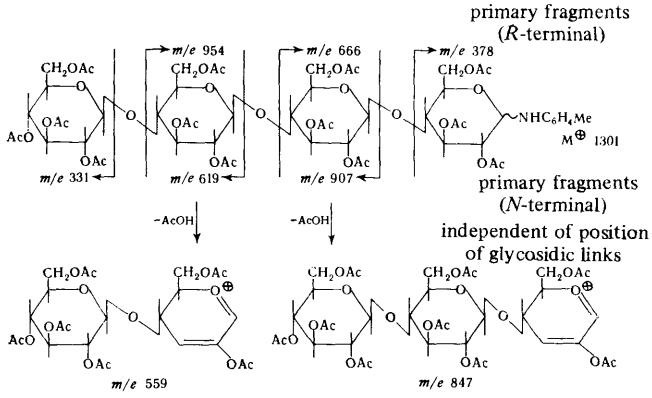


Figure 28. Dependence of ^{31}P chemical shifts (δ^+ and δ^-) of (+)- and (−)-ethoxymethylthiophosphinylthioglycolyl-valine on the concentration ratio $c^+/(c^+ + c^-)$.

The first work on the chemistry of nucleic acids included determination and comparison of the nucleotide composition of deoxyribonucleic acids in various lower and higher organisms, from which several characteristic features could be deduced (A. N. Belozerskii). A systematic search is being made for fundamental approaches to establishing the primary structure (i.e. the sequence of nucleotides), as yet in the simpler examples—transfer ribonucleic acids (A. A. Baev, D. G. Knorre). A promising way of studying the structure and functions of nucleic acids and their components is to modify them chemically, in particular with such specific agents as substituted hydroxylamines (N. K. Kochetkov, E. I. Budovskii). Compounds of nucleic acids with proteins are under investigation. Not only natural nucleoproteins but also model compounds with different types of amino-acid–nucleotide bond are being studied (M. A. Prokof'ev).

Development of the chemistry of carbohydrates in our country began with the work of P. P. Shorygin on the preparation of previously unknown cellulose ethers and esters, which was continued by A. E. Favorskii, S. N. Danilov, M. F. Shostakovskii, Z. A. Rogovin, N. I. Nikitin, M. M. Ushakov. Many studies were made of the degradation and oxidation of cellulose and other polysaccharides. The structure and the reaction mechanisms of starch, amyloses, glycogens, dextrans, etc. have been investigated. Much attention has been paid during the past two

decades to mono- and oligo-saccharides present in biologically important carbohydrate-containing polymers. Simple models of glycopeptides with various types of bonds have also been studied. The preparation and reactivity of carbohydrate phosphites and phosphinates—intermediates for the preparation of phosphorylated sugars—are being investigated (A. A. Petrov, E. E. Nifant'ev). Methods have been worked out for the synthesis of *C*-glycosides, in particular by applying the Wittig reaction to diverse phosphoranes (Yu. A. Zhdanov), and new methods of producing a glycosidic link (A. Ya. Khorlin, A. F. Bochkov, G. B. Elyakov). Effective methods are being developed for the structural analysis of carbohydrates. A mass-spectrometric method has been worked out for determining the sequence in oligosaccharides (see Scheme) (N. K. Kochetkov, O. S. Chizhov).



secondary fragments, the presence or absence of which depends on the position of the glycosidic links.

The chemistry of steroids has been investigated in the USSR since the 1930s, when M. I. Ushakov established the foundations of the synthesis of transformed steroids, in particular 6- and 16-methyl derivatives possessing strong physiological activity. The domestic manufacture of steroidal hormones based on cholesterol was established during the post-war period. In the 1950s work was begun in I. N. Nazarov's laboratory on a complete synthesis of steroidal compounds, and was developed by L. D. Bergel'son, I. V. Torgov, V. F. Kucherov, S. I. Zav'yalov, V. I. Maksimov. Microbiological and enzymatic transformations of steroids have been investigated by G. K. Skryabin and N. N. Suvorov.

Research on the synthesis of lipids has developed in several directions—the synthesis of natural fatty acids, the search for methods of synthesising glycerides and sphingolipids, and the synthesis of new types of phospholipids.

A thorough study of the most important branches of the chemistry of natural compounds enumerated above, together with the chemistry of antibiotics, vitamins, coenzymes, and alkaloids is being made in several institutes of the Academy of Sciences, among which the leading establishments are the Shemyakin Institute of Bio-organic Chemistry, Institute of Molecular Biology, Bakh Institute of Biochemistry, Protein Institute, Institute of Biological Physics, and Institute of the Biochemistry and the Physiology of Micro-organisms.

Systematic chemical and medico-biological investigations in the USSR resulted in the establishment of the present-day antibiotics industry, which produces all the most important antibiotics. Among the most significant chemical investigations on antibiotics are the discovery of chloramphenicol and its derivatives with the establishment of their structure (Shemyakin), the synthesis of cycloserine and study of the mechanism by which it functions (N. K. Kochetkov, R. M. Khomutov, M. Ya. Karpeiskii), determination of the absolute configuration of tetracyclines (M. N. Kolosov, A. I. Gurevich), elaboration of methods for the synthesis of penicillins and their analogues (I. L. Knunyants, I. T. Strukov, S. A. Giller), and general methods for separating mixtures of streptothricins (Khokhlov).

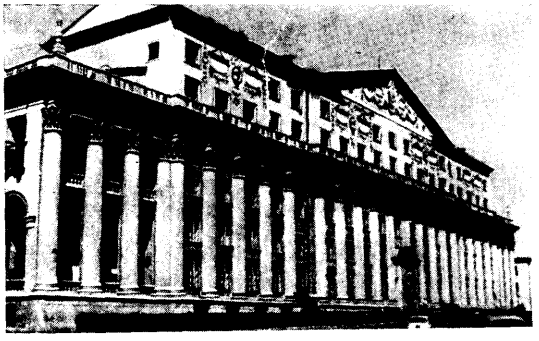
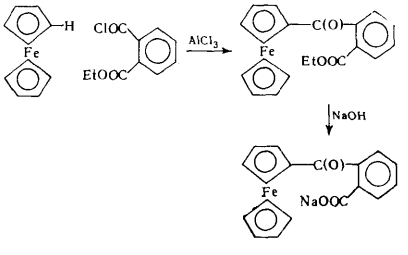


Figure 29. Shemyakin Institute of Bio-organic Chemistry of the USSR Academy of Sciences.

Studies of the chemistry of alkaloids, first begun by A. E. Chichibabin, were extended under the direction of A. P. Orekhov, N. A. Preobrazhenskii, A. S. Sadykov, S. Yu. Yunusov.

The complete structure has been determined for an important enzyme—the cytoplasmic aspartate aminotransferase from porcine heart muscle—containing 412 amino-acid residues (Fig. 30). This enzyme is one of the largest proteins whose structure has been deciphered (Ovchinnikov).

The achievements in the chemistry of natural compounds, together with advances in the organic chemistry of the most diverse classes of compounds, form the basis for such an important branch as the chemistry of medicinals and biologically active compounds. Among various new medicinal preparations mention must be made of ferroceron for the treatment of illnesses associated with an iron deficiency in the organism, e.g. iron-deficient anaemia of various aetiologies, ozaena, and paradentosis (A. N. Nesmeyanov). The active principle of ferroceron—sodium *o*-ferrocenylcarbonylbenzoate—is obtained by acylating ferrocene with ethyl *o*-chloroformylbenzoate:



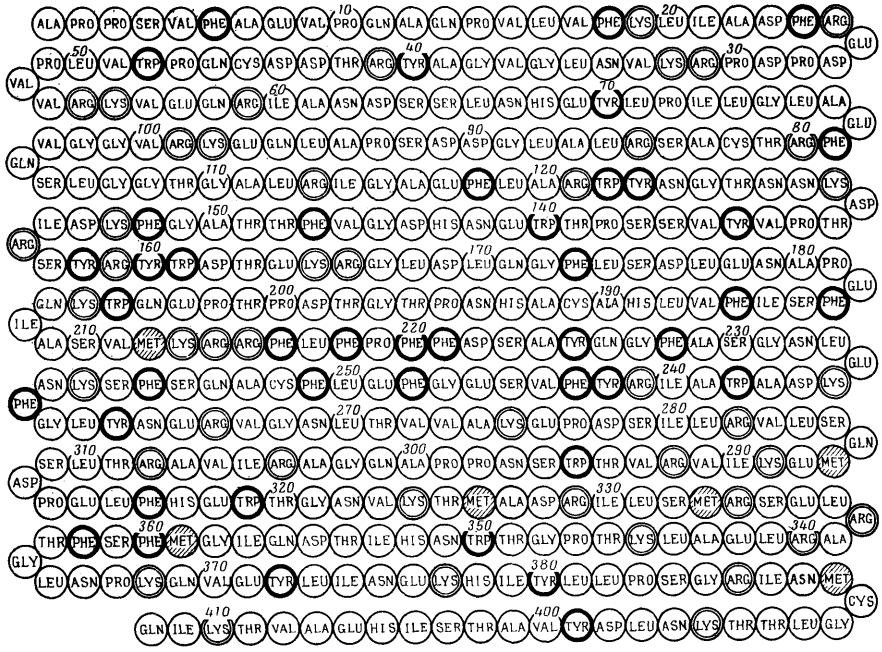


Figure 30. Amino-acid sequence of cytoplasmic aspartate aminotransferase from porcine heart muscle.

On Nesmeyanov's initiative the scientific foundations are being laid for the synthesis of artificial food—chemical and microbiological methods for the production of amino-acids, peptides, and proteins, research on the chemistry of odour and taste, study of the principles underlying the production of new types of foods. Recent years have seen the development of a convenient synthesis of DL-tryptophan by the cathodic reduction of indolylnitro-acrylates and their saturated analogues, conditions for the asymmetric synthesis of α-amino-acids in the proton exchange of racemic amino-acids on complex formation with metals of variable valency, and a synthesis of DL-glutamic acid, used as a flavouring agent (Belikov).

Convenient syntheses have been worked out for heterocyclic compounds of various structures, such as imidazolines, hydroxyhydropyrimidines, and dihydrotriazines, which are of interest with respect to their physiological activity (S. V. Rogozhin).

Petroleum Chemistry

Research on the chemistry of petroleum is associated with the names of D. I. Mendeleev, V. V. Markovnikov, N. D. Zelinskii, A. E. Favorskii, F. F. Beil'shtein [Beilstein], M. I. Konovalov, S. V. Lebedev, V. N. Ipat'ev, A. V. Topchiev, I. M, Gubkin, S. S. Nametkin. During the 1870–1890s Mendeleev studied Russia's oil-bearing deposits, foreseeing in petroleum an extremely valuable raw material for the production of organic compounds. He was the first to pose the question of the utilisation of natural gases, and put forward the idea of the subterranean gasification of coal. From the 1880s Markovnikov undertook a systematic study of petroleum, and proposed the name "naphthenes" for one of the types of hydrocarbons originating from petroleum. He isolated and identified many individual compounds, and studied their chemical and physical properties in comparison with model compounds. Zelinskii made many investigations on the interconversion of hydrocarbons, developed methods for the preparation of various compounds from petroleum raw material, and put forward a theory of the organic origin of petroleum.

Nametkin made investigations on the chemistry and technology of petroleum and natural gas. He elucidated a single mechanism for the nitrating and oxidising action of nitric acid on aliphatic and mono- and bi-cyclic hydrocarbons, studied the addition and the detachment of the elements of water and hydrogen halides to and from bicyclic compounds, as well as isomerisations of camphenic compounds, discovered the rearrangement bearing his name, and investigated the stereochemistry of mono- and bi-cyclic systems. Nametkin studied the composition of combustible natural gases and petroleums from various deposits, and investigated the chemical nature of solid hydrocarbons (paraffins and ceresins). He made various studies of oxidative cracking, catalytic aromatisation, the isomerisation of butenes into 2-methylpropene, and many other topics. He worked out valuable methods for analysing aromatic hydrocarbons, unsaturated hydrocarbons in gasolines produced by cracking, sulphur-containing compounds, and other compounds.

At the beginning of the century work on petroleum chemistry was conducted in college laboratories, mainly in Moscow University. The early years of the Soviet régime saw the foundation of specialised petroleum institutes, in which were elaborated the principles of several new manufacturing processes—the production of phenol and acetone, oxiran and methyloxiran, organic acids, alcohols, etc.—based on petroleum chemistry. The Moscow Petroleum-processing Works (directed by D. V. Ivanyukov) plays an important role in the introduction of new petroleum-chemical processes.

The main lines of development of petroleum chemistry are determined by the diverse tasks of present-day petrochemical production—study of the composition and properties of petroleums, establishment of scientific foundations for their processing and the production of various monomers, polymeric materials, synthetic rubber and fibres, surface-active agents and detergents, and solvents, and the synthesis of valuable chemical materials based on hydrocarbons. A large volume of research has been devoted to studying the composition of petroleums from different deposits (P. I. Sanin, A. F. Plate, G. D. Gal'pern, A. D. Petrov). Principles of a scientific classification of petroleums–combining chemical, geochemical, and technical aspects of the problem—have been formulated (A. A. Petrov, G. P. Kurbskii).

Hundreds of different hydrocarbons originating from petroleum have been identified. Chromatographic methods have been worked out for separating complex hydrocarbon mixtures, and also methods for isolating hydrocarbons having a certain structure. Many-sided investigations have been made of the interaction of complex compounds of metals of variable valency with hydrocarbons and non-hydrocarbon compounds of petroleum, which resulted in the suggestion of an original method for improving the quality of petroleum products (N. S. Nametkin).

A photochemical procedure has been worked out for isolating ash-forming elements from petroleums and petroleum products from various deposits in Georgia. It was shown that polycyclic aromatic hydrocarbons can sensitise the photochemical oxidation of naphthenes in mineral oils.

Organoelementary compounds present in petroleums—primarily organosulphur compounds (R. D. Obolentsev)—have been investigated. Yu. K. Yur'ev undertook the synthesis and spectroscopic examination of the many model thiolans required for the identification of those in sulphurous petroleums in the USSR. Studies have been made of the reactions involving cleavage of the thiophen and thiolan rings, which underly the industrial desulphurisation of petroleums.

A study has been made of the processes involved in pyrolysis, which is the chief industrial method for obtaining the main products—unsaturated and aromatic hydrocarbons—of petrochemical synthesis. In particular, a kinetic investigation has been made of the pyrolysis of alkanes in mixtures with alkenes, naphthenes, and alkylated arenes. The use of labelled atoms has enabled the dependence of the hydrogen concentration on the composition of the pyrolysable mixtures to be determined, and the elementary acts governing the interaction of hydrocarbons during pyrolysis to be elucidated (K. P. Lavrovskii, R. A. Kalinenko). Research is being conducted on a combined scheme for processing the liquid products of pyrolysis, involving the isolation of cyclopentadiene, methylcyclopentadiene, and aromatic hydrocarbons, together with the production of polymeric resins. A rapid process of thermal-contact pyrolysis has been elaborated which permits the efficient processing of all petroleum products, including crudes.

Carrying out chemical reactions in a plasma jet at 2000–3000°C is a promising method for obtaining several important petrochemical products (L. S. Polak). The topics studied in the field of plasma chemistry have been expanded significantly during recent years. The scientific foundations of a plasmachemical technology have been worked out—the production of acetylene and technical hydrogen from natural gas, unsaturated hydrocarbons from benzine and crude petroleum, and synthesis gas for the manufacture of vinyl chloride. These processes are in industrial operation at several chemical concerns.

The fundamental investigations by N. D. Zelinskii, B. A. Kazanskii, A. A. Balandin on the catalytic conversion of hydrocarbons formed the basis for a theory of hydrogenation and dehydrogenation catalysis and for introducing many reactions into practice. Highly efficient and selective catalysts have been developed, in particular for the hydrodemethylation of toluene and the dehydrocyclisation of hexane to produce benzene, and for the dehydrogenation of ethylbenzene to styrene. Mechanisms of the dehydrocyclisation of C_6–C_8 alkanes and alkenes have been studied. Processes of dehydrocondensation in the catalytic formation of resinous and carbonaceous products have been investigated (M. G. Gonikberg, M. I. Rozengart, I. I. Brusov, G. M. Marukyan, G. V. Isagulyants).

An economic process has been developed for the production of butadiene by the single-stage dehydrogenation of butane on an alumina–chrome catalyst (O. D. Sterligov). A palladium–zeolite catalyst has been developed for the isomerisation of hydrocarbons, a zeolite catalyst for the alkylation of benzene by alkenes, and catalysts containing added rare-earth metal oxides, which accelerate hydrogenation and dehydrogenation but produce no skeletal isomerisation (Kh. M. Minachev).

Research is being conducted on the use of π-allyl complexes of transition metals as polymerisation catalysts. Original catalytic systems have been created for the synthesis of *cis*-1,4-polybutadiene. New opportunities for stereospecific catalysis have been opened up. In order to obtain valuable chemical products, in particular novel monomers, broad investigations are being made on the dimerisation, codimerisation, oligomerisation, and co-oligomerisation of unsaturated hydrocarbons in the presence of combined catalysts (B. A. Dolgoplosk, B. A. Krentsel', G. A. Tolstikov, V. M. Vdovin, V. S. Aliev, M. M. Kaliberdo, V. S. Gutyrya).

New homogeneous catalysts, based on complexes of ruthenium, rhodium, palladium, and cobalt, have shown high selectivity: for example, it has been possible to hydrogenate *cis*-penta-1,3-diene to *trans*-pent-2-ene. Catalysts have been prepared comprising organometallic complexes of transition metals fixed to various carriers, including graphite (M. E. Vol'pin, B. A. Dolgoplosk, Yu. I. Ermakov).

Methods for the preparation of functional derivatives of hydrocarbons, especially oxygen-containing compounds, are being investigated. The principle of controlling liquid-phase oxidation by introducing so called stop-reagents—substances that convert reactive intermediates into compounds resistant to oxidation—has been developed (A. N. Bashkirov, V. V. Kamzolkin).

A combined study of the mechanisms of reactions occurring on fused iron catalysts, together with elucidation of the properties of the intermediate surface compounds, has enabled several catalytic syntheses to be predicted and accomplished (A. N. Bashkirov, Yu. A. Kogan, A. Ya. Rozovskii).

An industrially promising method—oxidative ammonolysis—for the preparation of nitrogen-containing derivatives of hydrocarbons has been applied to toluene, xylenes, pseudocumene, durene, and chlorinated hydrocarbons (S. D. Mekhtiev). A proposed process for obtaining acrylonitrile involves oxidative ammonolysis of propene on a fluidised catalyst bed (Institute of Catalysis of the Siberian Division of the USSR Academy of Sciences).

A series of comparative studies have been made of the chemistry of cyclic and unsaturated hydrocarbons and of silico-hydrocarbons. Besides broadening our views on the reactivity of these analogues, these investigations led to the production of interesting new materials, showing promise for use in the petrochemical and metallurgical industries as well as in several other branches of the national economy (N. S. Nametkin).

A petrochemical development is the chemistry of additives for improving the cleansing, dispersing, anti-wear, and other properties of motor and special oils (P. I. Sanin, A. M. Kuliev). A polymeric additive has been produced to ensure that high-alkane petroleums can be pumped through pipelines (V. P. Mamaev).

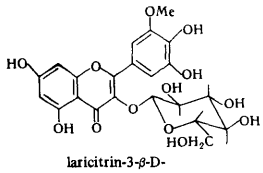
Chemistry of Wood

Significant results have been obtained in wood chemistry during recent years. The validity of regarding wood as a cross-linked polymer has been demonstrated. The number of cross-links in the cell walls of wood explains the changes in its properties and structure, which opens up the possibility of a purposeful variation in its properties.

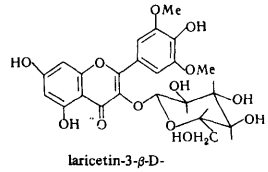
Phenolic phenylpropene compounds having a sulpho-group in the side-chain have been investigated as models of structural fragments of ligninsulphonic acids. The presence of the sulpho-group in this position is shown to stabilise the C_6–C_3 structural fragment of lignin. A procedure has been developed for preparing combined organic and mineral fertilisers based on hydrolytic lignin.

Application of salts of metals of variable valency permits controlled variation of the supermolecular structure and reactivity of cellulose (Institute of Physical Organic Chemistry of the Belorussian SSR Academy of Sciences). A technology is being worked out for a new nitric-acid method for obtaining cellulose, with use of the waste products as nitrogen-containing organic–mineral fertilisers. Fresh data have been obtained indicating that this method is promising for practical application.

Investigation of the interaction of levoglucosan with various di-isocyanates has shown that the hydroxypropylated material is suitable for the production of rigid polyurethan foams (Institute of Wood Chemistry of the Latvian SSR Academy of Sciences). Phenolic compounds from the needles, bark, and wood of conifer species of Siberia and the Far East have been studied. Two new compounds of the flavonoid series



laricitrin-3-β-D-glucopyranoside



laricetin-3-β-D-glucopyranoside

have been isolated from larch needles; they are of fundamental value for constructing a scheme of biogenesis for substances of this type (Irkutsk Institute of Organic Chemistry of the Siberian Division of the USSR Academy of Sciences).

Chemistry of Solid Fuels

M. V. Lomonosov, in his work "O sloyakh zemnykh [On the Earth's Strata]", formulated for the first time the view that coal is formed in stages from extinct plants, which have undergone the most complicated physicochemical transformations from wood through peat and lignite to coal.

An active part in establishing a science of fuel was taken by D. I. Mendeleev, V. V. Markovnikov, V. I. Vernadskii, N. D. Zelinskii, I. M. Gubkin, S. S. Nametkin, N. P. Chizhevskii, A. A. Skochinskii, Yu. A. Zhemchuzhnikov, N. M. Karavaev, A. B. Chernyshev, G. L. Stadnikov, A. F. Dobryanskii, and many others. The Committee on the Chemistry of Coal Tar and Coke, organised by the Academy of Sciences, did great work under the direction of A. E. Porai-Koshits and N. M. Karavaev. This Committee not only directed experimental work aimed at providing the growing organic synthetic industry with a continuous supply of raw material but also participated directly in studying the processes at undertakings with the aim of increasing the range of chemical products for organic synthesis based on the processing of coal.

An industrial classification of coals was worked out. The vast factual information that had accumulated on the qualitative characteristics of coals enabled native varieties to be differentiated according to their properties into power fuel for electrical generating stations and raw material for the production of high-quality coke with chemical products and materials (A. B. Chernyshov, N. G. Titov).

Studies were made on the possibility of expanding the raw-material base of coking by using abundant feebly coking coals. A theory of the formation of coke from mixtures of coals was put forward. L. M. Sapozhnikov's work on the thermal decomposition of coals and the formation of a plastic mass of carbon changed radically the view held on the effect of extreme temperatures, pressure, and oxidising and reducing media on structural changes in carbonaceous materials.

Theoretical researches were made on the genesis of coals, as a result of which new views were established on the nature of the geobiochemical processes involved in the transformation of plants into coal. A chemical theory was proposed for the formation of bogheads and the mixed humus–sapropelite origin of coals (Stadnikov). The petrological examination of coals has settled a wide range of questions concerning the classification and marking of coals, as well as the choice of raw material for industrial processing (Yu. A. Zhemchuzhnikov, I. L. Amosov, I. V. Eremin).

A fundamental scheme for the polymeric structure of the main organic substance in coals has been elaborated. It permitted generalisation of the concept of humic substances as monomeric molecular structures with fused aromatic rings and polyfunctional lateral substituents (V. I. Kasatochkin, L. L. Nesterenko). Great attention is paid to the thermal processing of coals, and catalytic methods for the hydrogenation and oxidation of hydrocarbons typical of the composition of fuels.

A procedure developed for the simultaneous hydrogenation of coal and a high-sulphur petroleum enables up to 50% of boiler fuel to be obtained with considerable quantities of motor fuel, phenols, benzene, and other chemical products (A. V. Lozovoi, A. A. Krichko). Promising methods have been studied for processing coals, peat, and bituminous shales by oxidation in alkaline medium with the production of various di- and poly-carboxylic acids (T. A. Kukharenko, A. S. Fomin).

The physicochemical and in particular thermodynamic investigation of the high-temperature processing of solid fuel led to an original method for the so called power-technical and power-chemical processing of fuel (A. B. Chernyshov, Z. F. Chukhanov). Chizhevskii carried out research with the aim of expanding the coal base of coking, and proposed an original design of coke-ovens.

Study of the distribution of rare elements and non-ferrous metals led to the so called "affinity series"

$$Ge > W > Ga > Be > Nb > Mo > Sc > Y > La > Zn$$

of these elements with respect to the organic matter in solid fossil fuels.

Processes have been worked out for obtaining a light porous filler (agloporite) for concrete by the heat-treatment of coal at 1100–1200°C.

The ion-exchange properties of peat can be increased by factors of 2.5–3 by oxidative degradation (N. I. Mitskivich, P. I. Bel'kevich, L. R. Chistova). The ammoniation of peat increases its moisture content, while its filtering power is diminished by factors of 10–15 (A. V. Tishkovich). Karavaev has completed many years of work on establishing the foundations of a general classification of fossil fuels.

Macromolecular Compounds

The chemistry of compounds of high molecular weight was founded as an independent branch at the beginning of this century. The concept of macromolecular substances as an important class of chemical compounds was due mainly to organic chemists. Research in this field began with the work of A. M. Butlerov, I. L. Kondakov, I. P. Ostromyslenskii, and P. P. Shorygin.

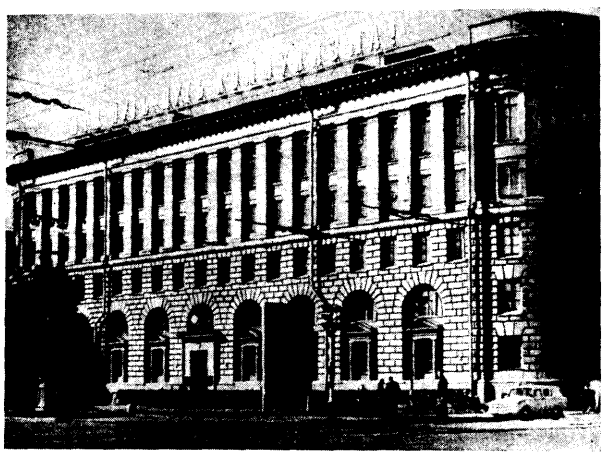


Figure 31. Institute of Macromolecular Compounds of the USSR Academy of Sciences.

S. V. Lebedev developed an industrial process for obtaining synthetic rubber based on butadiene. The study of polycondensation and polymerisation laid the foundations for the industrial production of phenol–formaldehyde resins, organosilicon polymers, synthetic rubbers, polymerisable oligomers, polymers for synthetic fibres, and other polymeric materials. Development of the science of polymerisation and isomerisation governed the growth of many branches of the chemistry of the monomers.

A. E. Favorskii, I. N. Nazarov, M. F. Shostakovskii suggested methods for obtaining ethynylvinylmethanols and vinyl ethers. These monomers have found wide application for the manufacture of various polymers and copolymers (adhesives, plasticisers, medicinals). K. A. Andrianov discovered convenient methods for the preparation of orthosilicic esters, and was the first to obtain polyorganosiloxanes, which have been widely used for the production of thermostable polymers employed for the thermal and electrical insulation of various articles, and the production of lubricants, plastics, rubbers, paints, and varnishes. Phosphorus-containing compounds (A. E. Arbuzov, B. A. Arbuzov, A. N. Pudovik, M. I. Kabachnik), organofluorine compounds (I. L. Knunyants), and various organoelementary compounds (A. N. Nesmeyanov) have been widely used for obtaining polymeric materials.

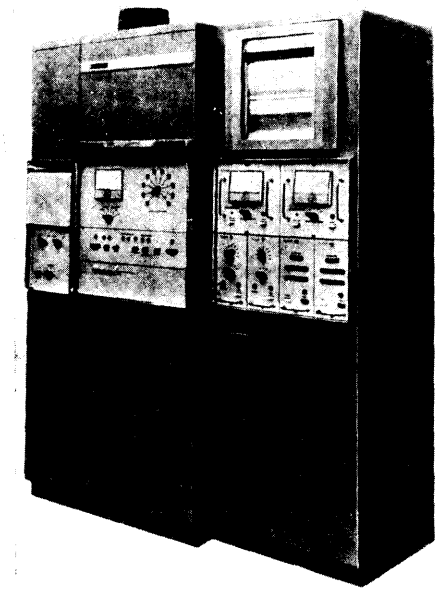


Figure 32. Automatic liquid chromatograph KhZh-1303 for determining molecular-weight distribution of polymers, developed by the Special Design Office of Analytical Instrumentation of the USSR Academy of Sciences and by the Institute of Macromolecular Compounds of the USSR Academy of Sciences.

The relations between the chemical structure and the reactivity of monomers have been studied. A new line of research began in the early 1960s, based on the possibility of varying the reactivity of monomers by complexing them with various substances. Investigations in this field, started by V. A. Kargin and V. A. Kabanov, offer the prospect of simulating the biosynthesis of polymeric compounds. The mechanisms of polymerisation and polycondensation have been investigated.

A theory of radical polymerisation and copolymerisation has been elaborated (S. S. Medvedev, Kh. S. Bagdasar'yan, A. D. Abkin). The kinetics and the mechanism of the redox initiation of chain polymerisation have been investigated (B. A. Dolgoplosk, E. I. Tinyakova), as well as the activation of radical polymerisation by complexing agents (V. A. Kargin, V. A. Kabanov, V. P. Zubov, E. B. Milovskaya, and others). Research on the elementary processes in the radical polymerisation of vinyl monomers and the cationic polymerisation of formaldehyde and oxirans led to the discovery of chain transfer (Medvedev) and of chain transfer with rupture (N. S. Enikolopov). These processes permitted control of the molecular weight, the molecular-weight distribution, and the structure of the polymers, and also enabled telomerisation to be accomplished (A. N. Nesmeyanov, R. Kh. Freidlina).

Broad investigations have been made of the uninhibited and inhibited heterophase polymerisation of polyfunctional monomers and oligomers to high degrees of conversion (G. P. Gladyshev, G. V. Korolev, N. N. Tvorogov). This work created a scientific basis for the industrial production and modification of several polymeric materials.

The influence of the supermolecular organisation of polymerising compounds on the kinetics of their conversion into chain and network polymers has been examined. Thus activation of the radical and ionic polymerisation of acrylic monomers and oligomers, due to a favourable arrangement of double bonds in liquid-crystalline and associated molecular aggregates of the liquid phase, has been detected and investigated (B. A. Krentsel', Yu. B. Amerik, N. N. Tvorogov, T. E. Lipatova), as well as in the crystallisation of monomers (V. A. Kargin, N. N. Semenov, V. A. Kalbanov, and others).

Work on polymerisation under extreme conditions has opened up a new line of research in the chemistry of polymerisation processes. Yu. S. Zaslavskii, A. A. Berlin, R. N. Zaslavskii, and M. I. Cherkashin investigated the polymerisation of various monomers and oligomers under the influence of friction, leading to the formation of polymer films which greatly diminished wear of the rubbing surfaces. N. S. Enikolopov and A. A. Zharov studied polymerisation under ultra-high pressure with shear. Work has been done on polymerisation in shock waves.

The mechanism of cationic polymerisation was first discussed by M. D. L'vov, G. G. Gustavson, and I. L. Kondakov at the end of the nineteenth century. S. S. Medvedev, A. R. Gantmakher, B. L. Erusalimskii investigated the mechanisms of the polymerisation of many unsaturated compounds in the presence of cationic catalysts, and in particular revealed the role of alkene–catalyst π-complexes. Specific aspects of the cationic polymerisation of rings appeared in papers by N. S. Enikolopov, S. G. Entelis, E. B. Lyudvig, and others.

Work on anionic polymerisation was begun by Lebedev, who made use of observations by A. A. Krakau and I. L. Kondakov that polymerisation might be accomplished in the presence of metallic sodium. The labours of S. S. Medvedev, A. R. Gantmakher, A. A. Korotkov, B. L. Erusalimskii elucidated many aspects of the kinetics and the mechanism, and established the effect of the nature of the alkali metal on the composition and structure of the polymers.

Studies of ionic telomerisation (A. A. Petrov, A. L. Klebanskii, M. F. Shostakovskii) yielded valuable products finding industrial application as polymeric materials.

Stereospecific polymerisation was studied by S. S. Medvedev, A. A. Korotkov, A. V. Topchiev, B. A. Dolgoplosk, E. I. Tinyakova, N. M. Chirkov, B. A. Krentsel', G. A. Razuvaev. The role of cobalt and titanium compounds in composite catalysts was established, and several novel catalytic systems were suggested, including π-allyl complexes for the polymerisation of diene hydrocarbons.

K. A. Andrianov, V. V. Korshak, S. R. Rafikov, L. B. Sokolov, S. V. Vinogradova made series of investigations on the mechanism of equilibrium and non-equilibrium polycondensation, revealing the effects of excess of reactants, simultaneous reactions, and experimental conditions on the mean molecular weights and the molecular-weight distribution. Berlin investigated the polycondensation of diols, polyols, and dibasic acids (or their derivatives) in the presence of unsaturated monobasic acids, and from the results worked out a general synthesis of polymerisable acrylic oligomers with terminal or regularly repeating reactive groups (condensation telomerisation). This work formed the scientific basis for the industrial production of several high polymers (polyamides, polyesters) and polymerisable oligomers (oligo(ether–acrylates) and their analogues).

The mechanism and the kinetics of the polyaddition of di-isocyanates to diols to form polyurethans have been studied (Yu. L. Spirin, T. E. Lipatova, S. G. Entelis, and others).

The development of such methods for synthesising polymers as oxidative dehydropolycondensation, polydiazotisation, polycoordination, polycyclisation, etc. led to the production of highly thermostable polymers having a system of conjugated aromatic and heterocyclic rings and exhibiting semiconductor and catalytic properties (V. V. Korshak, A. M. Sladkov, B. A. Krentsel', B. E. Davydov, Ya. M. Paushkin, I. L. Kotlyarevskii, A. A. Berlin, B. I. Liogon'kii, M. I. Cherkashin).

Among work promoting the industrial production of polymeric compounds and materials based on them mention must be made of investigations on the polymerisation of ethylene associated with the names of V. N. Ipat'ev, M. S. Nemtsov, A. I. Dintses, establishment of scientific principles for the manufacture of polypropylene (A. V. Topchiev, N. M. Chirkov, B. A. Krentsel'), and the production of Soviet synthetic rubbers (B. A. Dolgoplosk, A. I. Yakubchik, A. A. Korotkov, V. F. Evstratov).

Research aimed at obtaining poly(vinyl chloride) was initiated in our country by Ostromyslenskii in 1912. Development of this work led to organisation of the industrial production of polymers and copolymers of vinyl chloride. The work of S. M. Ushakov and P. P. Shorygin stimulated the industrial manufacture of polystyrene and poly(vinyl acetate), while the studies by G. S. Petrov mentioned above formed the basis for the production of phenol—formaldehyde and urea—formaldehyde resins and plastics. The industrial production of polyamides and aromatic polyesters is based on investigations by V. V. Korshak, I. L. Knunyants, Z. A. Rogovin, A. N. Nesmeyanov, R. Kh. Freidlina, A. A. Strepikheev, and others.

Compositions of oligomers with raw rubbers and thermoplastics were developed which enabled new industrial methods to be established for obtaining and modifying cured rubbers, elastomers, reinforced plastics, coatings, sealants, and other polymer materials (A. A. Berlin, A. S. Kuz'minskii, G. N. Petrov, I. S. Al'shits, M. S. Akutin, I. Ya. Kaplunov, and others).

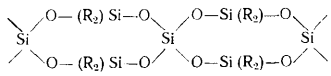
Study of the mechanochemistry of block and graft copolymerisation and reactions in the polymer chains laid the foundations for the industrial manufacture of highly impact-resistant polystyrene and poly(vinyl chloride), modified cellulosic fibres and cloth, and several other polymeric materials. Advances in the vulcanisation of

elastomers were due to original investigations by B. P. Zhukov, B. A. Dogadkin, and others.

A new field of polymer science—the chemistry of conjugated polymers—was opened up. Specific aspects of the supermolecular organisation and properties of these polymers were revealed, and the presence was demonstrated of low-lying triplet levels and paramagnetic centres influencing their reactivity and electrophysical properties (A. A. Ovchinnikov, L. A. Blyumenfel'd, A. A. Berlin, and others). The practical importance of these polymers is due to their use as photosensitive materials, organic semiconductors, inhibitors of the high-temperature degradation of elastomers and rigid-chain polymers, structural modifiers, and starting points for obtaining highly thermostable plastics.

Organosilicon polymers have acquired especial value among organoelementary polymers because of their astonishing combination of useful properties, high heat and frost resistance, excellent dielectric characteristics, good adhesive properties, absence of toxicity, etc. In 1937 Andrianov obtained the first patent in the world for the practical application of organosilicon compounds, and in 1940 he developed an industrial method for obtaining silicon tetrachloride—the most important starting material for the synthesis of polysiloxanes—by the reaction of chlorine with 35–65% ferrosilicon at 200°C. The mechanism of the formation of substituted orthosilicic esters was studied. Choice of a progressive technical procedure for obtaining organochlorosilanes in a fluidised bed enabled the large-scale industrial manufacture of methyl-, ethyl-, and phenyl-chlorosilanes to be organised.

The products of the simultaneous hydrolysis of di- and tri-functional organochlorosilanes were regarded as having a cyclolinear structure. The cohydrolysis of organochlorosilanes with aluminium chloride in alkaline media was used to obtain polyorganoaluminosiloxanes. Organospirocyclosiloxanes with the organosiloxane groups occupying a specified position in the spirocyclic ring



were prepared. Manufacture of a large range of organosilicon monomers and polymers was set up.

Study of the degradation and stabilisation of polymers was begun by S. V. Lebedev, B. A. Dolgoplosk, G. A. Razuvaev, V. A. Kargin, M. B. Neiman, A. S. Kuz'minskii. Kinetic investigations of the aging and stabilisation of polymers have been made by A. L. Buchachenko, G. P. Gladyshev, E. T. Denisov, V. V. Ershov, G. E. Zaikov, V. B. Miller, E. G. Rozantsev, D. Ya. Toptygin, V. Ya. Shlyapintokh, Yu. A. Shlyapnikov, and others. Studies have been made of the kinetics of oxidative degradation, the action of various stabilisers on the oxidation of polymers, and the synergic effect of several inhibitors. It has been discovered that chemical compounds that react rapidly with oxygen (or free radicals) to form inert products are able, when generated in polymer compositions or articles (as a result of the transformation of inert substances), to stabilise the polymeric materials against oxidative and/or thermal degradation at 300–400°C and above (Fig. 33).

Various iminoxyl radicals have been prepared which are widely used as "labels" and have proved effective stabilisers for several polymers. Work is being conducted on modifying the polymers to prolong the "life span" of polymeric compositions (N. S. Enikolopov, S. R. Rafikov, Z. A. Rogovin, Kh. U. Usmanov, N. A. Plate, and others).

The first investigations on the physical chemistry of polymers were aimed at studying their mechanical properties taking into account relaxation phenomena accompanying deformation and fracture. The results formed the basis of the contemporary physical chemistry of polymers (A. P. Aleksandrov, P. P. Kobeko, Yu. S. Lazurkin, V. A. Kargin, G. L. Slonimskii, M. V. Vol'kenshtein, S. E. Bresler, S. Ya. Frenkel', E. V. Kuvshinskii, G. I. Gurevich).

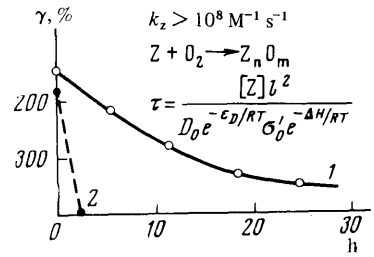


Figure 33. Stabilisation of thermostable polymers—variation in relative elongation at rupture for cured rubber based on SKTV-2 when aged in air (350°C): 1) stabilised specimen; 2) control.

The usual concepts valid for solutions of compounds of low molecular weight are shown to apply also to solutions of polymers. V. N. Tsvetkov investigated the latter in order to obtain information on the structure and conformation of the soluble molecules. A. A. Tager, V. P. Zubov studied the thermodynamics of the solutions, swelling, plasticisation, and gel formation. Research on the rheology of polymers was begun and developed by P. A. Rebinder and G. V. Vinogradov.

A. N. Zhurkov, G. M. Bartenev, V. E. Gul', A. L. Rabinovich, Yu. M. Malinskii developed theoretical ideas on the nature of the deformability and strength of polymers and reinforced plastics, and also studied the relaxation properties of polymers having rubberlike elasticity. V. A. Kargin and T. I. Sogolova established methods for modifying the supermolecular structure and physicomechanical properties of polymers.

Aspects of the physical chemistry of surface phenomena in polymer systems have been investigated by Yu. S. Lipatov, Yu. A. El'tekov, while the foundations for a theory of adhesion have been laid by B. V. Deryagin, V. E. Basin, S. S. Voyutskii. These investigations are not only of great theoretical importance but also of practical value, especially for the controlled production of adhesives, protective coatings, binders, reinforced plastics, etc.

INORGANIC CHEMISTRY

The inception of quantitative investigations on inorganic chemistry is connected with the work of M. V. Lomonosov. During the eighteenth century information accumulated on the composition and properties of various substances, and new elements were discovered. The establishment of the atomic—molecular doctrine in the nineteenth century, the discovery of the stoichiometric laws of chemical reaction, and the formulation of such concepts as atom, equivalent,

molecule, and valency enabled a start to be made in elaborating theoretical principles of inorganic chemistry.

D. I. Mendeleev's discovery of the Periodic Law and the Periodic System of the elements (1869) initiated a new stage in the development of chemistry. The discoveries of physics at the beginning of the twentieth century—the detection of radioactivity, the composite structure of the atom, and the quantum theory of atomic structure—faced inorganic chemistry with the task of studying the structure of atoms and molecules, and relating such structure to chemical properties.

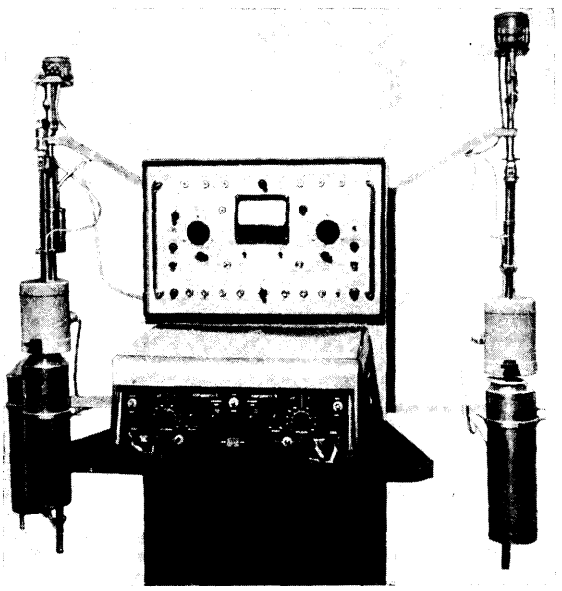


Figure 34. Automatic equipment for recording thermomechanical properties of polymers, developed in the Arbuzov Institute of Organic and Physical Chemistry of the USSR Academy of Sciences.

The Institute of Physicochemical Analysis, of which N. S. Kurnakov became director, and the Institute of Platinum under the direction of L. A. Chugaev were organised in Petrograd in 1918. These establishments were combined in 1934 with the Laboratory of General Chemistry as the Institute of General and Inorganic Chemistry. The Scientific Research Institute of Fertilisers, Insecticides, and Fungicides and the Institute of Chemical Reagents were founded in 1919, the State Institute of Applied Chemistry was established in 1920, and the Radium Institute headed by V. I. Vernadskii in 1922. Many other institutions and laboratories, concerned with all aspects of inorganic chemistry, were established in subsequent years.

Modern inorganic chemistry makes widespread use of the achievements of other branches of chemistry, the theoretical concepts and methods of physics, crystallography, crystal chemistry, and the theory of molecular structure. The principal fields of inorganic chemistry which have been most fully developed are—the chemistry of simple inorganic compounds, the chemistry of metals and alloys, the chemistry of the rare elements, radiochemistry, the chemistry of complex compounds, the chemistry of semiconductors, the chemistry of natural salts, and quantum inorganic chemistry.

Chemistry of Simple Compounds

Research on the chemistry of simple compounds came to be concerned with the structure and chemical properties of almost all elements and their simplest compounds. N. S. Kurnakov introduced the concepts of a chemical species, phases of variable composition, daltonides, and berthollides, and suggested the construction of equilibrium diagrams to represent the properties and stability of a chemical compound. Physicochemical analysis was used to study many of the simplest inorganic compounds; the unity of construction of diagrams for substances of different classes was demonstrated, compounds of unusual valency were detected, the wide distribution of phases of variable composition was established, and geometrical methods were developed for representing chemical systems (N. P. Radishchev, V. Ya. Anosov, A. G. Bergman, M. I. Ravich).

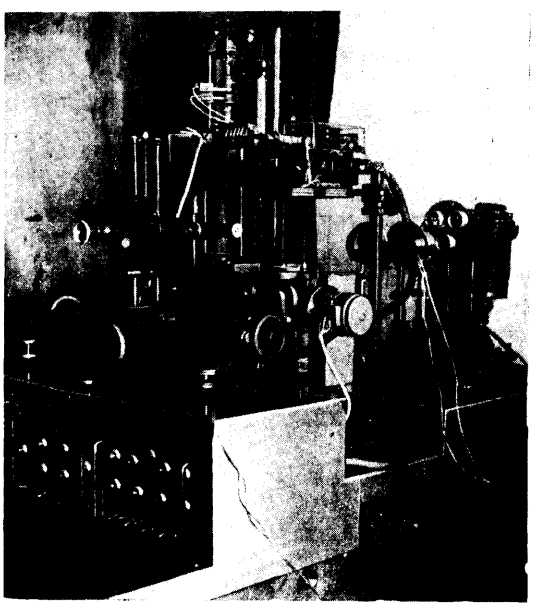


Figure 35. Opticomechanical apparatus for studying relaxation and creep in polymers (Arbuzov Institute of Organic and Physical Chemistry of the USSR Academy of Sciences).

During the 1930s physicochemical analysis became an objective method for studying complicated systems. Metals and alloys were investigated (V. A. Nemilov, N. V. Ageev, G. G. Urazov, V. I. Mikheeva), molten salts (A. G. Bergman, N. K. Voskresenskaya, N. S. Dombrovskaya, N. P. Luzhnaya), and multicomponent aqueous salt systems (V. I. Nikolaev, I. N. Lepeshkov). The chlorine metallurgy of rare and non-ferrous metals has been developed on the basis of the physicochemical analysis of systems involving chlorides of multivalent elements (G. G. Urazov, I. S. Morozov, and V. I. Evdokimov).

Methods of preparation of compounds of light elements, perchloric acid and its derivatives, hydrides of transition metals, hydroborons and their derivatives, etc. have undergone considerable development (S. Z. Makarov, A. F. Zhigach, V. I. Mikheeva, V. Ya. Rosolovskii, and others).

Many peroxides and ozonides have been obtained by I. I. Vol'nov. A series of investigations of the branched-chain decomposition of perchloric acid were made by V. Ya. Rosolovskii and G. B. Manelis.

Figure 36. Institute of Inorganic Chemistry of the Siberian Division of the USSR Academy of Sciences.

A new class of compounds—complex aluminium hydrides $AlH_3.nBH_3.mZ$, where Z is a nitrogen- or oxygen-containing ligand—have been prepared and subjected to physicochemical investigation at Moscow State University. These compounds were shown to be effective reductants and components of catalytic systems of the Ziegler–Natta type.

A. V. Novoselova has prepared novel polymeric beryllium alkoxoacetates $[Be(O.CO.CH_3)OR]_n$, as well as oxy- and hydroxy-acetates. Magnesium alkoxide halides have also been prepared, as promising catalysts for polymerisation processes.

The possibility of almost complete thermal dissociation of naturally occurring phosphates to give phosphorus pentoxide has been demonstrated by S. I. Vol'fkovich.

I. V. Tananaev, N. S. Nikolaev, and Yu. A. Buslaev have obtained important results on the acid–base equilibria of fluorides with hydrofluoric acid. A method developed for obtaining single crystals of copper(I) chloride gave a transparency equal to those of the best specimens in the world. Tungstates of thallium, barium, strontium, and the rare elements have been prepared and studied. Fluorides of Groups I–VI elements, oxofluorides, and polymeric fluorides have been studied by X-ray electron spectroscopy. Per-rhenates of copper, nickel, and lead have been prepared, as well as various barium chromates, niobates, and tantalates.

Developments have occurred in the chemistry of semiconductors (N. P. Sazhin) and dielectrics, and the chemistry of rare, trace, and rare-earth elements (I. V. Tananaev, K. A. Bol'shakov).

This is by no means a complete list of current researches on the preparation and properties of simple inorganic compounds.

The use of physical methods—X-ray diffraction, spectral methods of studying magnetic properties—is being developed in such investigations.

Methods have been elaborated for obtaining the pure metals necessary for radio-engineering and semiconductors. Under the direction of Yu. A. Zolotov investigations have been made on the extraction of more than twenty non-ferrous and noble metals by sulphur-containing organic compounds. Selective extractants have been proposed for copper, thallium, silver, and certain other metals both in the laboratory and in industrial use. Mixtures of a neutral and a cationic extractant have proved effective for the separation of transplutonic elements from rare-earth metals. L. F. Kuzina has worked out a new hydrogen-free process for the industrial production of metallic technetium.

Metals and Alloys

Many of the rules of alloy formation, methods of study, and preparation of alloys with valuable properties were first discovered and formulated by D. I. Mendeleev, N. S. Kurnakov, A. A. Baikov, P. M. Anosov, L. K. Chernov, E. S. Fedorov, A. A. Bochvar, A. A. Rzheshotarskii, and many others. An important aspect of the chemistry of metals is the character of their interatomic bonding. N. V. Ageev investigated the distribution of electron density in the interionic space, and showed that metals are bound by a continuous transfer of the electron cloud from one atom to the other.

Kurnakov established that the chemistry of alloys is the chemistry of continuous proportions: i.e. phases of variable composition (solid solutions) are formed, in which the component concentrations vary continuously. The properties of alloys are a continuous function of the component concentrations. The filling by electrons of energy bands in metallic crystals also obeys special rules.

The relation between the properties of metal—metal systems, in particular the heats of formation, and the structure of their electron shells has been shown in the work of Yu. M. Golutvin. The band theory (S. T. Konobeevskii) was of great value for understanding the solubility limits of metals one in another and the possibility of the formation of solid solutions. Research on the solid solutions formed in metallic systems was carried out over many years by N. S. Kurnakov, G. G. Urazov, N. I. Stepanov, A. T. Grigor'ev, V. A. Nemilov, P. Ya. Sal'dau, N. Kh. Abrikosov, O. S. Ivanov, I. I. Kornilov, V. I. Mikheeva, and many other scientists. It was shown that dissolution of the components in the formation of solid solutions is a special form of chemical interaction, and that this is accompanied in all cases by the evolution of heat owing to the formation of a chemical bond between atoms of the solute metal and molecules of the solvent.

Reactions occurring in solid solutions have been studied that lead to changes in the physical, mechanical, and other properties of the alloys (N. V. Ageev, A. A. Bochvar, S. A. Pogodin, V. N. Anosov, E. M. Savitskii, N. V. Grum-Grzhimailo, G. I. Chufarov). It was established that necessary conditions for the formation of solid solutions are isomorphism of the crystal structures of the separate components, similarity in size of their atoms, and a certain ratio of the electronegativity and ionisation potentials. A classification of solid solutions has been made.

The properties of solid solutions are currently being investigated in the Institute of General and Inorganic Chemistry, the Institute of Silicate Chemistry of the USSR Academy of Sciences, the Institute of Chemistry of the Ural Science Centre, and other institutions. It has been shown in particular that the ternary "alloy" based on zirconium dioxide ZrO_2–Y_2O_3–Nd_2O_3 possesses valuable electrophysical properties and refractoriness, and can be

recommended for the preparation of high-temperature electrodes of magnetohydrodynamic (MHD) generators (E. K. Keller). The properties of the hafnium dioxide–magnesium oxide system, which possesses high electrical conductivity, are being studied. A series of investigations is being made on the interaction, variation in composition of compounds, and polymorphic transitions in systems formed by alkali and rare-earth metal tungstates and molybdates. The solubility of magnesium, calcium, aluminium, lanthanum, neodymium, and zirconium oxides in $NaF-MgF_2$ melts and of lanthanum oxide in the $NaF-MgF_2(CaF_2, SrF_2, BaF_2)$ systems is under investigation.

Methods for the preparation and separation of novel compounds with special properties are being elaborated. The number of intermetallic compounds studied—binary, ternary, and multicomponent—has now reached 10 000; compounds of metals with non-metals—oxygen, hydrogen, nitrogen, silicon, boron, carbon—are also under investigation. Many of them possess special properties such as superconductivity, high-temperature strength, and hardness. A method has been worked out for obtaining intermetallic compounds with specified electrical and mechanical properties. Especially hard alloys are based on carbides of different metals—tungsten, titanium, cobalt, molybdenum, iron, etc. (N.S. Umanskii, G.V. Samsonov, V.I. Eremenko, I. I. Frantsevich, V. E. Ivanova, and others). A process has been worked out and realised under industrial conditions for the production of titanium carbonitride, from which can be obtained alloys at least as hard as those based on tungsten carbide.

Methods have been elaborated for the low-temperature preparation of oxonitrides, oxophosphides, and oxoborides of several transition metals (Yu. A. Buslaev). The properties of molybdenum disilicide, which possesses enhanced high-temperature strength, have been studied, and the production of heaters for high-temperature furnaces has been established.

A. G. Merzhanov proposed the self-propagating high-temperature synthesis method to obtain refractory compounds. Table 1 lists compounds of different classes obtained by this method (more than seventy are known), and shows that almost all of them possess properties such as heat resistance, chemical stability, hardness, etc. that are important for practical application. Compounds having melting points above 3500°K—TaC, HfC, NbC, ZrC, HfN, TaB_2—are especially interesting. A method has been worked out for obtaining zirconium carbide, one of the main constructional materials in nuclear technology. Conditions have been found under which the product has a high degree of purity.

Metallic compounds exhibiting superconductivity at the temperature of liquid helium are of great interest; about a thousand such compounds are known at the present time.

[Quantum Inorganic Chemistry]

The quantum chemistry of inorganic compounds is a young branch of inorganic chemistry, which has greatly developed only during recent years. Work in this field is done at the Institute of General and Inorganic Chemistry and the Institute of New Chemical Problems of the USSR Academy of Sciences, the Institute of Physical Chemistry of the Ukrainian SSR Academy of Sciences, the Institute of Chemistry of the Moldavian SSR, and other establishments.

During the 1950–1960s Ya. K. Syrkin and M. E. Dyatkina put forward several principles to form the basis for the further development of theoretical inorganic chemistry. Aspects of the participation of unshared pairs and vacant orbitals in chemical bonding were studied, a critical analysis was given of the concept of effective charge, and questions of chemical reactivity were considered.

Table 1. Compounds obtained by "spontaneously propagated high-temperature synthesis".

Compounds	Group in Periodic Table (metals)							Principal properties
	II	III	IV	V	VI	VII	VIII	
Nitrides	Mg_3N_2	BN AlN	TiN, ZrN, HfN	VN, NbN, TaN, Ta_2N	—	—	—	heat resistance, super- and semi-conductivity, chemical resistance, electrical and thermal insulation
Carbides	—	—	TiC, ZrC HfC, SiC	VC NbC, NbC, Nb_2C, TaC	WC	—	—	high m.p., great hardness, abrasives
Borides	MgB_2, MgB_4, MgB_6	—	TiB, TiB_2, ZrB_2, ZrB_4 HfB, HfB_2	VB, VB_2, NbB, NbB_2, TaB, TaB_2	CrB, CrB_2, MoB, Mo_2B, MoB_2, Mo_2B_5, WB, W_2B, WB_2	MnB	FeB NiB	resistance to molten metals, abrasive, small capture cross-section for neutrons
Silicides	—	—	TiSi, TiSi ZrSi, $ZrSi_2$	—	$MoSi_2$	—	—	high resistance to high-temp. oxidation
Chalcogenides			TiSe	$NbSe_2$, $TaSe_2$	MoS_2, $MoSe_2$	—	—	highly antifrictional
Solid solutions	TiC—WC, Ni—Al, MoS_2—NbS_2, BC—BN, NbC—NbN, TiC—TiN, TaC—TaN, TiB_2—MoB_2, $Nb_xZr_{1-x}C_yN_{1-y}$							great hardness, superconductivity, antifrictional

Calculations of coordination compounds by the method of molecular orbitals were initiated in the Structure Laboratory of the Institute of General and Inorganic Chemistry. Calculation of the ferrocene molecule (M. E. Dyatkina, E. M. Shustorovich) was an important stage in the development of a native quantum chemistry. The first non-empirical programme in our country for calculations of inorganic compounds by means of an electronic computer was worked out in the same laboratory jointly with the Lomonosov Moscow Institute of Fine Chemical Technology (M. E. Dyatkina, N. M. Klimenko, V. K. Belov, E. L. Rozenberg). Many fluorides and oxy-anions of non-transition elements have been calculated by means of this programme, which is used in several Soviet and foreign laboratories.

In the Institute of General and Inorganic Chemistry of the USSR Academy of Sciences a theory is being developed and systematic investigations are being made on X-ray-electron and X-ray spectra (V. I. Nefedov). Calculations are being made of the electronic structure of inorganic crystals (A. A. Levin).

In the Institute of Physical Chemistry of the Ukrainian SSR Academy of Sciences, under the direction of K. B. Yatsimirskii, a series of studies have been made on the application of crystal-field theory to atoms having f-electrons, experimental and theoretical work has been done on the interaction of ligands, and the role of the symmetry of the last occupied and first vacant molecular orbitals for the physicochemical characteristics of inorganic compounds has been established. In the Institute of Chemistry of the Moldavian SSR systematic investigations are being made on vibronic interactions, and chemical aspects of the Jahn–Teller effect are being studied (I. B. Bersuker). Calculations of atomic orbital energies have been made in the Institute of New Chemical Problems, and the results have been used to analyse the stereochemistry and thermodynamics of inorganic compounds.

Comprehensive calculations have been made on the fluorides of the inert gases (O. P. Charkin).

Increasing attention is now being paid to quantum-chemical calculations. Quantum chemistry provides the theoretical foundation for interpreting the results of physical investigations on inorganic compounds.

Crystal Chemistry

The development of crystal chemistry in our country is associated with the names of A. E. Fersman, A. F. Kapustinskii, N. V. Ageev, A. I. Kitaigorodskii, and other scientists.

The work of E. S. Makarov led to formulation of the principle of the structure of "interstitial phases" and to elucidation of the structure of berthollides and daltonides. G. B. Bokii examined processes of ordering in solid solutions, which suggested a crystal-chemical criterion for the composition of an ordered system. B. F. Ormont considered structural and thermodynamic aspects of the chemistry of defective crystals and phases of variable composition, as well as problems of interpreting the physicochemical properties and structure of real crystals.

V. G. Kuznetsov, G. B. Bokii, Z. G. Pinsker studied the crystal structure of semiconducting compounds. A systematic description has been given of the structure of several types of semiconductors.

N. V. Belov showed that a second, diortho-group Si_2O_7 exists in addition to the main Bragg structural unit—the orthosilicate tetrahedron—and that the "configuration" of silicate structures is determined primarily by the cations.

The crystal chemistry of minerals and their synthetic analogues has been developed by E. S. Makarov, V. A. Frank-Kamenetskii, Yu. A. Pyatenko.

Neutron diffraction, the Mössbauer effect, and other methods have been used to investigate double oxides A_2BO_5, and also ferroelectrics, antiferroelectrics, and ferromagnetics. This led to a crystal-chemical theory of ferroelectricity and to a new class of compounds—ferroelectromagnetics (G. S. Zhdanov).

An important branch of crystal chemistry is the study of complex compounds (G. B. Bokii, M. A. Porai-Koshits, G. S. Zhdanov, A. V. Ablov, T. I. Malinovskii, A. I. Kitaigorodskii, and others). The work of crystal chemists made it possible to establish the structure of various types of complexes, interpret their properties, and lay the foundation for theoretical concepts. Systematic structural investigations on compounds of cobalt, nickel, copper, zinc, palladium, and platinum established regularities in exchange of the coordination polyhedron and several peculiarities of the metal–ligand bond (Porai-Koshits).

Chemistry of Complex Compounds

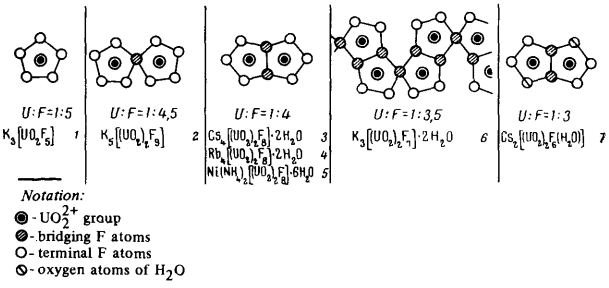
The founder of the chemistry of complex compounds in the Soviet Union was L. A. Chugaev, who discovered several inner-complex compounds of platinum, nickel, and other metals, and established the "rule of rings". The coordination theory of the structure of complex compounds was developed by L. A. Chugaev, I. I. Chernyaev, A. A. Grinberg, V. V. Lebedinskii, B. V. Nekrasov, N. K. Pshenitsin, and many other investigators. Chernyaev's rule of the *trans*-effect of ligands in complexes having a square configuration of the inner sphere underlay the study and preparation of new coordination compounds of platinum, rhodium, palladium, and other noble metals. Grinberg observed also a weaker *cis*-effect of ligands. He based a theory of the acid–base properties of complex compounds on platinum(II) complexes as example.

Several comprehensive investigations have recently been published on the interaction of ligands—a central trend in the chemistry of coordination compounds—revealing finer aspects of the metal–ligand bond. To them may be added an interesting treatment of the *trans*-effect (I. B. Bersuker, A. V. Ablov), K. B. Yatsimirskii's discovery of a kinetic effect in the interaction of ligands and the channels through which it is transmitted in complexes, and the establishment of a model of the *trans*-effect in six-coordinated complexes of transition metals containing a multiple metal–ligand bond (E. M. Shustorovich, Yu. A. Buslaev, M. A. Porai-Koshits).

Dozens of previously unknown complexes of platinum, rhodium, iridium, thorium, uranium, cobalt, nickel, iron, copper, zinc, and other metals have been obtained with various types of ligands containing nitroso-, nitro-, thiocyanato-, cyano-, and sulphato-groups. More than sixty new compounds of uranium and thorium were prepared in 1972 alone.

Developing the chemistry of the actinides, I. I. Chernyaev and R. N. Shchelokov established the law of the replacement of ligands in coordination compounds of uranyl and related complexing groups, which enabled them to prepare many new uranyl compounds. Examination of fluoride complexes of uranyl by X-ray diffraction (Yu. N. Mikhailov) revealed the presence of diverse structural motifs [Table 2].

Table 2.



Procedures based on complex formation have been worked out for separating many valuable metals, e.g. the platinum metals and gold, under both industrial and laboratory conditions. A method has been suggested for isolating copper, silver, and gold by means of sodium tetrahydroborate in the presence of complexing agents from baths used for the deposition of coatings.

Genetic series of complex compounds of uranium, thorium, plutonium, and zirconium have been obtained (I. I. Chernyaev, V. A. Golovnaya, G. V. Ellert, R. N. Shchelokov). Significant differences between complex compounds of radioactive elements and those of platinum metals are evident in the structure of the coordination sphere, the absence of a pronounced *trans*-effect, and a great "affinity" for oxygen-containing, not for nitrogen-containing, ligands. Many compounds predicted by coordination theory have been prepared.

I. V. Tananaev made a systematic study of fluoride and oxofluoride compounds of uranium, plutonium, and thorium, and the higher fluorides of elements of the chromium subgroup, vanadium, and titanium. He developed fluoride processes for the refining of uranium-containing materials.

D. I. Ryabchikov discovered the existence of a large new class of complex compounds of rare-earth metals, whose stability increased with atomic number from lanthanum to lutetium. An important role in the separation of rare-earth metals by the most diverse methods—liquid extraction, ion-exchange chromatography, fractional crystallisation, cathodic reduction—is played by complex formation. A new method of separation—partial complex formation—has been developed. New analytical procedures for rare-earth metals have also been established.

Heteropoly-compounds were investigated by E. A. Nikitina, and inner-complex compounds by S. A. Voznesenskii. A theory that complex formation is amphoteric in character was based on complexes having a non-metallic central atom (Ya. A. Fialkov). The thermodynamic and thermochemical parameters of complexes, used to determine their stability, have been studied by Yatsimirskii.

Direct experimental evidence has been obtained for the existence of stable complex molecules in the gas phase. Equimolecular complexes—$NaBeF_3$, $NaAlF_4$, $NaZrF_5$—and higher complexes—Li_2BeF_4, $(LiAlF_4)_2$, etc.—have been detected.

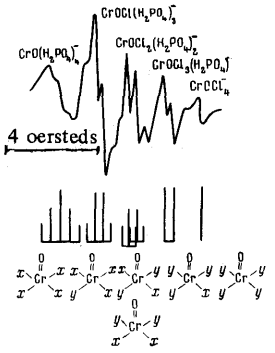


Figure 37. Electron spin resonance spectrum of chromium(V) complexes dissolved in phosphoric and hydrochloric acids.

The application of physical and physicochemical research methods—spectropolarimetry, dielectric measurements, electron spin resonance, nuclear magnetic resonance, etc.—will give valuable information on the structure of complex compounds. K. I. Zamaraev and N. N. Tikhomirova used e.s.r. to investigate the reactions of copper and molybdenum complexes. This method was combined with ultraviolet and infrared spectroscopy to study copper and cobalt complexes. A. N. Ermakov, P. N. Marov, and G. M. Larin are using e.s.r. to study the formation in solution, the nature of the bond, and the structure of coordination compounds of molybdenum(V), chromium(V), cobalt(II), copper(II), vanadium(IV), europium(II), and other paramagnetic ions. Labile *cis*- and *trans*-isomers of coordination compounds of yl ions (oxo-cations) have been discovered in a series of molybdenum(V) and chromium(V) complexes. Fig. 37 illustrates the e.s.r. spectrum of chromium(V) complexes dissolved in phosphoric and hydrochloric acids.

A theoretical model has been constructed for the interaction of ligands attached mainly by σ-bonds to the central atom. The *cis*-effect has been explained for compounds of non-transition elements from a single approach (V. I. Nefedov, Yu. A. Buslaev).

Chemistry of Rare Elements, Semiconducting Compounds, and Materials for Quantum Electronics

It is very important to obtain pure and superpure rare-earth metals, many of which could be separated only after the appearance of nuclear power and the production of their radioactive isotopes. A technology has also been elaborated for the production of pure zirconium, a constructional material for atomic reactors. This problem was one of the most difficult in the chemistry of the rare elements. Methods have been worked out and introduced into industry for obtaining ultrapure tellurium and selenium, necessary for the preparation of semiconductors, rubidium, caesium, beryllium, scandium, and germanium. The chemistry of simple and complex compounds of more than thirty rare elements (halides, oxides, phosphates, chalcogenides, acido-complexes with molecular ligands and with a metal–metal bond) is being studied in the Division of Rare Elements of the Institute of General and Inorganic Chemistry of the USSR Academy of Sciences (I. V. Tananaev).

During recent years new applications and new methods of isolation have been found for rare elements. For example, phosphors have been based on lanthanum and ytterbium orthophosphates activated with europium and terbium. Phosphors emitting in a specific region and very durable high-temperature binding materials have been obtained from scandium and gallium phosphates. Several procedures have been worked out for obtaining the spectra of sexivalent rhenium compounds in solution and determining their parameters, which are important for technical processes. New compounds of rhenium have been obtained, as well as polymeric compounds of this metal with heterochains. The problem of producing the ion-exchange resins required for purifying rare elements has been solved. Methods of separation by means of complex formation have been developed.

Many studies are connected with the chemistry of semiconductors. Carbides, silicides, fluorides, and borides of rare elements possess valuable properties. An important trend is the production of ceramet articles and glasses with additions of cerium, neodymium, praseodymium, and other metals.

The chemistry of semiconducting compounds, which has developed during recent decades, forms a separate branch of inorganic chemistry. Solutions have been obtained for the problem of obtaining highly pure germanium (N. P. Sazhin, D. A. Petrov, I. P. Alimarin, I. V. Shmanenkov, and others), silicon (B. A. Sakharov, M. I. Iglitsyn, and others), selenium, and tellurium. Semiconducting properties have been found in grey tin (A. I. Blum, N. A. Goryunova).

Semiconducting binary compounds were obtained by G. G. Urazov, N. A. Goryunova, A. R. Regel', N. P. Luzhna. The types of compounds that are now being prepared and studied are $A^{III}BV$ (BN, AlN, GaP, BP, BAs, InP, etc.), $A^{II}BVI$ (ZnS, ZnSe, ZnTe, CdS, HgS, etc.), $A_2^{III}B_3^{IV}$

(chalcogenides of gallium, indium, and thallium), chalcogenides of rare-earth metals, and many others. Bismuth and antimony chalcogenides are most often used for the production of semiconductors, and arsenic sulphides and selenides for semiconducting glasses. Semiconducting properties have been observed in many oxides (Cu_2O, ZnO, V_2O_5, UO_2, etc.), nitrides, carbides, and silicides of chromium, boron, manganese, iron, etc.

Many more complicated semiconducting compounds—$CuFeS_2$, $AgFeTe_2$, $Cu(Ag)Ge_2P_3$, $Cu_2(Ag_2)SnS_3(Se_3, Te_3)$, etc.—have been prepared and studied during recent years. Several criteria have been suggested for predicting the presence of semiconducting properties in tetrahedral ternary phases (N. A. Goryunova, V. P. Zhuze). Methods used to prepare semiconducting compounds comprise the decomposition of more complicated compounds, chemical transfer reactions, syntheses with counter-pressure, gas-phase reactions, purification by zone melting, etc.

Techniques have been developed for preparing semiconductors having specified properties. Materials have been produced for obtaining filamentous alloyed silicon crystals by gas-diffusion reactions. They have been used as a basis for sensitive miniature strain resistors and temperature and pressure sensors. A new process has been found for obtaining weakly alloyed epitaxial films of gallium arsenide on a strongly alloyed support. A rotating container heated by light has been suggested for growing crystals.

Several semiconducting compounds, e.g. antimony thioiodide, possess both piezoelectric and ferroelectric properties, which makes them promising for use in radioelectronics. Pressure–temperature–composition diagrams have been studied for the antimony(bismuth) iodide—sulphide(selenide) systems, which include the semiconducting ferroelectrics SbSI, BiSI, SbSeI, and BiSeI. Conditions for growing single crystals of these compounds from the gas phase and from the melt have been optimised. Single crystals of considerable size have been obtained with certain of them. Fundamental investigations have been made on complex phosphides and arsenides of the type $A^{II}B^{IV}C_2^V$, which show prospects for semiconductor and laser technology.

Physicochemical methods of analysis are used to obtain "equilibrium microdiagrams" for semiconductors and alloying additives (V. M. Glazov, V. S. Zemskov). These investigations make a considerable contribution to the theory of the alloying of semiconductors. Ternary systems based on antimonides of aluminium, gallium, indium, etc. have been examined. Departures from stoichiometry are under investigation (N. Kh. Abrikosov, M. S. Mirgalovskaya, and others). Physicochemical principles are being elucidated for the preparation of semiconducting materials, based on lead chalcogenides and their solid solutions, with specified properties (A. V. Novoselova and Ya. I. Gerasimov). Procedures have been worked out for the polarographic monitoring of the composition of single crystals with preliminary separation of the elements by ion-exchange chromatography.

Considerable progress has been made in the chemistry of materials for quantum generators and paramagnetic amplifiers. Special methods have been developed for growing crystals (S. A. Peskovetskii) and for producing crystals with a uniform distribution of impurities (S. V. Grum-Grzhimailo), and manufacture of the necessary compounds—the ethyl sulphates of lanthanum, gadolinium, and cerium, corundum (S. K. Popov), fluorite (I. V. Stepanov, B. P. Feofilov), calcium tungstate, etc.—has been set in motion. A search is being made for new materials for quantum electronics, in particular the production of chemical lasers (V. L. Tal'roze), and lasers based on liquid and vitreous media (G. V. Ellert). Methods are being worked out for obtaining ultrapure materials for the microelectronic, semiconductor, and other industries (G. G. Devyatykh).

Radiochemistry

Radiochemistry, which arose after the discovery of radioactivity by Henri Becquerel, began to develop in Russia at the beginning of the twentieth century, mainly in the laboratories of Moscow and St. Petersburg Universities. Study of the radioactive elements and their practical application have been the concern of V. I. Vernadskii, L. S. Kolavrat-Chervinskii, N. N. Beketov, A. P. Sokolov, V. I. Spitsyn, E. S. Bersuker, L. V. Pisarzhevskii, V. A. Borodovskii, K. P. Yakovlev, and many others.

V. G. Khlopin, B. A. Nikitin, A. E. Polesitskii, P. I. Tolmachev, M. A. Pasvik, A. P. Ratner, I. E. Starik investigated the partition of elements between a crystalline phase and a solution, and formulated a rule linking the distribution of trace elements with chemical composition and molecular structure.

Investigations of the distribution of compounds of radioactive elements between two liquid phases and the fundamental problems of extraction are of great practical importance (B. A. Nikitin, V. M. Vdovenko, V. V. Fomin, A. V. Nikolaev, I. P. Alimarin, Yu. A. Zolotov, and others). On the basis of these investigations extraction methods were worked out for the complete and partial separation of the radioelements in lumps of uranium, the isolation of uranium and other elements from industrial wastes, the separation of rare-earth metals, the partition of lanthanides from actinides, etc. Ratner put forward a quantitative theory of adsorption, which is important for separating rare elements on adsorbents and ion exchangers. Studies in this field were made by B. P. Nikol'skii, B. N. Laskorin, A. M. Trofimov, V. I. Paramonova.

Aspects of the qualitative and quantitative analysis of mixtures of rare-earth metals by ion exchange and complex formation, partition and paper chromatography, have been investigated by A. P. Vinogradov, D. I. Ryabchikov, K. V. Chmutov, A. K. Lavrukhina, and others. Significant results were obtained by A. D. Gel'man on the separation of transuranium elements—neptunium, plutonium, americium—by means of complexing agents. Starik examined the state of a substance under conditions of extreme dilution.

Radiochemical analysis—the separation, identification, purification, and quantitative determination of radioisotopes in natural specimens, irradiated targets, etc.—is very important in present-day radiochemistry. The analytical principles were worked out by Vinogradov, Khlopin, Polesitskii, Starik. Methods for the radiochemical analysis of the fission products of heavy nuclei and isotopes formed by the action of neutron and other types of irradiation have been elaborated by B. V. Kurchatov, Yu. M. Tolmachev, V. P. Shvedov, and others.

The establishment of nuclear reactors and accelerators led to the synthesis of new elements—from neptunium to element 107. G. N. Flerov was the first to synthesise elements having atomic numbers 104 and 105. Methods were worked out for isolating elements 106 and 107 from the products of the action of accelerated xenon ions, and for their identification.

Hitherto unknown isotopes and compounds have been obtained. The existence of californium, einsteinium, and fermium in the bivalent state has been discovered. V. I. Spitsyn, N. B. Mikheev, together with scientists at the Joint Institute for Nuclear Research (in the town of Dubna), obtained univalent mendelevium for the first time, the first element to be obtained in this state of oxidation, which is abnormal for actinides. An. N. Nesmeyanov developed a technique and regulations for obtaining technetium (No. 95) from a niobium and molybdenum target that had been exposed in a cyclotron, by extraction with an aliphatic ketone from sulphate solutions containing small quantities of fluoride and nitrate ions. B. F. Myasoedov developed a chromatographic method of ultrapurification from contamination with californium, providing a source of neutrons for small-scale equipment.

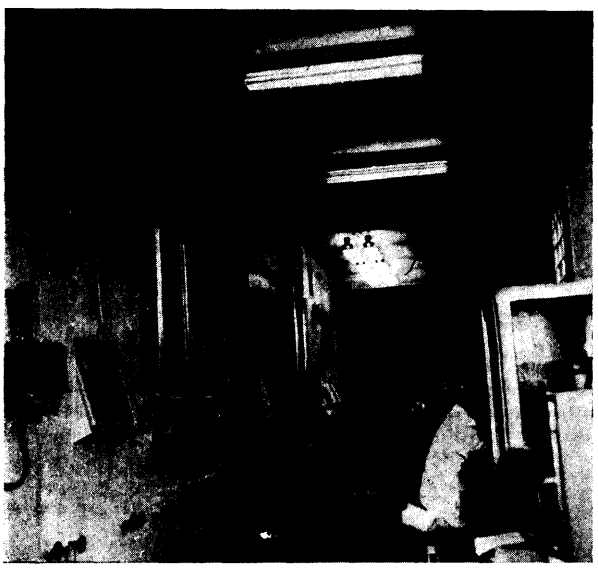


Figure 38. "Hot chambers" for work with highly radioactive substances (Institute of Physical Chemistry of the USSR Academy of Sciences).

Lavrukhina designed and constructed assemblies of low-background radiometric units permitting the examination of minute quantities of radioactive isotopes (down to 1 disintegration min^{-1} kg^{-1}) in large quantities of material (up to 1 kg). A method was proposed for determining subatmospheric dimensions of meteorites by radiochemical analysis of radioactive isotopes. A series of researches has been completed on the radiochemical analysis of the content of the cosmogenic isotopes—aluminium-26 and sodium-22—in a lunar regolith supplied by the automatic station Luna-16.

Great attention is being paid to the contamination of the environment with radioactive materials, the burial of wastes, the estimation of radioactivity in the vicinity of atomic installations, and problems of dosimetry (Spitsyn). An investigation of the behaviour in sea-water of fission products from a nuclear fuel (plutonium-239, ruthenium-106, technetium-99, cobalt-60, manganese-54, etc.) has been completed by V. V. Gromov. Study of the behaviour of radioactive isotopes and elements during their bioassimilation by phytoplankton under natural conditions in the South-eastern region of the Pacific Ocean has shown that radioactive fission products are efficiently assimilated and concentrated by the phytoplankton within 1–2 days. This promotes rapid transmission of the fission products of a nuclear fuel along the biological chain.

phytoplankton → zooplankton → fishes → man

which is a further justification for demanding a ban on the dumping of fission products in the ocean.

Almost all radioactive and stable isotopes—cobalt-60, caesium-137, strontium-90, phosphorus-32, iodine-131, boron-10, nitrogen-15, carbon-13, etc.—are now produced in the Soviet Union.

Chemistry of Natural Salts

The Soviet Union occupies the leading position in the world with respect to reserves, richness, and variety of composition of natural salts and brines.

Physical chemists and chemical hydrologists have made laboratory and field investigations of salt lakes in various regions of our country—the Crimea, Western and Eastern Siberia, the Caspian Depression, etc.—in which an important part was played by N. S. Kurnakov, V. I. Nikolaev, V. P. Il'inskii, S. Z. Makarov, B. L. Ronkin, I. N. Lepeshkov, M. G. Valyashko, Yu. P. Nikol'skaya, A. V. Nikolaev, and many others. New mineral salts were discovered, industrial methods for extracting salts were developed, and the salt equilibria in the lakes were studied, which contributed to optimising technical processes for the isolation of salts from natural brines.

In order to establish the genesis of the natural salts, systematic investigations were made of the solubility and other properties of complicated systems containing sulphates, hydrogen carbonates, carbonates, chlorides, and other salts. The results provided a justification for existing methods or led to new technical processes for obtaining salts from natural brines. S. I. Vol'fkovich worked out a process for converting mirabilite into sodium carbonate and ammonium sulphate—a valuable nitrogen fertiliser.

Investigations of great value for the national economy were made on potassium–magnesium deposits in the Solikamsk District, the Ural, Carpathian and Volga salt beds, where deposits having an increased potassium content and minerals containing boron were discovered, the potash beds of the Hissar Ridge and Tyubeg-tan in Uzbekistan, gameto-glauberitic deposits on the Tyan'-Shan in Kirgizia, deposits of epsomite, common salt, and gypsum in the Uzboi river bed in Turkmenia, and sylvinite–carnallite deposits at Starobino in Belorussia.

Phosphate beds have been investigated, and methods developed for enriching them and converting them into fertilisers, phosphorus, phosphoric acids, and other products (E. V. Britske, S. I. Vol'fkovich, A. I. Shereshevskii, N. N. Postnikov, M. L. Chepelevetskii, N. S. Kurnakov, A. G. Bergman, M. I. Ravich, L. G. Berg, F. M. Perel'man, A. B. Bekturov, M. N. Nabiev, M. E. Pozin, and many others). Thanks to these investigations the Soviet Union is able, not only to avoid importing phosphate minerals, but also to export its production to other countries.

The phase constitution, solubility, and thermal decomposition of natural carbonates and sulphates formed by the evaporation of sea-water have been examined. (These

compounds are used in water installations and for the production of building materials, plastics, and heat-insulating materials.) Ravich showed that salts that are almost insoluble in water under normal conditions become soluble at high temperatures (up to 600°C) and water-vapour pressures (up to 2500 atm). Problems involved in an optimal technology for processing natural deposits are being solved.

Great attention is being paid to detecting rare and trace elements, and isolating them from the salt ores. Thermographic, microthermal, and high-speed thermographic methods of analysis have been developed for this purpose, together with dilatometric phase analysis.

The chemistry of silicates is the basis of many important industries—cement, glass, ceramics, refractories, etc. Its task is to study methods for the preparation of silicate materials and their properties, as well as the processes occurring in them during operation. Silicate chemistry directly related to the technology of silicate manufacture has been the concern of N. V. Belov, P. A. Rebinder, P. P. Budnikov, N. A. Toropov, and many others.

Studies have been made on the structure of cement, the relation between its properties and mineralogical composition, the effect of mineralisers on processes of exchange, the processes involved in firing, and setting. Causes of the corrosion of cements have been elucidated, and measures developed for combating it (A. A. Baikov, S. I. Druzhinin, B. S. Shvetsov, and others). Technical processes have been worked out for obtaining special types of cement by the use of new types of raw material and industrial wastes, activators, surface-active additives, plasticisers, etc. The setting of cements at high temperatures and pressures has been investigated in connection with the production of ferroconcrete, polymer cement, etc. articles (M. M. Sychev, V. I. Korneev, V. N. Yung, V. A. Kind, B. V. Volkonskii, P. F. Konovalov, S. D. Makashev, V. B. Ratinov, O. P. Mchedlov-Petrosyan, S. I. Druzhinin, B. S. Shvetsov, I. L. Znachko-Yavorskii, A. P. Kreshkov, and many others).

Research has been undertaken on the chemistry of glass (D. S. Rozhdestvenskii, N. N. Kachalov, I. V. Grebenshchikov, G. Yu. Zhukovskii, A. A. Lebedeva, I. I. Kitaigorodskii, M. A. Bezborodov, M. A. Matveev). The technology of quartz glass has been developed by M. S. Maksimenko. Studies have been made to improve industrial processes and find ways of producing glass with special properties, glass–enamel refractory coatings, organosilicate materials, etc.

Recent decades have seen the establishment of a new branch of chemical science—the chemistry of the solid state—which studies chemical processes involving solid phases, determines the relation between the reactivity of solids and structural features, and elaborates a general theory of the controlled formation of solid compounds with the aim of producing effective new materials for present-day technology.

ANALYTICAL CHEMISTRY

Research on analytical chemistry in the Academy of Sciences originated with M. V. Lomonosov, who established the principles of quantitative chemical analysis and made numerous analyses of salts, minerals, and ores. Great contributions to the development of analytical chemistry were subsequently made by T. E. Lovits, V. M. Severgin, G. I. Gess [Hess], F. F. Beil'shtein [Beilstein].

During the early years of the Soviet State development began of a theory and new methods of analytical chemistry, especially those involved in solving applied problems of importance for the national economy. L. V. Pisarzhevskii, N. A. Tananaev, I. P. Alimarin, A. K. Babko, A. M. Dymov, and many others assisted in studying the natural resources of the country. Research was undertaken on the composition of rocks and minerals, as well as the contents of rare elements in various natural materials, and standard methods of analysis were developed for heavy chemical industry, metallurgical processes, ores, and useful fossils (V. I. Vernadskii, K. A. Nenadkevich, I. D. Borneman-Starynkevich, and others). Directly related investigations were made on the degree of purity of chemical compounds and the preparation of pure chemical reagents (V. V. Longinov, E. S. Przheval'skii, A. V. Rakovskii, A. E. Uspenskii).

Problems connected with developing chemical and physical methods of controlling the production of radium, uranium, and vanadium, separating them, and concentrating them were solved under the direction of V. G. Khlopin.

During the 1920–1930s analytical methods were developed for controlling production in works laboratories and for rapid analysis (N. A. Tananaev, A. M. Dymov, E. S. Przheval'skii, V. D. Voznesenskii, F. K. Gerke, I. P. Alimarin, A. M. Zan'ko, I. V. Tananaev, G. S. Landsberg, and others). Colorimetric, spectral, electrometric, and other methods of analysis became widely used. Great attention was paid also to standardising analytical methods.

The need to determine impurities in reagents and small quantities of rare elements in natural materials led to the appearance during the 1920s of special new, highly sensitive methods, including spot tests. A non-destructive method of analysis was developed for metals and alloys, as well as a fractional method of analysis (N. A. Tananaev).

Analysis by examining crystals under the microscope, established long ago by Lovits, was further developed. L. A. Chugaev, V. G. Khlopin, O. E. Zvyagintsev used a colorimetric method to analyse metals of the platinum group. Nikol'skii developed a method of potentiometric titration, and subsequently the theory of the glass electrode. Establishment of the first polarographic laboratories in our country is associated with the names of V. I. Vernadskii and A. P. Vinogradov. Internal electrolysis was established by Yu. Yu. Lur'e and Yu. A. Chernikhov, a sedimentometric method by N. A. Figurovskii, and a new form of volumetric analysis, vanadatometry, by V. S. Syrokomskii. The classic methods of analysis—gravimetric, titrimetric (A. K. Babko, I. V. Tananaev, I. P. Alimarin, I. M. Korenman, A. I. Busev, R. P. Lastovskii, and others)—have not lost their value. In the field of photometric analysis much attention has been paid to studying the mechanism of colour reactions, the processes of complex formation in solution. New reagents have been produced for the qualitative and quantitative determination and separation of almost all elements (V. I. Kuznetsov, N. S. Poluektov, S. V. Savvin, A. M. Lukin, and others).

Theoretical principles underlying the present search for new highly sensitive reagents have been established by L. M. Kul'berg (principle of functionally analytical and analytically active groups, and of the role of the nature of the metal) and by Kuznetsov (problems of the appearance of colour, use of the intramolecular dissociation of cyclic salts, mechanism of reactions with organic precipitants, etc.). N. P. Komar' studied the photometry of multicomponent mixtures, and K. B. Yatsimirskii developed a kinetic method of analysis. The luminescence method of

analysis established by S. I. Vavilov has been developed by M. E. Konstantinova-Shlezinger, E. A. Bozhevol'nov, D. P. Shcherbov, A. V. Karyakin, and others.

Spectral emission analysis is widely used to analyse metals, alloys, ores, and high-purity materials (D. S. Rozhdestvenskii, S. E. Frish, V. K. Prokof'ev, S. A. Borovik, A. N. Filippov, G. S. Lansberg, B. A. Lomakin, A. K. Rusanov). A rapid and accurate method of flame photometry has been developed by Poluektov. Studies by N. I. Tarasevich, V. V. Nedler, A. N. Zaidel' have been concerned with methods for the spectral analysis of ultrapure substances. A theory of emission spectroscopy has been elaborated during recent years, and processes occurring at the electrodes have been studied, as well as the mechanism of the vaporisation of material, excitation in the gas phase, etc. New modifications of the method are applied, in particular with the use of lasers. X-Ray spectral analysis has been developed by I. B. Borovskii, M. A. Blokhin, N. P. Il'in, N. F. Losev, Ya. E. Vainshtein This method is successfully applied to the analysis of metals, alloys, minerals, cements, and slags, as well as for phase analysis.

Polarography is widely used by A. M. Dymov, T. A. Kryukova, V. F. Toropova, I. P. Alimarin, S. B. Tsfasman. The theory of amalgam polarography is due to A. G. Stromberg; with accumulation on the mercury drop this method has been developed by S. I. Sinyakova, E. N. Vinogradova, A. G. Stromberg. Amperometric titration is widely used by I. P. Alimarin, O. A. Songina, Yu. I. Usatenko, V. A. Khadeev, and others. Potentiometric titration was further developed by N. A. Izmailov and then by A. P. Kreshkov, especially in non-aqueous media. High-frequency titration (V. A. Zarinskii) is used for the analytical control of production.

A promising and accurate coulometric method of titration has been used by M. S. Zakhar'evskii, A. Ogarev, F. I. Grishin. Several theoretical methods in the field of coulometry have been developed by P. K. Agasyan, who has studied the interrelationship among the various electrochemical methods.

Gas analysis forms a separate branch of analytical chemistry. Gas analysers of various types, in particular photocolorimetric, have been produced. Determination of the content of gases in metals, which is extremely important for the metallurgical industries, began to be developed by N. P. Chizhevskii, P. S. Lebedev, Yu. A. Klyachko, Z. M. Turovtseva.

Gas-chromatographic analysis, which is widely employed at the present time both for analytical and preparative purposes in scientific research and for the control of production, is sensitive, accurate, and simple. Such methods have been developed by A. A. Zhukhovitskii and N. M. Turkel'taub, who have elaborated new forms—chromathermography, a dynamic thermal method, vacancy chromatography, stepwise chromatography, chromatography without a carrier gas. V. G. Berezkin has studied the application of gas chromatography to analytical chemistry.

Mass spectroscopy is used to analyse solids—pure substances, semiconductors, materials for nuclear technology. V. L. Tal'roze has developed a method combining chromatography and mass spectrometry (chromatographic mass spectrometry).

The development of radiochemistry and the atomic industry provided the opportunity for new radiochemical methods of analysis. Radioactivation analysis has been widely used by I. P. Alimarin and Yu. V. Yakovlev. Natural radioisotopes came to be utilised as indicators. Analytical methods have been based also on the scattering or the absorption of β- or γ-rays. X-Radiometry, isotopic dilution, and radiometric titration have also been developed.

Optical methods of analysis have been widely used. Refractometry has been elaborated by B. V. Ioffe, and spectropolarimetry is successfully applied by A. P. Terent'ev, V. M. Potapov, E. G. Rukhadze.

Special types of analysis—micro and ultramicro—utilise various chemical and physicochemical techniques. Ultramicroanalysis involving use of a microscope has been developed by I. P. Alimarin and M. N. Petrikova. These lines of attack have been applied to the analysis of minerals and ores in geochemistry.

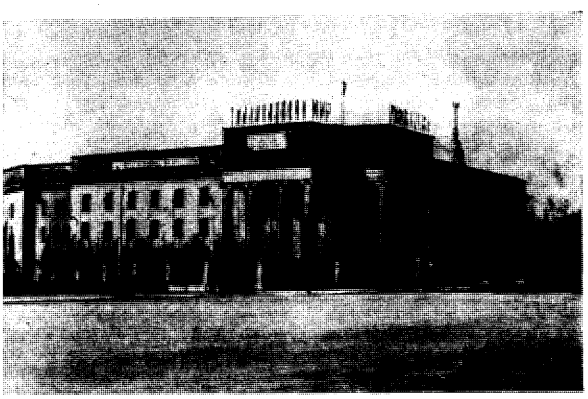


Figure 39. Vernadskii Institute of Geochemistry and Analytical Chemistry.

The problem of the analysis and control of production of atomic materials in our country has been successfully solved (A. P. Vinogradov, P. N. Palei, D. I. Ryabchikov, B. P. Nikol'skii, I. P. Alimarin, I. E. Starik, I. V. Tananaev). The efforts of a group of scientists of the USSR Academy of Sciences and of branch scientific research institutes (I. P. Alimarin, N. P. Sazhin, Yu. A. Zolotov, M. S. Chupakhin, Yu. V. Yakovlev, A. V. Karyakin, Z. M. Turovtseva, L. L. Kupin) have been concentrated on solving the problem of obtaining and analysing pure materials (high-purity metals, semiconducting materials, and chemical reagents).

A considerable contribution to the development of the analytical chemistry of rare elements and rare-earth metals has been made by A. P. Vinogradov, I. P. Alimarin, D. N. Ryabchikov, A. N. Ermakov, M. M. Senyavin, A. I. Ponomareva, and others.

The wide use of synthetic and natural organic compounds in industry and scientific research has stimulated the development of new methods of organic analysis. Important studies are being made in several institutes of the USSR Academy of Sciences on the elementary and functional analysis of organic substances using physical and physicochemical methods (A. P. Terent'eva, M. O. Korshun, V. A. Klimova, N. E. Gel'man).

The wide range of facilities of modern analytical chemistry has been applied in examining materials from the lunar surface procured by Soviet automatic stations.

Unique data have been obtained on the composition and structure of lunar rocks, the significance of which it is difficult to overestimate.

The growth of science and technology presents analytical chemistry with new problems—to enhance accuracy and sensitivity, accelerate the analysis, evolve methods of local analysis and remote analysis, and to automate analytical control.

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Within the confines of a single paper, of course, it is impossible to cover all lines of chemical research, even in general form. For this reason there may have been omissions of names, which is especially unfortunate both intrinsically and because the Reviewer feels the deepest respect for his scientific colleagues both of the past and of the present day. Nevertheless, the hope should be expressed that this outline will reinstate in the reader's memory the glorious historic road travelled by chemistry in our country, and recall the herculean, selfless, and enthusiastic labours, filled with romance, of many generations of Russian chemists.

The USSR Academy of Sciences, in celebrating its 250th anniversary, can be justly proud of the names of its illustrious scientific chemists, who over the ages have glorified Russian chemical science.

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Intermediate Compounds in Enzymic Catalysis and Their Kinetic Investigation

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Reactions catalysed by enzymes usually involve the successive formation of several intermediate compounds (enzyme-substrate complexes, covalent intermediates, conformers of the enzyme or the substrate). Kinetic methods have provided a fertile approach to the investigation of such labile intermediates. The Review summarises the kinetic laws of catalytic reactions involving labile intermediates in prestationary and stationary states. The relaxation kinetics of a multistage catalytic reaction is also examined.
The investigation of labile intermediate compounds is inseparably connected with the development of methods of "fast" kinetics. The Review therefore discusses "flow", "flash", and "temperature jump" methods and the possibility of applying them to enzymic reactions. Rather more detailed consideration is given to the formal kinetics of the appearance of intermediate compounds in reactions of the most thoroughly studied enzymes-catalase, α-chymotrypsin, peroxidase, ribonuclease, and aspartate aminotransferase. A list of 236 references is included.

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I. INTRODUCTION

Physical organic chemistry is paying increasing attention to research on reactions involving biopolymer catalysts[1,2], because knowledge of the specific mechanisms through which enzymes accelerate chemical reactions should help to elucidate the driving forces of enzymic catalysis. As a result, application of the principles of the action of the active centres functioning in enzymes might facilitate solving the problem of producing selective chemical catalysts with controllable properties[3-5].

The efforts of several scientific biochemical schools during the past decade have produced considerable progress in research on catalysis by enzymes[1,2,6]. Investigations in this field are developing in two main directions: (i) the structures both of enzymes and of the active centres are being studied, the most valuable information being given by X-ray diffraction[7-9]; and (ii) a study is being made of the dynamics of enzymic action, i.e. the sequence of changes undergone by a substrate molecule at an active centre of the enzyme, leading to formation of a product molecule. The present Review is devoted mainly to discussing the achievements of the latter group of investigations.

A fundamental idea in enzymic catalysis is the multistage transformation of substances under the influence of a protein catalyst. This was first pointed out by Michaelis and Menten[10], who concluded that the mechanism of the action of invertase involves formation of an intermediate enzyme-substrate complex (a Michaelis complex)†.

Subsequently a detailed investigation of other enzymic systems confirmed that reactions involving biological catalysts actually comprise the successive formation of several intermediate compounds (non-covalent enzyme-substrate complexes, covalently formed intermediate compounds, conformers of enzyme or substrate). Thus study of the mechanism of enzyme action encounters the specific problem of determining the number and nature of intermediate compounds involved. These intermediates are usually extremely labile, and in rare cases can be isolated in individual form[1]. Chemical kinetic methods have proved very fruitful for investigating such labile intermediates.

The present Review summarises the kinetic laws observed in enzymic reactions, paying attention primarily to the kinetic evidence for intermediate compounds in both transitional and stationary stages of the reaction. More detailed acquaintance with procedural features of the kinetic methods used can be obtained by referring to reviews[1,11-13]. Certain formal kinetic aspects of the investigation of intermediate compounds in enzymic catalysis may prove useful also for analysing other classes of reactions likewise involving labile intermediates.

The simplest general mechanism of a multistage consecutive catalytic reaction occurring on an active centre of an enzyme E and involving a substance S (the substrate) can be written

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_1 \dots \underset{k_{-i}}{\overset{k_i}{\rightleftharpoons}} X_i \rightleftharpoons \dots X_n \underset{k_{-(n+1)}}{\overset{k_{(n+1)}}{\rightleftharpoons}} E + P \qquad (1)$$

where the X_i ($i = 1, 2, 3, \dots, n$) are intermediate compounds, P is the reaction product, and k_i and k_{-i} are the rate constants of forward and reverse elementary steps. This scheme covers both unimolecular [k_i, $i \neq 1$, $-(n+1)$] and bimolecular [k_1, $k_{-(n+1)}$] elementary reactions. According to the laws of chemical kinetics a differential equation describing the variation of concentration with time can be written for each of the $n + 3$ participants in the reaction. Only $n + 1$ of the resulting $n + 3$ differential equations are linearly independent, since the variable

† The term "Michaelis complex" often implies the primary non-covalent enzyme-substrate complex. This is not quite exact, since the "saturation" observed in the dependence of reaction velocity on substrate concentration, which indicates the existence of a "Michaelis complex", may represent the presence of any other intermediate compound in the reaction, including one formed covalently. In its general meaning the term "Michaelis complex" represents the totality of intermediate compounds in enzymic catalysis.

component concentrations are related by the two linear algebraic equations of material balance

$$[E]_0 = [E] + \sum_{i=1}^{n} [X_i]$$
$$[S]_0 = [S] + [P] + \sum_{i=1}^{n} [X_i] \quad (2)$$

Thus the progress of all the elementary reactions in scheme (1) with time is described by the set of $n + 1$ differential equations

$$\begin{aligned}
&\frac{d[X_1]}{dt} + (k_{-1} + k_2)[X_1] = k_1[E][S] + k_{-2}[X_2] \\
&\vdots \quad \cdots \\
&\frac{d[X_i]}{dt} + (k_{-i} + k_{i+1})[X_i] = k_i[X_{i-1}] + k_{-(i+1)}[X_{i+1}] \\
&\vdots \quad \cdots \\
&\frac{d[X_n]}{dt} + (k_{-n} + k_{(n+1)})[X_n] = k_n[X_{n-1}] + k_{-(n+1)}[E][P] \\
&\frac{d[P]}{dt} + k_{-(n+1)}[P][E] = k_{(n+1)}[X_n]
\end{aligned} \quad (3)$$

together with the two algebraic equations (2). Simultaneous solution of Eqns. (2) and (3) yields expressions for all the reaction components as functions of time. The above differential and algebraic equations constitute a non-linear set with constant coefficients (non-linear because of the presence of second-order terms containing the products of variable concentrations—$k_1[E][S]$ and $k_{-(n+1)}[E][P]$). A solution can be found by numerical integration on a digital computer[14] or by simulation on an analogue computer[15]. The character of the transitional processes in enzymic reactions involving intermediate compounds has been investigated qualitatively for various initial conditions[16]. However, the possibility of an analytical solution of the set of equations (2) and (3) is of the greatest interest for comparing the reaction mechanism with experimental kinetic results. This task can be simplified considerably by using certain conditions permitting transformation to a linear set of equations. In the kinetic analysis of the mechanism of the action of enzymes three approaches based on the premises simplifying the formal kinetic treatment—(*a*) kinetics of reactions in the transitional stage or "prestationary" kinetics, (*o*) kinetics of steady-state enzymic conversion, and (*c*) relaxation kinetics—have at present found the greatest development and application. These approaches and their application to the investigation of reaction mechanisms will be examined in detail below with reaction (1) as example.

II. TRANSITIONAL STAGE OF REACTION

1. "Prestationary" Kinetics of an Enzymic Reaction

The non-linear set of equations (2) and (3) can be simplified by conducting the bimolecular stages of reaction (1) under pseudounimolecular conditions, i.e. in the presence of a large excess of one of the reactants. Changes in the concentration of this reactant with time can then be neglected, so that the bimolecular terms in the differential equations (3) become linearly dependent only on the variable concentration of one of the reactants. This approach is usually made for the analytical treatment of so called "prestationary" kinetics.

With $[S]_0 \gg [E]_0$ and only slight occurrence of reaction (1) ($[P] \simeq 0$ is formally equivalent to formation of the product P at an irreversible stage of the reaction, $k_{-(n+1)} = 0$) under conditions such that consumption of the substrate can be neglected, $[S] = [S]_0$, the set of equations (2) and (3) becomes

$$\left\{\begin{aligned}
&\frac{d[X_1]}{dt} + (k_{-1} + k_2)[X_1] = k_1[S_0][E] + k_{-2}[X_2] \\
&\vdots \quad \cdots \\
&\frac{d[X_i]}{dt} + (k_{-i} + k_{i+1})[X_i] = k_1[S]_0[E] + k_{-2}[X_2] \\
&\vdots \\
&\frac{d[X_n]}{dt} + (k_{-n} + k_{n+1})[X_n] = k_n[X_{n-1}] \\
&[E]_0 = [E] + \sum_{i=1}^{n} [X_i]
\end{aligned}\right. \quad (4)$$

$$\frac{d[P]}{dt} = k_{(n+1)}[X_n] \quad (5)$$

Several standard procedures—reduction to a single linear differential equation of higher order, application of Laplace transforms, etc.—are available for solving sets of linear differential equations[17]. The method of solution in the kinetic analysis of complicated chemical reactions has been described[18-22], and several approaches to a solution have been discussed for the progress of enzymic reactions[15,23-26]. The use of graph theory for these purposes has been described[27,28].

The general solution of Eqns. (4) is

$$[X_n] = \sum_{j=1}^{n} A_j e^{\lambda_j t} + B \quad (6)$$

where the λ_j are the n eigen values or real roots of the corresponding characteristic equation of order n. The quantity $-1/\lambda_j$ has the dimension of time and is a complicated function of the elementary rate constants of reaction (1). Particular solutions describing the time variation of the concentrations of all intermediate compounds X_i can be obtained from the general solution (6) by introducing initial conditions. The dependence of the concentration of the reaction product on time follows from the differential equation (5) when (6) is substituted and the resulting expression is integrated:

$$[P] = k_{n+1} \sum_{j=1}^{n} \frac{A_j}{\lambda_j} (e^{\lambda_j t} - 1) + k_{n+1} B t \quad (7)$$

Equations (6) and (7) generalise for n intermediate compounds earlier equations obtained for the kinetics of reactions involving one intermediate[29-33]

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X \xrightarrow{k_2} E + P \quad (8)$$

or two intermediates[15,34]

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_1 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} X_2 \xrightarrow{k_3} E + P \quad (9)$$

Considering scheme (8) in greater detail, we find that the time variation of the concentration of the intermediate X is given by

$$[X] = \frac{k_1[S]_0[E]_0}{k_{-1} + k_2 + k_1[S]_0} (1 - e^{-t/\tau}) \quad (10)$$

Analysis of the curve corresponding to function (10) (Fig. 1*A*) enables the characteristic time τ to be determined. The dependence of τ^{-1} on the substrate concentration

$$\tau^{-1} = k_1[S]_0 + k_{-1} + k_2 \qquad (11)$$

will then yield the formation and decomposition rate constants k_1 and $k_{-1} + k_2$ of the intermediate compound.

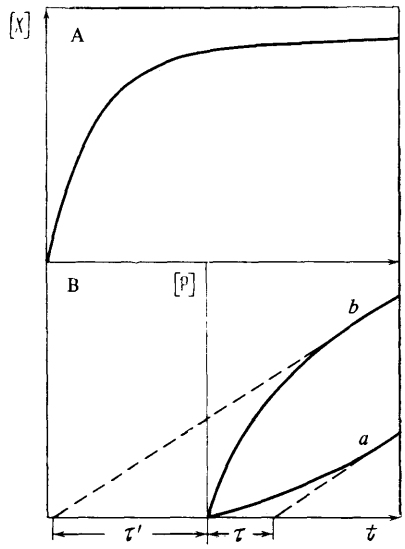


Figure 1. Kinetics of an enzymic reaction involving one intermediate under prestationary conditions.
(A) Dependence of concentration of intermediate compound X on time for the prestationary occurrence of the reaction by mechanism (8). (B) Rate curve for the prestationary formation of the product by different mechanisms:
a) Michaelis–Menten (scheme 8); *b*) Henry (scheme 14).

If direct experimental observation of X is difficult, information on the presence of such intermediate and on the reaction mechanism can be obtained by examining the kinetics of formation of the final product. The concentration of P as a function of time is given [32] by

$$[P] = \frac{k_2[E]_0[S]_0}{[S]_0 + K_m}t + \frac{k_1k_2[E]_0[S]_0}{k_1[S]_0 + k_{-1} + k_2}\left(e^{-(k_1[S]_0 + k_{-1} + k_2)t} - 1\right) \qquad (12)$$

where $K_m = (k_{-1} + k_2)/k_1$. The [P] curve approaches asymptotically a straight line whose slope is the steady-state rate of the process (Fig. 1*B*, curve *a*):

$$v_{stat} = \left(\frac{d[P]}{dt}\right)_{max} = \frac{k_2[E]_0[S]_0}{[S]_0 + K_m} \qquad (13)$$

Formula (11) holds for the observed induction period τ. The presence of an induction period in the product–time curve (in the absence of a chain or autocatalytic reaction) is a reliable indication of the presence of an intermediate (or at least one intermediate—see below). Analysis of the dependence of $(d[P]/dt)_{max}$ and τ on the enzyme and substrate concentrations will enable rate constants to be determined for all the elementary reactions.

Consecutive formation of an enzyme–substrate complex (Michaelis–Menten, scheme 8) and its concurrent formation

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \qquad (14)$$
$$E + S \xrightarrow{k_2} P + E$$

(Henry [35]) can be distinguished by the formal kinetic analysis of enzymic reactions in the prestationary state. Scheme (14), which assumes the formation of an unreactive complex ES and a bimolecular reaction of the substrate with the free enzyme, leads to the steady-rate equation (13) for scheme (8). However, significant differences have been found [36] between the kinetics of reactions (8) and (14) in the prestationary stage. No induction period is present in the product–time curve for reaction (14) (Fig. 1*B*, curve *b*), and the asymptote corresponding to the steady state makes the negative intercept

$$\tau' = -\frac{[S]_0}{k_1K_m(K_m + [S]_0)} \qquad (15)$$

on the abscissa axis. Mechanisms (8) and (14) can be distinguished also by the methods of relaxation kinetics [37].

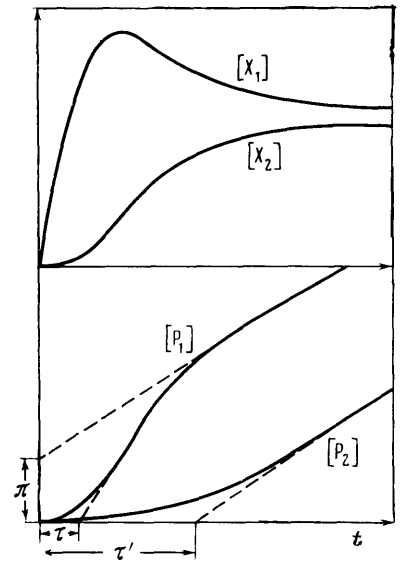


Figure 2. Prestationary kinetics of the formation of intermediates and products for a three-stage mechanism (16).

The mechanism of the action of proteolytic enzymes has been discussed in detail in terms of the formation of two intermediates and two products

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_1 \rightarrow X_2 \overset{k_3}{\rightarrow} E + P_2 \qquad (16)$$
$$\searrow P_1$$

Fig. 2 illustrates the variation of $[X_1]$ and $[X_2]$. The analytical time dependence of the concentration of product P_1 (Fig. 2) is [38]

$$[P_1] = \frac{k_2R}{Q}t + \frac{k_2N}{G}(e^{Gt} - 1) + \frac{k_2M}{F}(e^{Ft} - 1) \qquad (17)$$

where R, Q, F, G, M, and N are functions of the rate constants k_1, k_{-1}, k_2, and k_3. All the elementary rate constants of mechanism (16) can be determined[38] by analysing the steady-state reaction velocity and also τ, τ', and π

$$\tau = \frac{1}{k_1[S]_0 + K_m}; \quad K_m = \frac{k_2 + k_{-1}}{k_1} \tag{18}$$

$$\tau' = \frac{k_2^2 - k_1 k_2 [S]_0}{k_1 k_3 (k_2 + k_3)([S]_0 + K_m')}; \quad K_m' = K_m \frac{k_3}{k_2 + k_3} \tag{19}$$

$$\pi = [E]_0 \left\{ \frac{k_2^2 [S]_0^2}{(k_2 + k_3)^2 ([S]_0 + K_m')^2} - \frac{k_2 k_3^2 [S]_0}{k_1 (k_2 + k_3)^2 ([S]_0 + K_m')^2} \right\} \tag{20}$$

as functions of enzyme and substrate concentrations (see also Fig. 2).

We must emphasise an important general kinetic peculiarity of multistage catalytic reactions of type (1) in the prestationary state. Equations (6) and (7) show that the functional time dependence of the concentration of intermediate compounds is given by the sum of n exponential terms and a constant, whereas that of the concentration of the final product is represented by the sum of n exponential terms $(e^{\lambda_j t} - 1)$ together with a linear function of time. Hence the number of exponential terms in Eqns. (6) and (7) corresponds to the number of intermediate compounds in reaction (1) (cf. in particular mechanisms (8) and (16) with Eqns. (10) and (17)). Thus a reaction involving n intermediate compounds will ideally yield an experimental set of n characteristic times. In an actual experiment, however, a smaller number of exponential terms may be observed, primarily because of the method of recording the kinetic curve. The most widely used spectrophotometric method requires appreciable spectral differences between the components of reaction (1). Furthermore, the time resolution of the apparatus imposes significant limitations. A characteristic time can be determined experimentally only provided that it exceeds the "dead" time of the apparatus. As a consequence of these limitations, the number of exponential terms observed experimentally will give only an estimate of the minimum number of intermediate compounds involved in the reaction.

2. Experimental Methods

The kinetics of the prestationary stage of enzymic reactions (approximated by the above restriction to excess of one of the reactants and a slight extent of conversion of the substrate) has been studied mainly by flow methods. Such methods for measuring the kinetics of fast reactions in solution were first used by Hartridge and Roughton[39-41] and have since been developed by Chance[42-47]. At the present time the stopped-flow method is most widely used[48-53,181]. The main feature of flow methods is the rapid mixing of solutions of the reactants in a specially designed mixing chamber. Much attention has been paid to the problem of efficient mixing[11,54]. The main conclusion was that rate constants determined by means of flow apparatus can be regarded as reliable only for reactions with half-lives exceeding 0.2–1 ms. The "dead" time of current flow equipment is about 0.1–0.3 ms[50,51,55]. Nevertheless, the development of sufficiently simple and convenient apparatus has led to the widespread use of flow methods (especially the stopped-flow method) for studying intermediate compounds in enzymic reactions. Table 1 lists the enzymic systems that have been studied by flow methods.

The use of flash photolysis in enzymology will further increase the resolving power of apparatus for investigating non-stationary kinetics[109-112]. In contrast to flow methods, the flash method does not require rapid mixing of the reactants. With use of a photosensitive substrate precursor, capable of conversion into the substrate by the action of light, two parameters—(i) duration of the flash and (ii) time of photochemical formation of the substrate—govern the "dead" time of the method[110]. The xenon pulse technique yields powerful flashes of light lasting 10–100 ms.[113] The duration of a flash can be shortened without diminishing the power by use of a laser technique[111]. The duration of the photochemical reaction may be quite short.

Table 1.

Enzyme	Substrate or activator	Ref.
Alcohol dehydrogenase	aromatic aldehydes	56
	p-nitrosodimethylaniline	57
	benzaldehyde, acetaldehyde	58-60
α-Amylase	*o*-nitrophenol-α-maltose	61
Hydroxylase	*p*-hydroxybenzoic acid	62
Glyceraldehyde phosphate dehydrogenase	NAD*	63
Glutamate dehydrogenase	glutamic acid	64,65
Enolase	interaction of subunits	66
Carbamate kinase	carbamoyl phosphate, ADP**	67
Carbonic anhydrase	sulphonamides	68,69
	Zn^{2+}	70
Carboxypeptidase A	*N*-dansylated peptides	71
Catalase	hydrogen peroxide	72
Catalase-hydrogen peroxide	hydrogen peroxide, ethanol	72,73
Xanthin oxidase	xanthin oxygen	74
Lactate dehydrogenase	NAD*, lactic acid	75-77
D-Amino-acid oxidase	β-chloroalanine	78
Papain	nitrophenyl esters of benzyloxycarbonyl-glycine	79
	p-nitrophenyl ester of benzyloxycarbonyl-L-lysine	80
Peroxidase	hydrogen peroxide, ethyl and methyl hydroperoxides	81
Peroxidase-hydrogen peroxide	ascorbic acid, quinol	73
	cytochrome C	82
	hexacyanoferrate(II)	83
Staphylococcal nuclease	isomerisation (pH jump)	84
Trypsin	ethyl ester of *N*-benzoyl-L-arginine	31,86
	p-nitroanilide of *N*-benzoyl-L-arginine	87
	p-nitrophenyl acetate	108
	structural changes	89
Tryptophan synthetase	L-serine, indole, tryptophan	90
Ficin	ethyl ester of *N*-acetyl-L-arginine	31,86
	p-nitrophenyl hippurate	88
	p-nitrophenyl ester of benzyloxycarbonyl-L-lysine	80
Chymotrypsin	*p*-nitrophenyl acetate	85,91-94
	methyl and ethyl esters of *N*-acetylated L-amino-acids	95-100
	amide of *N*-furovlacryloyl-L-tryptophan	98
	methyl ester of *N*-furoylacryloyl-L-tryptophan	99
	p-nitrophenyl esters of *N*-benzyloxycarbonyl-L-amino-acids	101,102
	N-furoylacryloyl-L-tryptophan (pH jump)	103
	cyclic sulphonates	104
	Proflavin	105
Cytochrome C	Cr^{2+}	106
Alkaline phosphatase	*O*-*p*-phenylazophenyl phosphorothioate	107

[* NAD = nicotinamide–adenine dinucleotide.]
[** ADP = adenosine diphosphate.]

Catalase, peroxidase, and α-chymotrypsin have been studied in greatest detail by the above methods, and therefore the mechanism by which these enzymes function will be more fully discussed below.

3. α-Chymotrypsin

The proteolytic enzyme α-chymotrypsin catalyses the hydrolysis of peptide linkages, as well as that of ester and amide bonds in synthetic model substrates. The first hint that an intermediate compound of the enzyme with the acidic portion of the substrate is formed at the stage of

formation of the main product P_1 (scheme 16) was Hartley and Kilby's observation[114,115] that the separation of *p*-nitrophenol in the hydrolysis of *p*-nitrophenyl acetate by α-chymotrypsin takes place in two stages: an initial "burst" of *p*-nitrophenol in approximately stoichiometric concentration with respect to the added enzyme is followed by a slower, steady-state further hydrolysis of the substrate (a critique of the conclusions of this research will be found in Ref. 1). Careful investigation of the kinetics of both stages by later workers[85,91-94], using the stopped-flow method, showed that the rate curve for the separation of *p*-nitrophenol is described by Eqn. (17) provided that $k_1[S]_0 \gg k_2$, k_3. The time variation of $[P_1]$ then assumes the simpler form[91]

$$[P_1] = At + B(1 - e^{-kt}) \tag{21}$$

$$A = \frac{\frac{k_2 k_3}{k_2 + k_3}[E]_0[S]_0}{[S]_0 + K_m \frac{k_3}{k_2 + k_3}}; \quad K_m = \frac{k_{-1} + k_3}{k_1} \tag{22}$$

$$B = \frac{\left(\frac{k_2[S]_0}{K_m + [S]_0}\right)^2 [E]_0}{\left(\frac{k_2[S]_0}{K_m + [S]_0} + k_3\right)^2} \tag{23}$$

$$k = \frac{k_2[S_0]}{K_m + [S]_0} + k_3 \tag{24}$$

In fact, when $[S]_0 \gg K_m$ and $k_2 \gg k_3$, we have $B = [E]_0$, so that the initial "burst" of *p*-nitrophenol corresponds to the initial concentration of the enzyme (Fig. 3)‡. These results established the presence of the intermediate compound X_2 (the acylated enzyme), which was subsequently shown to be the ester of the hydroxyl group of serine-195, present in the active centre of the enzyme, and the acyl part of the substrate[117,118]§.

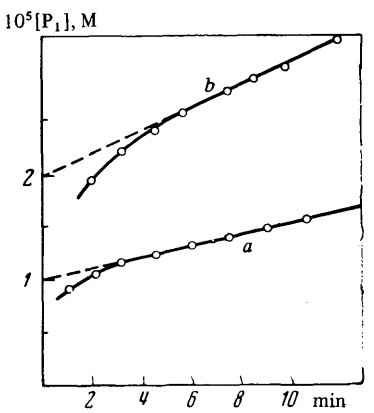


Figure 3. Kinetics of the formation of *p*-nitrophenol in the hydrolysis of *p*-nitrophenyl acetate catalysed by α-chymotrypsin[115] (enzyme concentration for curve *b* double that for *a*).

‡ Current methods for determining the concentration of active centres in many enzymes are based on this principle[116].

§ Several acylated enzymes, which are stable at low pH, have been isolated in pure form (acetylchymotrypsin[117], the homologous series of acylated enzymes formed by aliphatic carboxylic acids from C_1 to C_7[119], *cis*- and *trans*-isomers of cinnamoylchymotrypsin[120-122], etc.).

The kinetics of acylation of the active centre in α-chymotrypsin by *p'*-nitrophenyl *trans*-*p*-nitrocinnamate has been studied[110] by flash photolysis using the *cis*-ester as photosensitive substrate precursor. Steric features of the active centre are such that the reactivity of the *trans*-isomers of substrate derivatives of β-arylacrylic acids exceeds that of the corresponding *cis*-isomers by factors of 10^3–10^4 (*trans*-specificity)[123]. The action of a flash of light on a solution of α-chymotrypsin with *p'*-nitrophenyl *cis*-*p*-nitrocinnamate forms the highly reactive *trans*-isomer, which acylates the active centre of the enzyme. Spectrophotometric monitoring of the separation of *p*-nitrophenol was used to study the kinetics of the reaction.

p-Nitrophenyl acetate and the other substrates used in the above researches are relatively unreactive ("non-specific") substrates of α-chymotrypsin. Gutfreund and Sturtevant[91,92] suggested that the catalysis by chymotrypsin of specific ester substrates derived from α-*N*-acylated L-amino-acids takes place by the same mechanism (16) as does the hydrolysis of *p*-nitrophenyl acetate. Special attention was paid to proving this hypothesis[96-100].

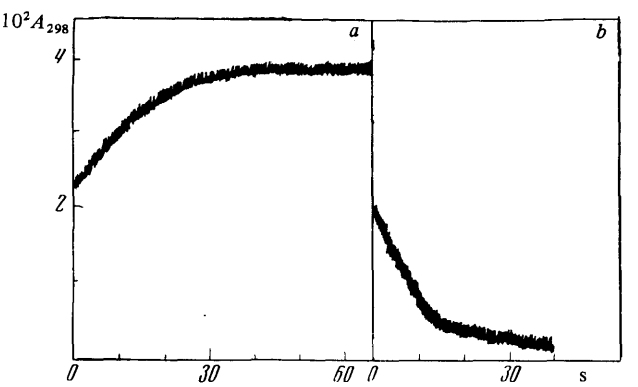


Figure 4. Prestationary kinetics of the hydrolysis of the methyl ester of *N*-acetyl-L-phenylalanine investigated by stopped-flow method[98]: *a*) variation of optical density when 3.7×10^{-5} M α-chymotrypsin and 0.017 M substrate solutions are mixed at pH 3.2; *b*) pH of solution obtained in expt. (*a*) raised from 3.2 to 5.7.

Formation of an acylated enzyme in the hydrolysis of the ethyl ester of *N*-furoylacryloyl-L-tyrosine is indicated by the effect that separation of the alcohol anticipates establishment of a steady-state concentration of the intermediate compound (as with *p*-nitrophenyl acetate).[95] Direct kinetic confirmation of the formation of intermediate compounds X_1 and X_2 in the catalysed hydrolysis of esters of *N*-acylated L-amino-acids has been obtained[98,124]. In the latter case analysis of the reaction kinetics at the wavelengths of absorption by the intermediate compounds (~ 290 nm) revealed that the rate curve was represented by the sum of at least two exponential terms, which according to Eqn. (6) indicates the formation of at least two intermediate compounds. Thus mixing a solution of α-chymotrypsin with the methyl ester of *N*-acetyl-L-phenylalanine produces a rapid, kinetically unresolved variation of the spectrum (with a half-time < 3 ms), which evidently indicates formation of the primary enzyme–substrate complex X_1; this is followed by slow formation of the acylated enzyme (Fig. 4, curve *a*). In the steady

state, under conditions such that consumption of the substrate can be neglected, the concentration of the acylated enzyme remains constant; consumption of the substrate ultimately leads to disappearance of the intermediate compounds from the solution (curve *b*). A similar pattern is found in the chymotrypsin hydrolysis of other specific ester substrates—the methyl esters of the *N*-acetylated amino-acids L-tyrosine, L-tryptophan, and L-leucine, and also the ethyl ester of *N*-acetyl-L-tyrosine—the acylation rate curves for all these substrates being used to determine the formation and hydrolysis rate constants k_2 and k_3 of the acylated enzymes by means of Eqn. (24).[124]

The rate of hydrolysis of amides is limited at the stage of formation of the acylated enzymes ($k_2 \ll k_3$)[97,98]. A more detailed picture of formation of the enzyme–substrate complex X_1 could be obtained for this class of substrates. Use of a combined "stopped flow–temperature jump" apparatus (see below) showed[98] that formation of a reactive enzyme–substrate complex in the hydrolysis of *N*-furoylacryloyl-L-tryptophanamide involves formation of a metastable intermediate compound:

$$E + S \underset{10^4\ s^{-1}}{\overset{6\cdot10^7\ M^{-1}\ s^{-1}}{\rightleftharpoons}} ES \underset{30\ s^{-1}}{\overset{1.5\ s^{-1}}{\rightleftharpoons}} ES' \rightarrow E + P \qquad (25)$$

The rate constants of formation of the primary complex ES and of the conformational change ES $\rightleftharpoons$ ES′ (scheme 25) were determined from an analysis of the rate curve described by the sum of two exponential terms.

The conformational mobility of the active centre of α-chymotrypsin was discovered kinetically from an analysis of the interaction of the acridine colorant Proflavin with the active centre. Analysis of the kinetics of complex formation shows[105] that the active centre exists in solution as two conformations, which are able to bind the colorant at significantly different rates. The concentration ratio of the conformers depends on the pH.

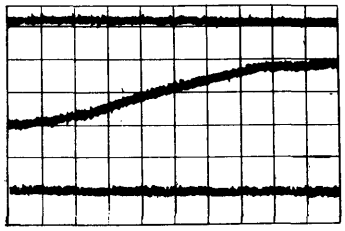


Figure 5. Oscillogram of variations of transmittance after the flash exposure of *cis*-*p*-nitrocinnamoylchymotrypsin (0.1 M KCl + 0.01 M KH_2PO_4 (pH 8.8) at 25°C). The horizontal lines mark 0 and 100% transmittance, and the time base is 0.25 s per large division[109].

A conformational change in the active centre has been recorded at the hydrolysis stage of the acylated enzyme in the hydrolysis of *trans*-*p*-nitrocinnamoylchymotrypsin induced by flash exposure of the *cis*-isomer[109]. Such exposure at the absorption wavelength of the cinnamoyl chromophore (320–360 nm) produces a variation in optical density comprising three kinetically resolved processes (Fig. 5). The reaction mechanism involves three stages:

$$cis\text{-EA} \overset{h\nu}{\rightleftharpoons} trans\text{-EA}' \overset{k}{\rightarrow} trans\text{-EA} \overset{k_3}{\rightarrow} E + P \qquad (26)$$

The spectrophotometric analysis and the pH dependence show that the first, rapid stage involves photochemical *cis*–*trans* isomerisation of the cinnamoyl group in the active centre of the enzyme, whereas the slow concluding stage entails hydrolysis of the resulting *trans*-isomer. The induction period observed on the rate curve for separation of *trans*-nitrocinnamic acid (the stage *trans*-EA′ → *trans*-EA) is probably associated with specific conformational changes in the active centre, which will thus acquire a catalytically active structure.

Thus the detailed kinetic analysis which has hitherto been made of reactions catalysed by α-chymotrypsin shows that the mechanism by which the enzyme acts involves labile intermediate compounds comprising the covalently formed acetylated enzyme, non-covalent complexes, and conformers of the enzyme.

4. Catalase and Peroxidase

The visible absorption spectra of the complexes formed by the haem-containing enzymes—catalase and peroxidase—with hydrogen peroxide and organic peroxides differ substantially from those of the original enzymes. This enabled Chance to monitor directly the formation and consumption of these labile intermediates by the accelerated- and stopped-flow methods using highly sensitive spectrophotometric apparatus[72,73,81,82].

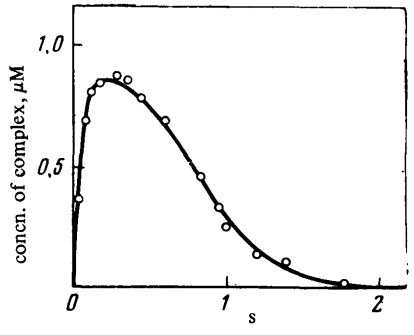


Figure 6. Variation of concentration of peroxidase–hydrogen peroxide complex when 1.0 μM peroxidase and 4.0 μM H_2O_2 solutions are mixed (pH 4.0).[126]

Rapid mixing of solutions of catalase with hydrogen peroxide enabled the rates of formation of the complexes formed by the enzyme with hydrogen peroxide and with organic peroxides to be recorded, as well as the slower rate of disappearance resulting from consumption of the peroxy-compound (Fig. 6). The rate of disappearance of the complex is increased by the presence of electron-donating substrates (aliphatic alcohols and glycols were used for this purpose)[125,128]. These results suggested that the mechanism of the peroxidase action of catalase involved a stage of formation of an intermediate enzyme–substrate compound and a stage of bimolecular reaction of this compound with a donor molecule AH_2:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow[(AH_2)]{k_2} E + P \qquad (27)$$

The formal kinetic description of a two-substrate reaction with one intermediate compound has been discussed [32,125-127]. Provided that the concentration of the second substrate remains almost unchanged during the reaction ($[AH_2] \gg [E]_0$, $[S]_0$) the kinetics of reaction (27) is described by the equations

$$\frac{d[S]}{dt} = k_{-1}[ES] - k_1([E]_0 - [ES])[S] \quad (28)$$

$$\frac{d[ES]}{dt} = k_1([E]_0 - [ES])[S] - (k_{-1} + k_2[AH_2]_0)[ES] \quad (29)$$

The rate constant k_1 was determined [125] in conformity with Eqn. (29) from the initial rate of formation of the intermediate compound when formation of the complex has not proceeded far:

$$k_1 \cong \frac{1}{([E]_0 - [ES])[S]_0} \cdot \frac{d[ES]}{dt} \quad (30)$$

Adding Eqns. (28) and (29) yields the relation

$$\frac{d[S]}{dt} + \frac{d[ES]}{dt} = -k_4[AH_2]_0[ES] \quad (31)$$

Integration of this formula for complete consumption of intermediate compound and substrate ($t = 0$, $[S] = [S]_0$, $[ES] = 0$; $t \to \infty$, $[S] = 0$, $[ES] = 0$) gives

$$k_2 = \frac{[S]_0 \int_0^\infty}{[AH_2]_0 \cdot \int_0^\infty [ES]\,dt} \quad (32)$$

which enables us to find the rate constant k_2 (scheme 27). The integral $\int_0^\infty [ES]dt$ was evaluated numerically from the area bounded by the kinetic curve representing formation and consumption of the enzyme–substrate complex (Fig. 4). Reaction of the complex ES with the donor molecule is bimolecular, but does not involve formation of an enzyme–peroxide–donor ternary complex [129]. Thus the value of k_2 determined for the catalase–methyl hydroperoxide–methanol system was found to be independent of the methanol concentration (0.2–0.08 M).

According to Chance [125] the mechanism of the catalase action of catalase does not differ significantly from that of its peroxidase action. A second hydrogen peroxide molecule acts as donor in this case:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \xrightarrow[[S]]{k_2} E + P \quad (33)$$

The mechanism of catalysis by peroxidase is more complicated than the reaction mechanisms involving catalase. Peroxidase forms at comparable rates two spectroscopically distinct complexes with hydrogen peroxide. Complex (I) is formed immediately on the addition of hydrogen peroxide, and is an unstable green compound rapidly converted into the red complex (II). This conversion takes place more rapidly in the presence of a hydrogen-donor. The general scheme of the process based on fast kinetic measurements can be written [125,130]

$$E + H_2O_2 \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES^I \xrightarrow[(AH_2)]{k_3} ES^{II} \xrightarrow[(AH_2)]{k_4} E \quad (34)$$

$$\searrow AH^\cdot \qquad \searrow AH^\cdot$$

$$2AH^\cdot \to A + AH_2$$

III. STATIONARY STAGE OF REACTION

1. Multistage Catalytic Reactions

Steady-state occurrence of reaction (1) permits considerable simplification of its kinetic description. Experience shows that a steady state is usually established some time after the start of the reaction. This follows from Eqns. (6) and (7), since, at sufficiently large values of t, the concentrations of the intermediate compounds reach constant (stationary) values

$$[X_n]_{t\to\infty} = B \quad (35)$$

while the concentration of the product increases linearly with time

$$[P]_{t\to\infty} = k_{n+1}Bt - k_{n+1}\sum_{j=1}^{n}\frac{A_j}{\lambda_j} \quad (36)$$

provided that consumption of the substrate during the initial period of reaction can in effect be neglected.

The conditions limiting the validity of using the equations of stationary kinetics to investigate the mechanisms of enzymic reactions have been analysed [15,131,132]. If the rate of change of the concentration of the intermediate compounds X_i is much smaller than the rates of change of the concentrations of reaction products and starting materials, each of the derivatives of the intermediate concentrations can be equated to zero: $d[X_i]/dt = 0$ (see Eqns. 3). The problem reduces to the simultaneous solution of $n + 2$ algebraic equations and one differential equation [133-136]. The steady-state reaction velocity in this case is given by the usual Michaelis equation for reversible reactions

$$v = \frac{\frac{V_S}{K_S}[S]_0 - \frac{V_P}{K_P}[P]_0}{1 + [S]_0/K_S + [P]_0/K_P} \quad (37)$$

in which, however, the parameters—the maximum rates V_S, V_P and the Michaelis constants K_S, K_P—are functions of the rate constants of the elementary stages. These quantities have been expressed in terms of the rate constants of the kinetic scheme (1). [133]

Many papers have appeared on the theory of stationary kinetics and its practical application to investigating the specific mechanisms of enzymic reactions [15,131-145]. It must be noted, however, that study of the steady-state kinetics of an enzymic reaction is of very limited value for an understanding of the multistage mechanism of enzyme action. The primary reason is that in general, without the use of additional data, experimental rate constants cannot be assigned unambiguously to elementary chemical stages, since the dependence of the rate of the process on the initial concentrations of S and P will yield only the four kinetic parameters—K_S, K_P and V_S, V_P—whereas the number of rate constants of elementary reactions in process (1) is $2(n + 1)$. Determination of all the elementary constants of reaction (1) obviously becomes impossible when $n > 1$.

Nevertheless, lower limits to rate constants of elementary stages can be determined from steady-state kinetics. The reason is that the parameters of the stationary kinetics are determined by the limiting stage. The lower limit to the rate constant of any unimolecular stage in the forward direction of reaction (1) is given by [133]

$$k_{i+1} \geqslant \frac{V_S}{[E_0]}; \quad i \neq 0 \quad (38)$$

Similarly, for the reverse reaction we have

$$k_{-i} \geqslant \frac{V_P}{[E]_0}; \quad i \neq n+1 \quad (39)$$

These formulae enable data on the stationary kinetics of enzymic reactions to be analysed, and the rates of the slowest stages to be estimated. For this purpose Table 2 lists values of $V_{max}/[E]_0$ for several enzyme systems [12].

These results represent the efficiency of enzymic catalysis. Table 2 shows that rate constants of the limiting processes of unimolecular conversion of intermediate compounds lie in the range 10^2–10^3 s^{-1} for the majority of enzymes.

Table 2.

Enzyme	$V_{max}/[E]_0$, s^{-1}	Enzyme	$V_{max}/[E]_0$, s^{-1}
Acetylcholinesterase	10^3	Kinase	10^3
Chymotrypsin	10^2–10^3	Urease	10^4
Trypsin	10^2–10^3	Fumarase	10^3
Ribonuclease	10^2	Aldolase	10^2
Papain	10	Dehydrogenase	10^3
Carboxypeptidase	10^2	Catalase	10^7
Myosin-ATPase*	10^2	Peroxidase	10

[* ATP = adenosine triphosphate.]

Lower limits to the rate constants can be determined[133] also for the bimolecular stages of reaction (1). They are respectively

$$k_1 \geqslant \frac{V_S + V_P}{[E]_0 K_S} \tag{40}$$

$$k_{-(n+1)} \geqslant \frac{V_S + V_P}{[E]_0 K_P} \tag{41}$$

Table 3 gives the results of analyses[12,133] of the limiting values of rate constants for several specific enzymic reactions. The minimum value of the bimolecular rate constant k_1 for certain reactions (of fumarase) approaches the limit predicted by the theory of reactions controlled by diffusion of the reactants.

The study of stationary kinetics may be useful, not only for estimating lower limits to the reactivity of intermediate compounds, but also for obtaining more detailed information on their properties. However, this requires that the reaction mechanism should be sufficiently well known. As example we consider some results of the investigation of catalysis by α-chymotrypsin.

2. Steady-state Kinetic Study of Intermediate Acylated Enzyme in Catalysis by α-Chymotrypsin

Investigation of the prestationary kinetics of reactions catalysed by α-chymotrypsin showed that the mechanism of catalysis involved a stage of formation and hydrolysis of an intermediate acylated enzyme (scheme 16). The steady-state rate of such a reaction is described by the equation[146]

$$v = \frac{k_{cat}\,[E]_0[S]_0}{K_{m(app)} + [S]_0} \tag{42}$$

where

$$k_{cat.} = k_2k_3/k_2 + k_3 \tag{43}$$

$$K_{m(app)} = K_S k_3/k_3 + k_2; \quad K_S = \frac{k_{-1} + k_2}{k_1} \tag{44}$$

Equations (42)–(44) indicate that the experimental parameters k_{cat} and $K_{m(app)}$ are complicated functions of the rate constants of both chemical stages of the enzymic process. Hence it follows that, with comparable values of k_2 and k_3, such parameters do not characterise the reactivity of any individual intermediate. Nevertheless, abundant experimental information, describing the reactivity both of the enzyme–substrate complex and of the intermediate acylated enzyme, has now been obtained from stationary kinetic data. Apart from certain indirect methods[146] two main approaches have been used for analysing reactivity in catalysis by α-chymotrypsin.

Table 3.

Enzyme	Substrate	$k_{1,min}$, $M^{-1}\,s^{-1}$
β-Amylase	amylose	5.8×10^7
Urease	urea	5.0×10^6
ATPase	ATP	8×10^6
Cytochrome C reductase	cytochrome C	9×10^7
Acetylcholinesterase	acetylcholine	10^9
Fumarase	fumaric acid	0.5×10^8
	L-malic acid	1.6×10^8
	fumaric acid at zero ionic strength	3×10^{10}

(a) Investigation of substrates with a known limiting stage

The rate constant of the limiting stage can be determined from steady-state kinetic data k_{cat} and $K_{m(app)}$ only if the difference in reactivity between the intermediate species ES and EA is sufficiently large. This is evident from Eqns. (42)–(44), whence it follows that, when $k_2 \gg k_3$,

$$k_{cat.} = k_3; \quad K_{m(app)} = K_S k_3/k_2 \tag{45}$$

Different relations hold when $k_3 \gg k_2$:

$$k_{cat.} = k_2; \quad K_{m(app)} = K_S \tag{46}$$

This approach has been used[147–150] to analyse the relation between structure and reactivity k_3 of the intermediate acylated enzymes formed in the hydrolysis of p-nitrophenyl esters of aliphatic carboxylic acids (C_1–C_7).

(b) Determination of elementary constants by selective action on rates of individual stages of enzymic reaction

Use of this method has been considered for a reaction with a single intermediate[151–153]. The approach has been analysed[154–161] for the three-stage catalytic reaction mechanism (16). Thus the reversible inhibiting effect of heavy-metal cations on the acylation stage k_2 of α-chymotrypsin[162–165] or even the effect of the ionic strength of the solution[155] on the same stage has been used for this purpose. Fig. 7 illustrates the effect of ionic strength on the steady-state hydrolysis of the ethyl ester of *N*-benzoyl-L-tyrosine in the presence of α-chymotrypsin. The abscissa of the point of intersection gives[155] the value of $-1/K_S$, and the ordinate $1/k_3$.

However, the method which has been most greatly developed and systematically applied to reactions involving migration of an acyl group is that of competing reactions,

based on competition between water and an added nucleophilic reagent for reaction with the acylated enzyme[156-159, 166]. According to the scheme

$$E + S \underset{}{\overset{K_S}{\rightleftharpoons}} ES \xrightarrow{k_2} EA \begin{cases} \xrightarrow{k_3[H_2O]} E + P_2 \\ \xrightarrow{k_4[N]} E + P_3 \end{cases} \quad (47)$$

the experimental parameters are related to the concentration of the nucleophile by the formulae

$$k_{cat(1)} = \frac{k_2(k_3 + k_4[N])}{k_2 + k_3 + k_4[N]} \quad (48)$$

$$k_{cat(2)} = \frac{k_2 k_3}{k_2 + k_3 + k_4[N]} \quad (49)$$

$$K_{m(app)} = K_S \frac{k_3 + k_4[N]}{k_2 + k_3 + k_4[N]} \quad (50)$$

where $k_{cat(1)}$ and $k_{cat(2)}$ are the kinetic parameters determined by means of Eqn. (42) for the steady-state rates of formation of the products P_1 and P_2 respectively. From the dependence of k_{cat} and $K_{m(app)}$ on the concentration of the added nucleophile, using Eqns. (48)–(50), we can determine separately the rate constants at the stages of acylation and hydrolysis of the acylated enzymes, as well as the equilibrium constant K_S.

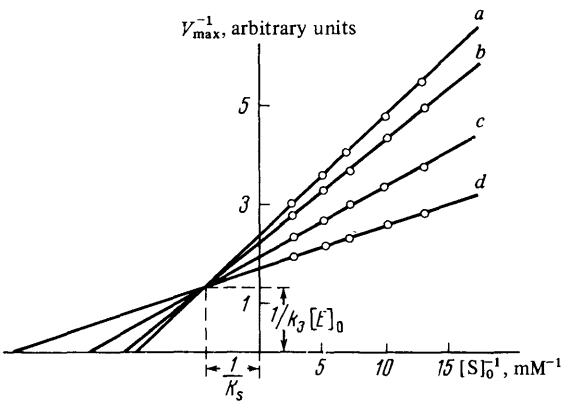


Figure 7. Dependence of initial steady-state rate of α-chymotrypsin hydrolysis of ethyl ester of *N*-benzoyl-L-tyrosine (6 vol.% of acetonitrile with pH 7.8 (pH-stat) at 25°C) on ionic strength (KCl, M): *a*) 0.1; *b*) 0.2; *c*) 0.5.[155]

Among the disadvantages of this technique are uncertainty on the mechanism of the effect of the nucleophile on the acylated enzyme and also the need to allow for the inhibiting effect of the nucleophile[158].

This approach has found systematic application in an investigation[158,159] of the reactivity of intermediate acylated enzymes using butane-1,4-diol as added nucleophile. Rate constants of formation and hydrolysis have been determined[159] for the homologous series of acylated enzymes formed by *N*-acylated derivatives of L-amino-acids. The results enabled certain conclusions to be drawn on the structure of the active centre and the mechanism of the specificity of α-chymotrypsin[147,160].

IV. METHODS OF RELAXATION KINETICS

1. Multistage Catalytic Reactions

Relaxation methods of investigating the kinetics of chemical reactions are based on the principle that, when a system is subjected to a rapid external constraint (change of temperature, pressure, or electric field), the time required for the system to reach a new equilibrium (or stationary) state will depend on the rate of chemical reaction (or sometimes on the rate of diffusion of the reactants). Transition of the system to the new equilibrium reactant concentrations is termed "chemical relaxation"[167]. The external constraint perturbing the system may be either discontinuous (temperature jump, pressure, or electric field pulse) or periodic (ultrasonic absorption). The resolving power of relaxation methods lies between 10^{-5} s (temperature jump) and 10^{-10} s (absorption of ultrasound)[11-13,26]. Formal aspects of the relaxation kinetics of complicated chemical reactions have been discussed[12,26,168,182].

The relaxation kinetics of an enzymic reaction involving *n* intermediate compounds (reaction 1) was analysed by Hammes and Alberty[169] and also by Eigen and Hammes[12]. With the system at equilibrium the concentrations

$$[\bar{E}],\ [\bar{S}],\ [\bar{X}_1] \ldots [\bar{X}_n],\ [\bar{P}]$$

of all the species are constant. When a rapid external constraint is applied, the reactant concentrations assume new values corresponding to the new equilibrium. The instantaneous concentrations of the components can be written

$$([\bar{E}]+\Delta[E]),\ ([\bar{S}]+\Delta[S]),\ ([\bar{X}_1]+\Delta[X_1]) \ldots ([\bar{X}_n]+\Delta[X_n]),\ ([\bar{P}]+\Delta[P]),$$

where the symbol Δ denotes the changes in the reactant concentrations. In order to find the functional dependence of each component concentration on time, we must solve Eqns. (2) and (3). This set of equations will be linear if the displacement of the equilibrium is small. The bimolecular terms $k_1[E][S]$ and $k_{n+1}[E][P]$, which are responsible for the non-linearity of the system, can then be written

$$k_1([\bar{S}]+\Delta[S])([\bar{E}]+\Delta[E]) = k_1([\bar{E}][\bar{S}]+[\bar{E}]\Delta[S]+ +[\bar{S}]\Delta[E]+\Delta[S]\Delta[E])$$

and hence

$$k_{(n+1)}([\bar{E}][\bar{P}]+[\bar{E}]\Delta[P]+[\bar{P}]\Delta[E]+\Delta[P]\Delta[E]).$$

For a small shift of the equilibrium, terms containing Δ^2 can be neglected. Hence Eqns. (2) and (3) can be simplified to

$$\frac{d\Delta[S]}{dt} = a_{1,1}\Delta[S] + \sum_{j=1}^{n} a_{i,j+1}\Delta[X_j]$$
$$\frac{d\Delta[X_j]}{dt} = a_{j,1}\Delta[S] + \sum_{j=1}^{n} a_{i,j}\Delta[X_j] \quad (51)$$

where the constants $a_{i,j}$ are functions of the rate constants of the elementary chemical reactions and the initial equilibrium concentrations of the components of the reaction

$$E + S \underset{k_{2,1}}{\overset{k_{1,2}}{\rightleftharpoons}} X_1 \underset{k_{3,2}}{\overset{k_{2,3}}{\rightleftharpoons}} \ldots \rightleftarrows X \rightleftarrows \ldots \underset{k_{n+1,n}}{\overset{k_{n,n+1}}{\rightleftharpoons}} X_n \underset{k_{n+2,n+1}}{\overset{k_{n+1,n+2}}{\rightleftharpoons}} E + P \quad (52)$$

Somewhat as for the set of equations (4), a general solution can be sought (accurate to a constant) in the form

$$\Delta[S] = \sum_{j=1}^{n+1} A_j e^{\lambda_j t}$$
$$\Delta[X_j] = \sum_{j=1}^{n+1} B_{i,j} e^{\lambda_j t} \quad (53)$$

where the λ_j are the roots of the characteristic equation of degree $n + 1$.

An important conclusion which follows from the above survey is that, when n intermediate compounds are involved, the number of exponential terms is $n + 1$. Thus the number of exponentials observed experimentally can be regarded as a criterion of the minimum number of intermediate compounds taking part in the reaction. The measured relaxation times $-1/\lambda_j$ are functions of all the rate constants of elementary reactions and the equilibrium concentrations of the reactants.

Table 4.

Enzyme	Substrate or activator	Ref.
Alcohol dehydrogenase	NAD-imidazole	176
Aspartate aminotransferase	aspartic, glutamic, oxosuccinic, oxoglutaric acids	177
	α-methylaspartic acid	178
	erythro-β-hydroxyaspartic acid	179
Aspartate transcarbamoylase	5-bromocytidine phosphate	180
	carbamoyl phosphate, L-malic and succinic acids	183-185
Glyceraldehyde 3-phosphate dehydrogenase	NAD	186-192
Acid phosphatase	*p*-nitrophenyl phosphate	193
Creatine kinase	creatine phosphate	194
Lactate dehydrogenase	NADH	195,196
Lysozyme	saccharides	197,198
	Biebrich Scarlet	199
Malate dehydrogenase	NADH, malic acid	200,201
Pyruvate kinase	bivalent metal ions, ADP	202
Ribonuclease	nucleotides	202-209
	isomerisation	210-213
Serine dehydrogenase	isomerisation	214
Serine transhydroxymethylase	glycine	215
Trypsin	isomerisation	210,211
	proflavin-benzamidine	174,216
Tryptophan synthetase	L-serine, indole, tryptophan	217,218
Urease	urea	219
Flavodoxin	interaction of coenzyme with apoprotein	220-222
Chymotrypsin	Proflavin	175,223,224
	Proflavin and methyl ester of *N*-toluene-*p*-sulphonyl-L-arginine	225
	Biebrich Scarlet	226
	isomerisation	211
Cytochrome C	hexacyanoferrate(II)	175

Particular cases of scheme (52) (one and two intermediate compounds) and specific approaches to determining the rate constants of elementary stages have been described[13,167-173]. It has been shown[13,26,174] that data on relaxation amplitudes may prove useful, besides kinetic data (relaxation times), in the analysis of reaction mechanisms.

Many enzyme systems have now been studied by relaxation methods. Those listed in Table 4 have been examined mainly by the temperature-jump method. A rapid change of temperature is usually effected by discharging a high-voltage capacitor through the reaction cell containing, in addition to the reactants, a certain quantity of an inert electrolyte to lower the electrical resistance. A temperature change of 3–10 deg occurs within 10^{-6} s.[11-13] Equipment combining stopped-flow and temperature-jump apparatus was proposed for the kinetic investigation of fast reversible stages preceding the *irreversiole* limiting stage[175]. The temperature jump can be effected in an interval from milliseconds to a few seconds after cessation of flow. Further shortening of the "dead" time of the "temperature jump" method entails the use of laser illumination to heat up the reaction cell[227,228].

The possibilities of using flash photolysis to study the relaxation kinetics of enzyme reactions have been discussed[229-231]. In this case the equilibrium is changed as a consequence of a concerted fast photochemical reaction. Light-induced rapid changes in pH (flash-induced pH jump) merit special attention[229].

2. Aspartate Transaminase and Ribonuclease

A review[232] of the study of enzyme reactions by relaxation methods discusses the mechanisms of the following—(i) reactions of aspartate transaminase with amino- and keto-acids, (ii) reaction of cytochrome C with ferrocyanide, (iii) reaction of alcohol dehydrogenase with NAD–imidazole and the combination of NADH with malate and lactate dehydrogenases, (iv) hydrolysis of *p*-nitrophenyl phosphate by acid phosphatase, and (v) reactions of pancreatic ribonuclease A. Table 4 shows that the reaction mechanisms of aspartate transaminase and ribonuclease have been studied in greatest detail. These examples give an idea both of the possibilities of relaxation kinetics and of the achievements of enzymology in investigating the mechanisms of enzymic catalysis.

Aspartate aminotransferase (AAT) catalyses the reversible transfer of an amino-group between aspartic and oxoglutaric acids with the formation of oxosuccinic and glutamic acids:

$$\begin{array}{l} \overset{\ominus}{\mathrm{COO}}\mathrm{CH_2CH}\overset{\ominus}{\mathrm{COO}} + \overset{\ominus}{\mathrm{COO}}(\mathrm{CH_2})_2\,\mathrm{COC}\overset{\ominus}{\mathrm{OO}} \xrightleftharpoons{\mathrm{AAT}} \\ \quad\quad\quad\

studied, and rate constants characterising the individual stages were determined (or estimated). The spectral characteristics of the intermediates showed them to be probably covalent compounds of the substrate with pyridoxal phosphate, including Schiff bases.

Besides the stages that were studied, more rapid spectral changes were observed in the reaction of aspartate aminotransferase, whose kinetics could not be analysed by the temperature-jump technique. In order to slow down these stages, the reaction of the enzyme with certain modified substrates was investigated. The analogous L-α-methylaspartic acid is a competitive inhibitor of amino-acid substrates and able to form an aldimine with pyridoxal phosphate on the enzyme. Because of the presence of the α-methyl group, however, transamination cannot take place. Kinetic study of this system by a combined "stopped-flow–temperature jump" method revealed that the reaction occurred in three stages[178]:

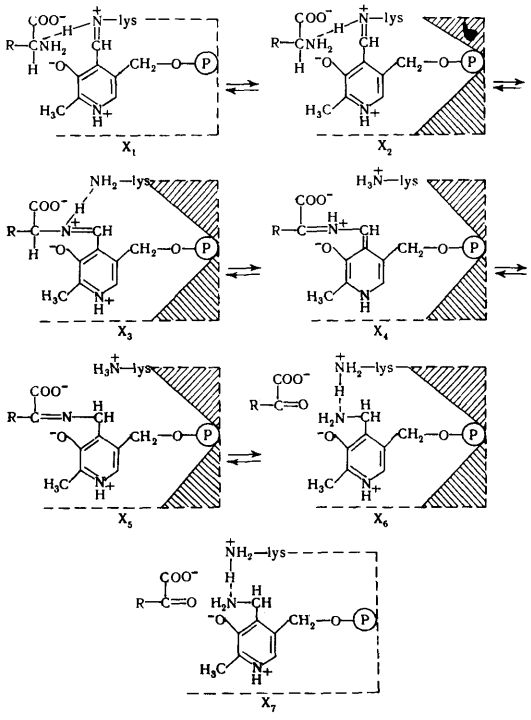
$$E + S \rightleftarrows X_1 \rightleftarrows X_2 \rightleftarrows X_3 \qquad (56)$$

All the rate constants in this mechanism were determined, and the spectral properties of the intermediate compounds were studied. The reaction was regarded[178] as involving formation of a primary complex X_1, followed by a conformational change ($X_1 \rightleftharpoons X_2$) and formation of an aldimine X_3.

The *erythro*-isomer of L-β-hydroxyaspartic acid is a substrate of the enzyme, but transamination occurs very slowly. Eight relaxation times were detected[179] in the reaction of this substrate with aspartate transaminase. The simplest mechanism consistent with this finding is

$$E_l + S \rightleftarrows X_1 \rightleftarrows X_2 \rightleftarrows X_3 \rightleftarrows X_4 \rightleftarrows X_5 \rightleftarrows X_6 \rightleftarrows X_7 \rightleftarrows E_m + S' \qquad (57)$$

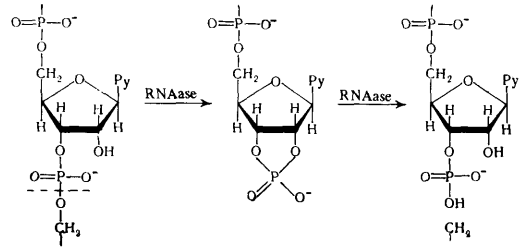
where S' represents the keto-form of the substrate. Detailed analysis of the concentration dependence of relaxation times and equilibrium constants enabled 14 and 16 rate constants to be calculated representing mechanism (57). Furthermore, the spectral characteristics of the intermediates were determined. A suggested reaction mechanism consistent with the results can be represented by the scheme[234]



(58)

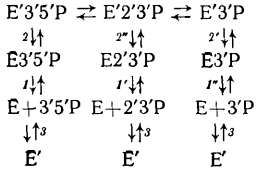
The first three intermediates have spectral characteristics similar to those of compounds X_1, X_2, and X_3 in the reaction of L-α-methylaspartic acid, and at these stages the reaction probably also terminates in formation of an aldimine (X_3). The intermediate X_4 has absorption maxima at 460 and 490 nm, the molar absorption at the latter wavelength exceeding 10^5 M^{-1} cm^{-1}. According to the authors[179] this compound has a quinoid structure; the other three compounds have absorption maxima in the region of 330 nm and are ketimines (scheme 58).

Hammes studied the mechanism of the action of ribonuclease A in as great detail as that of catalysis by aspartate aminotransferase[203–209]. The reaction catalysed by the former enzyme involves transesterification of a 3',5'-dinucleotide with formation of a 2',3'-cyclophosphate, followed by hydrolysis of the cyclic phosphate with formation of a 3'-nucleotide:



(59)

Synthetic substrates were used to investigate the relaxation kinetics, which considerably simplified the kinetic analysis. The interaction of the enzyme was studied with all three classes of substrates. On the basis of these investigations the "minimal" mechanism



(60)

was suggested. With each class of substrates (3',5'-dinucleotides, 2',3'-cyclophosphates, and 3'-nucleotides) the reaction involves a bimolecular stage of formation of the primary complex (stages *1*, *1'*, *1''*), followed by its isomerisation (stages *2*, *2'*, *2''*). Furthermore, examination of the free enzyme showed that it existed in two conformations (stage *3*). Comparison of these kinetic results with X-ray diffraction data[235,236] enabled a detailed mechanism to be postulated for the action of the enzyme[209,232].

The investigations on the mechanisms of the action of aspartate aminotransferase and ribonuclease A provide an excellent illustration of the possibilities and achievements of "fast" kinetic methods for studying the mechanisms of enzymic catalysis. The results of these investigations may be instructive for the choice of approaches to the study of other catalytic systems.

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Fixation of Nitrogen in Solution in the Presence of Transition Metal Complexes

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The review presents the results of studies in the last decade on the reduction of molecular nitrogen in aprotic and protic media. The products, intermediate complexes, and mechanisms of these reactions are considered. The relation between the mechanisms of the N_2 reduction reactions discovered recently and the mechanism of biological nitrogen fixation is discussed. The bibliography includes 161 references.

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I. INTRODUCTION

Ten years have elapsed since the discovery by Vol'pin and Shur of the first system fixing molecular nitrogen in solutions of transition metal complexes[1]. During this period, the concepts of the chemistry of N_2 have undergone radical changes. In the first place it was found that nitrogen readily reacts with many low-valent transition metal derivatives to form complex nitrides and also derivatives of hydrazine and organonitrogen compounds. In a study of the reaction of hydrazine with $RuCl_3$ in 1965, Allen and Senoff obtained for the first time a complex of molecular nitrogen[2]. After several months, a similar complex was obtained directly from molecular nitrogen[3]. These studies gave rise to a new field of coordination compounds in which N_2 enters as a ligand into the coordination sphere of the metal. It was discovered that in the formation of complexes nitrogen can be very reactive, competing successfully for a coordination site with ammonia and water, for example, and complexes containing N_2 in the coordination sphere are sometimes very stable and withstand heating to 200°C.

Contrary to the expectations of the chemists who synthesised them, the N_2 complexes discovered in the first years proved to be incapable of activating nitrogen with respect to further reactions, for example with respect to reduction to ammonia. It was not until 1969 that intermediate nitrogen complexes capable of undergoing further reactions were detected[4] and in some cases subsequently isolated and investigated.

Finally, systems in which nitrogen is reduced to hydrazine and ammonia in aqueous and aqueous alcoholic solutions in the presence of molybdenum and vanadium complexes, sometimes even at room temperature and atmospheric pressure[5,6], were discovered in 1970.

Thus nitrogen ceased to be an inert gas, which had been thought capable of reacting under the usual conditions only with metallic lithium. On the other hand, the biological fixation of nitrogen achieved by many bacteria and algae in the presence of water and oxygen at the normal temtemperatures and pressures, which had previously been completely puzzling, has now lost its unique features.

The studies on the biological fixation of nitrogen in recent years permit conclusions concerning the mechanism of this reaction. The involvement of transition metal (iron and molybdenum) compounds in the reduction of N_2 can now be regarded as proved and the relation between the enzymatic process and its chemical models is becoming increasingly clear. Whereas previously biological fixation of nitrogen, which indicated the possibility in principle of N_2 reactions under mild conditions, led chemists to seek non-enzymatic model systems, nowadays further progress towards the understanding of the mechanism of the enzymatic process is undoubtedly associated with the investigation of non-biological models, where the investigation of the mechanism is always simpler than in biological systems.

Further simulation of the biological fixation of nitrogen and the study of the mechanism of enzymatic fixation can probably be carried out simultaneously, with a comparison of the results of experiments under enzymatic and non-enzymatic conditions. Such a comparison will be made in the concluding section of the present review.

The review does not deal with the results of studies on stable nitrogen complexes with transition metal compounds (see for example the reviews in the literature[7-9] concerning these substances).

II. GENERAL CONSIDERATIONS

Nitrogen fixation is understood as a process involving complete or partial dissociation of the N≡N bond. This process can be oxidation or reduction of nitrogen depending on whether the electronegativity of the atoms forming a bond with nitrogen is greater or smaller than that of nitrogen. Since reactions in which nitrogen is oxidised by molecular oxygen with formation of oxidation products such as N_2O, NO, NO_2, and N_2O_5 are endothermic, at low temperatures the equilibria are displaced towards the formation of free N_2 and O_2. Oxidants more powerful than oxygen are capable, in principle, of oxidising nitrogen; for example, it has been stated that molecular oxygen in its excited singlet state reacts with N_2 to form nitrogen oxides[10]. Oxygen atoms and carbenes can react with nitrogen to form N_2O and diazo-compounds[11-14]. However, the majority of known reactions involving nitrogen, which occur under mild conditions, may be regarded as reductive. Reagents which are thermodynamically capable of interacting with N_2, including metals and hydrogen, behave

as electron donors in relation to N_2. This review is therefore concerned with the reduction of molecular nitrogen in solutions.

The nitrogen molecule has certain characteristic features which distinguish it from other related unsaturated compounds, for example acetylene (see, for example, Borod'ko and Shilov [7]).

In the first place, in the dissociation of a triple bond most of the energy (about 130 out of 225 kcal) is consumed in the dissociation of the first linkage [15,16]. This determines the stability of the nitrogen molecule in relation to one- or two-electron reactions, i.e. reactions in which the dissociation of one π-linkage in nitrogen results in the formation of one or two new linkages with the latter. For example, the H_2 molecule and even the H atom are incapable of adding to nitrogen, since the formation of a single N–H bond (on addition of the H atom) or of two N–H bonds (on addition of the H_2 molecule) do not compensate the energy expended on the dissociation of the π-linkage in the nitrogen molecule (and of the H–H bond when H_2 is added) and these reactions are strongly endothermic:

$$\cdot H + N_2 \rightarrow \cdot N_2H - 21 \text{ kcal, (Ref.16)}$$

$$H_2 + N_2 \rightarrow N_2H_2 - 49 \text{ kcal.}$$

On the other hand, similar reactions involving carbon–carbon π-linkages are strongly exothermic. For example, we have for acetylene

$$\cdot H + C_2H_2 \rightarrow \cdot C_2H_3 + 40 \text{ kcal,}$$

$$H_2 + C_2H_2 \rightarrow C_2H_4 + 42 \text{ kcal.}$$

After the dissociation of the first π-linkage in nitrogen and the formation of an azo-compound, further successive dissociations of each of the remaining two linkages requires much less energy, so that, following the addition of three H_2 molecules to the N_2 molecule, the overall energy of the N–H bonds compensates the energy expended on the dissociation of the triple bond and the overall ammonia formation reaction is exothermic. These thermodynamic characteristics of the reactions of molecular nitrogen to a large extent determine its behaviour on reduction.

Only very powerful reducing agents (such as metallic lithium) are capable of undergoing the one-electron reactions

$$\cdot X + N_2 \rightarrow X{-}N{=}N\cdot$$

The intermediate formation of the $\cdot N_2H$ radical in aqueous solution, suggested by Bauer [17], appears very unlikely at present.

The two-electron processes $X_2 + N_2 \rightarrow XN_2X$ are much more favourable from the thermodynamic standpoint and are probably more common. However, if one begins with molecular hydrogen, then not only the reaction where the final product is di-imide(N_2H_2) but also the hydrogenation of nitrogen to ammonia with the intermediate formation of di-imide cannot occur at normal temperatures, since the activation energy for this reaction must be not less than 49 kcal, which corresponds to a negligible rate. This explains the finding that the usual hydrogenation catalysts, which catalyse the addition of hydrogen to olefins and acetylenes, are incapable of catalysing the hydrogenation of nitrogen.

In order to explain the reduction of nitrogen via the N_2H_2 stage under mild conditions (for example under the conditions of the biological fixation of nitrogen), it has been suggested [18] that the formation of N_2H_2 may be accompanied by the coupled exothermic oxidation reaction, the energy of which exceeds the deficit of energy for the formation of N_2H_2. Later, it was shown that the biological fixation of nitrogen does not require coupled oxidation, so that this mechanism is not obligatory (although of course in certain yet unknown cases it may operate).

New possibilities of obviating the thermodynamic difficulties in the reduction of molecular nitrogen are discovered when account is taken of the formation of intermediate mononuclear and dinuclear complexes of nitrogen with transition metal compounds:

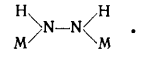
$$M + N_2 \rightleftarrows MN_2;\ MN_2 + M' \rightleftarrows MN_2M'.$$

Here and henceforth M is a transition metal compound.

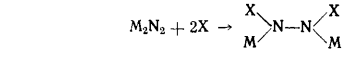
The reduction potential of M (as usually understood, i.e. corresponding to a one-electron transfer)† can be much lower in the formation of the complex than is required for the dissociation of a single π-linkage in the nitrogen molecule (the complexes formed are stabilised by the interaction of the filled *d* orbitals of M and the π orbitals of nitrogen). The subsequent two-electron reduction of nitrogen in the complex, even with the intermediate formation of di-imide, can be facilitated when di-imide forms a complex with M or M', [19] the heat of formation of the di-imide complex being greater than the heat of formation of the complex with molecular nitrogen.

Indeed, comparatively stable complexes of metal compounds with di-imide and its derivatives are known, although hitherto they have been obtained largely from sources other than molecular nitrogen. For example, when hydrazine reacts with $CuCl_2$, a copper(I) complex of di-imide is formed [20]. It has been shown by X-ray diffraction analysis [21] that zero-valent nickel forms a mononuclear complex with azobenzene, which has a structure of the type of π-complexes with olefins, where the interatomic distance $r(N{-}N) = 1.385$ Å, which is close to the length of a single N–N bond in hydrazine and evidently corresponds to an appreciable electron transfer to N_2Ph_2. The authors [21] regard this complex as a model of the intermediate complex with N_2H_2 in nitrogen fixation.

If a complex of this kind has a dinuclear structure, it can evidently be regarded as a hydrazine derivative:



In this connection it is easy to imagine a mechanism [7,16] in which the initial dinuclear complex with N_2 is converted into a hydrazine derivative in a single stage under the influence of an additional two-electron reducing agent 2X:



The dissociation of two π-linkages at once in the four-electron reduction under the influence of four atoms of a one-electron reducing agent is much more favourable on energy grounds than the dissociation of a single π-linkage in a two-electron process. Thus the reaction

$$N_2 + 2H_2 \rightarrow N_2H_4 - 22 \text{ kcal}$$

involves the expenditure of 27 kcal less than in the formation of di-imide from N_2 and H_2.

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†The reduction potential E_0 is reckoned from the hydrogen potential and corresponds to the free energy of the reaction $M + H^+ \rightarrow M^+ + \frac{1}{2}H_2$ at pH 0. In the present review we are dealing with reducing agents more powerful than hydrogen and having negative values of E_0. The potential will be regarded as higher or lower if its absolute value is correspondingly greater or smaller.

Thus the M_2N_2 complex can play the role of a seed where the subsequent four-electron process removes or diminishes the thermodynamic difficulties which exist in successive one- or two-electron reduction.

The reducing agent X can exist in solution independently of the complex or can be linked to M (for example, the hydrogen atom in the hydride M–H linkage). A fairly common special case of this "four-electron" mechanism may involve the employment of additional electrons from one or both atoms of M forming the complex with N_2. For example, one can formulate the reactions

1. $M_2N_2 + X \rightarrow M{=}N{-}\overset{\displaystyle X}{\overset{|}{N}}{-}M$
2. $2M + N_2 \rightarrow M{=}N{-}N{=}M$ or

(in the second case the dinuclear complex is evidently no longer a hydrazine derivative). The latter reaction is possible when M is a fairly powerful two-electron reducing agent.

It is significant that the formation of complexes with transition metals makes it possible to distribute the dissociation energy of the π-linkages of N_2 in uniform steps, while the "usual" one- or two-electron reduction requires the main energy expenditure in the first stage, i.e. requires a particularly powerful reducing agent.

The consideration of the reduction of nitrogen in protic media, in particular in an aqueous medium, is of considerable interest. In this instance, which occurs, for example, in the biological fixation of nitrogen, solven protons are employed for forming the hydrogen atoms of ammonia:

$$N_2 + 6\bar{e} + 6H^+ \rightarrow NH_3 .$$

The thermodynamics of the successive reduction of nitrogen becomes more favourable in aqueous solution compared with non-polar media, since ammonia, hydrazine, and probably di-imide are hydrated in water with a considerable energy gain, while the initial molecular nitrogen is hardly hydrated at all. The table below lists the enthalpies of formation of ammonia and the intermediates from the elements in the gas phase, in water, and acid solution.

	$N_2 \xrightarrow{H_2} N_2H_2$	$N_2H_2 \xrightarrow{H_2} N_2H_4$	$N_2H_4 \xrightarrow{H_2} 2NH_3$
$\Delta H_{298(gas)}$, kcal mole^{-1}	49	22.7	−22
(Soln. H_2O)	(33.5) *	8.2	−38.4
(Soln. in acid)		−1.8	−64

*On the assumption that the heat of hydration of N_2H_2 is close to the heat of hydration of the N_2H_4 molecule and two NH_3 molecules.

However, in the aqueous phase the reaction with the intermediate formation of di-imide requires reducing agents which are more powerful than molecular hydrogen. An approximate estimate yields −1.1 V for the reduction potential of di-imide in water. Under these conditions, a new difficulty arises in the aqueous solution because reducing agents having reduction potentials much higher than that of molecular hydrogen cannot exist in water, since they must react with the latter to form molecular hydrogen:

$$M + H_2O \rightarrow M^+ + OH^- + \tfrac{1}{2}H_2 .$$

Therefore one- or two-electron reduction of nitrogen in aqueous solution with the intermediate formation of N_2H_2 is virtually impossible.

The reduction potential of M can be much lower than −1.1 V if a four-electron reduction mechanism is adopted. Reducing agents having a reduction potential sufficient to convert nitrogen into hydrazine (−0.23 V) are known and can exist in aqueous solution (for example Cr^{2+} or V^{2+} salts).

Protonation of N_2 in the M_2N_2 complex by an acid or the formation of a hydrogen bond with a water molecule facilitates the four-electron reduction with formation of a hydrazine derivative:

$$M_2N_2 \overset{H^+}{\rightleftarrows} M{=}N{-}\overset{\displaystyle +}{\underset{\displaystyle H}{N}}{=}M \leftrightarrow M{=}N{-}\underset{\displaystyle H}{N}{-}M^+ \xrightarrow{H^+} N_2H_4 .$$

Thus the four-electron mechanism of the reduction of nitrogen with formation of a dinuclear complex ensures, in principle, the possibility of reducing N_2 to hydrazine (as the intermediate or final product) in an aqueous medium.

However, when the reaction proceeds via hydrazine or its derivative, the free energy of the process (bearing in mind the impossibility of the existence of an unduly powerful reducing agent in aqueous solution) must be close to zero. This imposes significant limitations on the thermodynamic properties of the catalyst M which ensures the reduction of nitrogen. Its reduction potential must not be higher than that of the reducing agent and, on the other hand, it cannot be too small, since M must itself be a reducing agent strong enough to reduce nitrogen.

Under these conditions, it is necessary that the heat of formation of the complex M_2N_2 should also be optimal. With increase and decrease of the stability of the complex, the rate of reaction should rapidly decrease, in the first case owing to a decreased rate of reduction of bound nitrogen and in the second owing to a lower concentration of the intermediate complex.

Apparently the stability of dinuclear complexes with N_2 can vary within wide limits and is not related directly to the reduction potential of M, since many stable N_2 complexes are known both with powerful and weak reducing agents. Thus, in order to select a catalyst M for an aqueous medium, capable of catalysing the reducing of nitrogen with formation of hydrazine as an intermediate or final product, one must begin with the fact that both the reduction potential of M and the M–N bond energy must be restricted to comparatively narrow limits. It becomes clear from the foregoing discussion why rapid reduction of nitrogen in an aqueous medium must be a rare exception among the large number of reduction systems. We may note that a combination of suitable thermodynamic properties of the catalyst M is by itself insufficient for the reaction with nitrogen, since the reaction requires that M must have also a suitable ligand environment (a free site for nitrogen, accessibility to the action of the reducing agent) and the two atoms M in the initial complex must be separated by an appropriate distance.

Table 1 shows that on passing to acid media it is possible to employ even weaker reducing agents, since protonation stabilises the resulting hydrazine (or ammonia). However, one must bear in mind that at low pH values the reaction between the reducing agent and water to liberate hydrogen, which is usually catalysed by acids, is accelerated.

The increase of pH on passing to alkaline media can increase the reduction potential of M, since in the reaction

$$M + OH^- \rightarrow MOH + e$$

the reduction potential increases linearly with pH ($E_0 = E_0^0 + 0.059pH$). However, one must also take into account the fact that in the reactions

$$N_2 + 4e + 4H_2O \rightarrow N_2H_4 + 4OH^-,$$
$$N_2 + 6e + 6H_2O \rightarrow 2NH_3 + 6OH^-,$$

and also in

$$2e + H_2O \rightarrow {}^1/_2H_2 + OH^-,$$

the reduction potentials of NH_3, N_2H_4, and H_2 likewise increase linearly with pH, the slope being the same as for M and therefore the difference between the reduction potentials ΔE will be independent of pH. An alkaline medium will in fact favour the thermodynamics of the reduction of nitrogen in those cases where the dependence of the redox potential on Ph is more marked than for hydrazine, which should imply the formation in an alkaline medium of certain new compounds which are more powerful reducing agents than the compound existing in an acid medium [as, for example, in the case of titanium(II) salts, which are moderately strong reducing agents in an acid medium, while in an alkaline medium they liberate hydrogen from water]. Evidently, this corresponds to the formation of ionised species with a high effective negative charge at the metal atom of the reducing agent.

This discussion is based on the assumption that the most economical pathway to the reduction of nitrogen from the standpoint of energy expenditure is the formation of hydrazine derivatives from the complex with N_2.

If account is taken of the possibility of six-electron reduction of nitrogen directly to ammonia, then the process should, in principle, be achieved by weaker reducing agents. However, the probability of such a mechanism is itself apparently very low, since it requires simultaneous and considerable shifts of a large number of nuclei in a single step[22].

Thus preliminary consideration of the possible involvement of transition metal compounds in the reactions involving the reduction of molecular nitrogen shows how the formation of intermediate complexes can give rise to a mechanism in which the thermodynamic difficulties involved in the reduction of N_2 are overcome.

III. REDUCTION OF NITROGEN IN APROTIC MEDIA

1. Nitrogen-fixing Systems

Vol'pin and Shur discovered in 1964 the reduction of nitrogen at room temperature in ethereal and hydrocarbon media in the presence of transition metal compounds ($CrCl_3$, $MoCl_5$, WCl_6, $FeCl_3$, $TiCl_4$) when they react with powerful reducing agents ($LiAlH_4$, EtMgBr, i-Bu_3Al).[1] Ammonia was isolated after the hydrolysis of the reaction product in the presence of nitrogen. The results were then confirmed[23] in experiments with labelled $^{15}N_2$ nitrogen.

Some of these and similar systems were known previously and were used in catalysis, particularly as catalysts of the polymerisation and hydrogenation of olefins and acetylenes. Thus their capacity to activate unsaturated compounds was known.

Moreover, many investigators flushed their systems with nitrogen, which they regarded as inert and there is evidence (see, for example, Refs. 24 and 25) that in the presence of nitrogen certain differences in the behaviour of such systems compared with that *in vacuo* or in an atmosphere of argon were observed even before 1964. Nitrogen sometimes retarded the catalytic polyermisation reaction. Ammonia was actually isolated from the products of the reaction carried out in an atmosphere of nitrogen. Nevertheless, the widely held view that nitrogen is inert evidently prevented many investigators from reaching definite conclusions concerning this reaction before 1964 and this is why Vol'pin and Shur's work initiated a new stage in the study of the reduction of nitrogen in solution.

In the first experiments of Vol'pin and Shur appreciable yields of the reduction product [up to 25% of ammonia (after the hydrolysis of the product) relative to the amount of transition metal employed] was observed at comparatively high nitrogen pressures (150 atm). Soon Vol'pin and his coworkers succeeded in obtaining more active systems. Thus in the reaction of N_2 with the products of the reaction of Cp_2TiCl_2($Cp = \pi$-C_5H_5) with EtMgBr in ether the yield of ammonia (after hydrolysis) was 67% per mole of the titanium compound employed, even at atmospheric pressure[26]. On increasing the pressure, the yield of ammonia became nearly quantitative.

Later it was shown[27] that free metals, for example, magnesium activated by iodine, can be used as reducing agents and that simple purely inorganic systems such as $TiCl_4 + Mg(MgI_2) + N_2$ can be used to reduce nitrogen.

Evidently, the role of the non-transition metal or the organometallic compound consists primarily in the reduction of the transition metal compound, such reduction being known to proceed frequently via alkyl or aryl derivatives of transition metals. Indeed, it has been found[28] that the reduction of nitrogen can be carried out also without a specially added reducing agent on heating solutions of dialkyl and diaryl derivatives Cp_2TiR_2 in an atmosphere of N_2. In this case nitrogen is reduced under the influence of low-valent titanium derivatives formed as intermediates or as final products of the thermal decomposition of the organotitanium compounds.

The reduction of nitrogen (albeit with a low yield of the product) has been observed also on heating with nitrogen a previously prepared solution of dicyclopentadienyltitanium(II).[28] Thus molecular nitrogen was found to be capable of reacting in solution with many transition metal compounds.

Subsequent studies in many laboratories in different countries led to the discovery of various systems interacting with nitrogen (see the appropriate reviews[24,25,29-33]).

The range of transition elements and reducing agents is now very large: Henrici-Olive and Olive[34] and also van Tamelen et al.[35] used successfully as reducing agents naphthalene derivatives of alkali metals (lithium, sodium, and potassium). Bayer and Schurig[36] showed that alkali metals (Li, Na, K, Rb, and Cs), alkaline earth metals (Mg and K), and the lanthanides (La and Ce) can serve as reducing agents.

Bell and Brintzinger obtained about 1 mole of ammonia (after hydrolysis) per mole of $FeCl_3$ using as a reducing agent the doubly charged anion formed by treating 2,6-dimethylnaphthalene with lithium[37].

Apart from the transition metal compounds already mentioned, vanadium[34,38], manganese[39], and cobalt[27,39] chlorides, tetraalkoxy-derivatives of titanium[40-43], vanadium, chromium, molybdenum, manganese, and nickel acetylacetonates[40], cyclopentadienyl derivatives of zirconium[36] and niobium[44], and triphenylphosphine complexes of titanium[45] and iron[39] proved to be active.

Negative results have also been published. For example, dicyclopentadienyltitanium dichloride, which forms an exceptionally active system with organomagnesium compounds, does not reduce nitrogen in the presence of tri-

isobutylaluminium[30]. The explanation is probably that in the latter case the reduction terminates with the formation of stable titanium(III) complexes[46,47]. Cobalt and manganese compounds proved to be inactive in many cases[30].

Nickel, palladium, copper, and platinum compounds apparently could not be used at all in systems reducing N_2 in solutions[1,30,39].

The yields of ammonia (after the hydrolysis of the products) are extremely varied and in different systems can amount to between a fraction per cent and one mole of ammonia per mole of the transition metal compound employed. In several cases between one and two moles of ammonia are formed per mole of the transition metal.

It was reasonable to attempt the catalytic reduction of nitrogen, for example by a catalytic hydrogenation process. It was found that hydrogen usually inhibits the reaction, lowering the yield of the product[36,40,48] even in those systems where catalytic hydrogenation of olefins is possible. In some cases hydrogen does not have much influence on the yields of products (for example, in the reactions involving vanadyl and molybdenyl acetylacetonates with LiBu). In certain systems, for example, $Ti(OEt)_4$ + $(i\text{-}Bu)_3Al + N_2$, an appreciable increase of the yield of ammonia (after hydrolysis) was observed following the introduction of molecular hydrogen[40]. However, with increase of hydrogen pressure, the yield of ammonia passes through a maximum (increasing approximately by a factor of 1.5) and then falls.

In none of the instances was catalytic hydrogenation observed. However, Vol'pin and his coworkers[39,49,50] achieved the catalytic reduction of nitrogen under the influence of a more powerful reducing agent. Thus metallic aluminium reduces nitrogen at 130°C and a pressure of 100 atm in the presence of titanium tetrachloride and aluminium bromide. Metallic aluminium without additives is known to react with nitrogen only at much higher temperatures. The yield of ammonia after hydrolysis can reach hundreds of ammonia molecules per molecule of the added titanium compound. The reaction takes place in benzene or aluminium bromide melt, which (like titanium tetrachloride) is necessary for catalytic reduction.

Lithium aluminium hydride can be used as a reducing agent instead of aluminium. In this case up to 100 moles of ammonia (after hydrolysis) per mole of the initial titanium tetrachloride can be formed even at 60–70°C when the reactions are performed in a molten mixture of aluminium bromide and chloride. A catalytic system can also be obtained (up to 10 moles of ammonia per mole of titanium) when the nitrogen–hydrogen mixture is heated to 130°C with a mixture of $(BuO)_4Ti + (i\text{-}Bu)_3Al + AlBr_3$ in the presence of benzene. Hydrogen activates the system in this case, since in its absence only two moles of ammonia per mole of titanium are obtained.

Here we may note that, although catalytic hydrogenation of nitrogen has not so far been observed in solutions, Japanese workers showed recently that the introduction of alkali metals strongly activates heterogeneous catalysts of the gas-phase synthesis of ammonia. Thus Tamaru and coworkers[51,52] observed that the reaction of iron, cobalt, titanium, and molybdenum complexes of phthalocyanines with metallic sodium resulted in the formation of a donor–acceptor complex which can catalyse the synthesis of ammonia from nitrogen and hydrogen starting from a temperature as low as 110°C. Ozaki, Aika, and Hori[53,54] showed that alkali metals sharply increase the catalytic activity of ruthenium, osmium, iron, molybdenum, and other metals in the synthesis of ammonia, ruthenium activated by potassium being capable of catalysing the reaction at a temperature as low as 146°C and atmospheric pressure. There is no doubt that alkali metals enhance the electron-donating properties of the metal atoms in the catalyst (this is shown particularly by the activity series Cs > K > Na), which apparently occurs in many instances also in the fixation of nitrogen in solutions.

Van Tamelen and coworkers[42] achieved the cyclic hydrolysis-reduction in the $(i\text{-}C_3H_7O)_4Ti + NaNp + N_2$ system in tetrahydrofuran (THF). By adding successively small amounts of isopropyl alcohol, it was possible to hydrolyse the product to ammonia and then regenerate it with metallic sodium, after which it was again capable of reacting with nitrogen. Thus it was possible to accumulate up to 3.4 moles of ammonia per mole of titanium alkoxide in the course of 5 such cycles. Following the addition of aluminium tri-isopropoxide, the system was capable of forming 2.75 moles of ammonia per mole of titanium in only one cycle.

Van Tamelen and coworkers also reported the electrochemical reduction of nitrogen[41,43] in dimethoxyethane at a nichrome cathode using an aluminium anode. After eleven days at 40 V, the formation of 10.2 millimoles of ammonia (6.1 moles of ammonia per mole of titanium) was observed. It was noted that an appreciable amount of aluminium (15.1 millimoles) was lost under these conditions from the anode during electrolysis and that aluminium could apparently also behave as a reducing agent.

The reduction of nitrogen in solutions is usually inhibited by compounds such as carbon monoxide and acetylenes[24,29]. Moisture and oxygen naturally also reduce the yield since they interact with nitrogen-reducing systems.

2. Reaction Products

Nitrides. Ammonia is usually formed in the hydrolysis of the nitrogen reduction products in aprotic media. Among the products which hydrolyse with formation of ammonia, amides, imides (M–NH_2, M–NH–M), or nitrides might have been expected, since ammonia itself should not be stable in nitrogen-reducing systems containing metals or organometallic compounds.

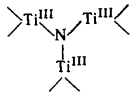
Soon after the first reports by Vol'pin, it was observed[55] that in the products of the reaction carried out in $(C_2D_5)_2O$ and using C_2D_5MgBr as the reducing agent the ammonium salt formed after decomposition of acid does not contain deuterium atoms. This evidently indicates that before hydrolysis the product did not contain deuterium atoms linked to nitrogen, i.e. that it was probably a nitride.

This conclusion was confirmed further by the observation (of ammonia) in a number of studies of systems in which the reactants did not contain nitrogen at all (for example $TiCl_4 + Mg + MgI_2 + N_2$).

If the involvement of the solvent in the reaction is not postulated, there is virtually no doubt about the formation of nitrides as the products in such a system. Aluminium nitride is evidently the product of the reduction of nitrogen in the catalytic system $Al + TiCl_4 + AlBr_3 + N_2$ (where the reduction can be carried out in the aluminium bromide melt). The detailed structures of the nitride products are unknown for the majority of the systems.

Vol'pin and coworkers[39,50] found that the complex $C_6H_6TiCl_2 2AlCl_3$, obtained in the reduction of titanium tetrachloride by aluminium in the presence of aluminium chloride and benzene by the method of Natta et al.[56],

reacts with nitrogen at 130°C with formation of the compound having the elemental composition $(C_6H_6)[TiCl_2 2AlCl_3]_3N$ and hydrolysed with formation of ammonia. This product is probably a complex nitride incorporating three titanium atoms per nitrogen atom:



A thorough investigation of the products of the reaction of nitrogen in the system $TiCl_3(THF)_3 + Mg + N_2$ and $VCl_3(THF)_3 + Mg + N_2$ was carried out by Yamamoto and coworkers [57,58]. In both systems the reaction proceeds at room temperature and atmospheric pressure, the amount of ammonia formed not exceeding one mole per mole of the transition metal. After the absorption of 0.5 mole of nitrogen per mole of titanium in the first system (2.5 gramme-atoms of magnesium are employed at the same time), a black diamagnetic powder with the composition $TiNMg_2Cl_2(THF)$ can be isolated from solution and the stoichiometry of the process can be represented by the equation

$$TiCl_3(THF)_3 + 2.5Mg + 0.5N_2 \rightarrow TiNMg_2Cl_4THF + 0.5MgCl_2(THF)_2 .$$

When the product is decomposed by HCl, ammonia and hydrogen are formed. The structure of the molecule formed in the reaction with nitrogen is not clear, but it is probably not monomeric and cannot be represented as a derivative of titanium(III) and magnesium(II), this being indicated by the evolution of hydrogen in the reaction with HCl. A complex of bipyridyl with zero-valent magnesium can be isolated when the reaction product is treated with bipyridyl. In terms of its chemical properties, the product behaves as a nitride: it evolves ammonia on hydrolysis, does not evolve nitrogen on heating to 200°C and, on treatment with pyridine, bipyridyl, and benzoyl chloride, magnesium can be removed from the product either partly or completely, but the nitrogen formed in these processes remains bound to titanium and can be evolved in the form of ammonia only by hydrolysis.

The reaction with nitrogen in the system $VCl_3(THF)_3 + Mg + N_2$ proceeds similarly (although somewhat more slowly), the product being the complex $VNMg_2Cl_2(THF)$. It is also diamagnetic, does not evolve nitrogen on heating, and hydrolyses with evolution of ammonia, i.e. it is evidently a complex nitride. However, nitrides are not the only possible products of the reduction of nitrogen in such systems.

As already stated, in certain cases hydrogen increases the yield of ammonia after the hydrolysis of the reaction products [40]. Presumably in certain instances it enters into the composition of the product. Indeed, it has been found [59] that hydrogen atoms are linked to the nitrogen atoms, i.e. a complex imide M–NH–M may be formed in this case.

In an early study by Van Tamelen [60] metallic potassium was added to a solution containing a suspension of dialkoxytitanium dichloride and nitrogen was passed into the system. The formation of free ammonia, which was driven out of the system with the nitrogen, was then observed. The evolution of ammonia continued for several weeks and after its cessation the addition of metallic potassium gave rise to the formation of fresh ammonia. The overall yield of ammonia reached only 10–15% relative to titanium. If, as claimed by the authors, ammonia is not formed owing to the traces of moisture in nitrogen, presumably the solvent serves as a source of hydrogen atoms by reacting with the nitride, which is the primary product.

Organonitrogen compounds. The studies by Vol'pin and coworkers [30,61-64] first established the possibility of forming organonitrogen compounds in the reduction of molecular nitrogen with isolation of aromatic amines after hydrolysis. In the systems $Cp_2TiCl_2 + LiPh + N_2$ and $Cp_2TiPh_2 + LiPh + N_2$ in ether the hydrolysis of the products of the reaction with nitrogen (20°C, N_2 pressure 100 atm) led to the detection of aniline (0.15 mole of aniline together with 0.65 mole of ammonia per mole of the titanium compound).

When *p*-tolyl-lithium or *m*-tolyl-lithium are employed as the reducing agents, mainly *p*- and *m*-toluidines respectively are found in the reaction products, i.e. nitrogen largely replaces the lithium.

In the presence of *o*-tolyl-lithium a mixture of all three isomers is found in the product. The authors suggest that the isomers are produced via the intermediate formation of dihydrobenzene in a complex with titanium. In analogous systems involving aliphatic organolithium compounds only insignificant yields of aliphatic amines were observed.

Van Tamelen and Rudler demonstrated the possibility of obtaining organonitrogen compounds by treating the nitrides formed as primary products with compounds containing the carbonyl group [65]. Thus when ketones or acid chlorides are added to the reaction product subsequent to the absorption of nitrogen in the $Cp_2TiCl_2 + Mg + N_2$ system, amines or nitriles are formed in the reaction mixture after several days.

$$R_2CO \rightarrow R_2CHNH_2 + (R_2CH)_2NH ,$$
$$RCOCl \rightarrow RCN .$$

These data indicate a comparatively high reactivity of the nitride derivatives, which distinguishes them from the usual nitrides, formed, for example, on combustion of metals in nitrogen. Subsequently such reactions were investigated by Dormond et al. [66]

Hydrazine. In 1969 studies by two groups of investigators demonstrated simultaneously that, in addition to ammonia, hydrazine may be formed in nitrogen-fixing systems in aprotic media [4,67], i.e. a product of incomplete reduction of nitrogen may be observed after the hydrolysis of the primary products.

In the system $(i\text{-}C_3H_7O)Ti + NaNp + N_2$ in THF [67] the yield of hydrazine following the hydrolysis of the products increased with decrease of the molar ratio $[Ti^{IV}]/[NaNp]$ to give maximum yields of 15–19% (relative to titanium), ammonia being formed together with hydrazine (the ratio $2NH_3/N_2H_4$ varied in the range 3.3–5). The compound forming hydrazine can be reduced further to nitrides by an excess of NaNp.

When $(i\text{-}C_3H_7O)_4Ti$ is replaced by $CoCl_2$, $MoCl_5$, WCl_6, $CrCl_3$, $NiBr_2$, or $FeCl_3$, hydrazine is not formed.

A complex of molecular nitrogen, dissociating reversibly with evolution of nitrogen (see below), is formed in the system $Cp_2TiCl_2 + i\text{-}C_3H_7MgCl + N_2$ at low temperatures (between −80° and −100°C) [4,68]. At −60°C in the presence of excess isopropylmagnesium chloride nitrogen is reduced, evidently via the intermediate formation of the above complex, to a hydrazine derivative, which hydrolyses to form N_2H_4. At such low temperatures nitrides are hardly formed and subsequent reduction to ammonia derivatives proceeds only above 0°C.

Appreciable yields of hydrazine were obtained later in reactions with nitrogen in the systems $TiCl_4 + Al + AlBr_3$, [39] $FeCl_3(Ph_3P)_2 + i\text{-}C_3H_7MgCl$, [69] $MoCl_5 + i\text{-}C_3H_7MgCl$, [69] $FeCl_3 + LiPh$, [70] and $FeCl_3 + Mg$. [71] The results of some of these studies will be discussed in greater detail in the next section.

3. The Mechanism of the Reduction of Nitrogen in Aprotic Media

Many systems capable of reducing nitrogen in aprotic media in the presence of many transition metal compounds, various reducing agents, in different solutions, and under different reduction conditions refute the idea that the reaction mechanism is always the same. In most cases even the nature of the nitride reduction products is still obscure and the reaction mechanism can be discussed only in the broadest outline. The reduction of nitrogen was sometimes investigated in order to elucidate the reaction mechanism, but the results obtained in these studies are also frequently contradictory, are being revised, and cannot be regarded as unambiguous.

The involvement of powerful reducing agents together with transition metal compounds made it necessary to assume from the very beginning that N_2 is activated by compounds of transition metals in a low state of oxidation which are formed under the influence of reducing agents.

Such activation must involve the formation of a complex of nitrogen and the metal atom and, as early as 1966, it was possible to suggest on the basis of general considerations and certain analogies, including the analogy with the reaction of methylene and nitrogen discovered at that time [13,14],

$$CH_2 + N_2 \rightleftarrows CH_2N_2 ,$$

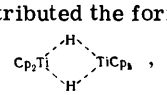
that nitrogen is activated by "carbene-like" compounds such as $Ti^{II}d^2$ and $Fe^{II}d^6$. However, the specific mechanism of the reduction remained unknown and various workers put forward different hypotheses to account for the results.

The involvement of hydrides in the reduction of nitrogen. It has been shown that hydrides which evolve hydrogen on hydrolysis (HD under the influence of D_2O) are formed in many nitrogen-fixing systems. The involvement of hydride linkages in catalytic reactions, particularly in the hydrogenation of olefins, suggested that the M–H bond can be involved also in the reduction of nitrogen, for example by the insertion of the N_2 molecule with formation of M–N=N–H.

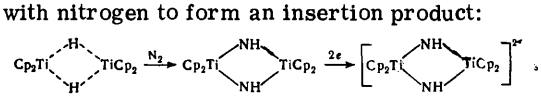
Systems incorporating Cp_2TiCl_2, which are homogeneous and in certain cases (for example, with EtMgBr) effectively reduce nitrogen even at atmospheric pressure, have been investigated in greatest detail from the standpoint of the mechanism. It has been established [55] that hydrides are formed in this system together with nitrides simultaneously with the reduction of nitrogen.

The inhibiting effect of hydrogen, which was observed for many nitrogen-fixing systems (see above), can be explained by the fact that the hydrides formed in the reaction of low-valent transition metal derivatives with hydrogen are mostly inactive in relation to nitrogen.

Nevertheless, on the basis of ESR data for the Cp_2TiCl_2 + EtMgBr + N_2 system, Brintzinger [72] concluded that the hydride, to which he attributed the formula



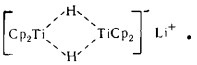
reacts with nitrogen to form an insertion product:



This hypothesis, which is attractive in view of its simplicity, was subsequently extended to biological nitrogen fixation [73]. However, it was not confirmed in subsequent investigations.

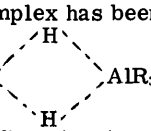
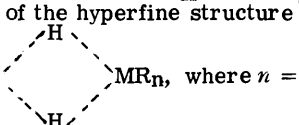
In the first place, this mechanism contradicts data [55] showing the absence of NH groups in the product. Moreover, as shown subsequently by Brintzinger himself [74], the ESR signal which has been attributed to the product of the reaction with nitrogen is not in practice associated with the nitrogen. The triplet signal of the dihydride was found to belong to a monomeric species to which Brintzinger attributed the formula of the anion $[Cp_2TiH_2]^-$. [74] This dihydride does not change in the presence of nitrogen [36] and is probably a side product.

Henrici-Olive and Olive showed by the ESR method that a species containing two hydrogen atoms per tervalent titanium atom is formed in the system Cp_2TiCl_2 + LiNp. [75] In this case the hyperfine structure of the spectrum indicates the involvement of the lithium atom in the complex and the formula of a dimer with titanium in different valent states (bivalent, tervalent) was attributed to this complex: [31]



It is suggested that nitrogen forms a complex with bivalent titanium, this being followed by reduction under the influence of lithium naphthalide.

A similar dinuclear structure of the hydride has been suggested for the system Cp_2TiCl_2 + EtMgBr, [31] it being postulated that the reaction of nitrogen with bivalent titanium in the complex does not alter the ESR signal of the titanium(III) hydride, which remains unchanged.

Presumably the hydride products are in reality related to the hydride complex observed previously—the product of the reaction of Cp_2TiCl_2 with $(i\text{-}Bu)_3Al$ and of Cp_2TiCl_2 with $(i\text{-}Bu)_2AlH$). This complex has been investigated by ESR and the formula  was attributed to it on the basis of the hyperfine structure [76]. The general formula  where n = 2, 1, or 0 for aluminium, magnesium, lithium (or sodium) respectively, can probably be attributed to the dihydride complexes. Like their aluminium precursor, titanium(III) dihydride complexes involving magnesium, lithium, and sodium are evidently inactive with respect to nitrogen and are side products.

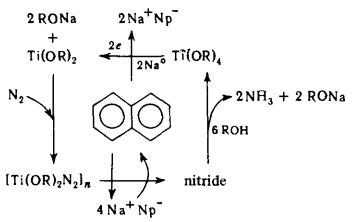
The formation of hydrides inactive in relation to nitrogen apparently constitutes a general phenomenon in the reduction of nitrogen in aprotic media. However, as already mentioned, in certain cases nitrogen can also increase the yield of the reduction product. In these systems, which usually contain alkoxy-derivatives of titanium, one cannot rule out the involvement of hydrides in the fixation of nitrogen, but the available data are still insufficient for more specific conclusions concerning the mechanism.

The degree of oxidation of the transition metal. The degree of oxidation of the transition metal in compounds active with respect to nitrogen has been discussed in a number of studies. Most of these refer to systems including titanocene derivatives. On the basis of ESR data, Vol'pin and coworkers [27] concluded that in these systems the reaction with nitrogen begins after the disappearance of titanium(III), i.e. the degree of oxidation of titanium is less than three. It has been concluded [77] that the Cp_2Ti^- ion [which may be regarded as a derivative of

titanium(I)] reacts with nitrogen. As already stated, Olive suggested that titanium(II) in a complex with a hydride derivative of titanium(III) is active in relation to nitrogen.

Maskill and Pratt [78] and Bayer and Schurig [36] postulated that zero-valent titanium complexes are active.

Bivalent titanium compounds were assumed to be active by van Tamelen and coworkers [32]. Thus in systems incorporating $Ti(OR)_4$, which have been investigated in greatest detail in these studies and which permit cyclic hydrolysis-reduction, the following mechanism in which the $Ti(OR)_2$ species reacts with nitrogen has been adopted [79]:



Titanium(II) and vanadium(II) complexes are assumed to be active in relation to nitrogen by Yamamoto et al. [37] in the systems $TiCl_3(THF)_3$ + Mg and $VCl_3(THF)_3$ + Mg. The study of the reduction of nitrogen in the systems VCl_3 + LiNp and $CrCl_3$ + LiNp [31,80] by ESR showed that the metals in these systems must be very highly reduced.

We may note that precisely in these instances, evidently involving very powerful reducing agents, the yield of ammonia per atom M under the conditions of high Red/M ratios reaches 2. It is interesting to note that the yield of reduction products in the VCl_3 + LiNp + N_2 system depends on the order in which the reducing agent and the vanadium compound are mixed in an atmosphere of nitrogen [38]. If a solution of lithium naphthalide is added to a solution of VCl_3, the amount of nitrogen absorbed reaches 0.39 mole per mole of VCl_3. If, on the other hand, a VCl_3 solution is added to a solution of lithium naphthalide, up to 0.7 mole of N_2 is reduced.

Kinetic data and preliminary conclusions concerning the structure of the intermediate complexes. Maskill and Pratt [78,81] employed a kinetic approach for the homogeneous system Cp_2TiCl_2 + EtMgBr + N_2. They established that, when the system is flushed with nitrogen, the species formed on reduction of dicyclopentadienyltitanium dichloride which is active with respect to nitrogen can exist for a long time in the absence of nitrogen, since the yield of products and the rate of their accumulation depend little on whether nitrogen is passed in immediately after mixing the reactant or after a long time‡. It was discovered that, above 0.5 atm, the rate of reaction is independent of the nitrogen pressure and, in the presence of a sufficient excess of the reducing agent, is independent of the concentration of ethylmagnesium bromide. Under these conditions, the rate was found to be proportional to the square of the initial concentration of the titanium compound.

‡We may note that in the study of Nechiporenko et al. [55] the yield fell sharply when nitrogen was introduced to the reaction mixture only when some time elapsed after the mixing of the reactants. Evidently, this difference from the result of Maskill and Pratt [81] is due to the fact that the system of Nechiporenko et al. [55] was static and the gases evolved could react with the active species. Indeed, it was subsequently shown that ethylene in the system investigated forms the π-crotyl complex $Cp_2Ti(\pi\text{-}C_4H_7)$. [82]

The results indicate the formation of a dinuclear complex when two reduced titanium derivatives interact. Evidently the interaction determines the rate of the entire process when the nitrogen pressure is in excess of 0.5 atm and the subsequent reaction with nitrogen proceeds rapidly. It is interesting to note that qualitatively similar kinetics (proportionality to the square of the concentration of the transition metal compound, the attainment of a limiting rate with respect to the nitrogen and reducing agent concentrations) were observed subsequently in a study of another homogeneous system—$FeCl_3$ + LiPh + N_2 (see below) [70]. In this case one can also conclude that a dinuclear complex is formed.

In the systems investigated by Yamamoto [37], $TiCl_3(THF)_3$ + Mg + N_2 and $VCl_3(THF)_3$ + Mg + N_2, the rate of reaction in THF is consistent with first order with respect to the concentration of the initial chlorides, the amount of unconsumed magnesium, and the N_2 pressure. The amount of reduced nitrogen does not, however, exceed one molecule for two titanium atoms. Hence, it follows that the most probable mechanism involves the formation of a complex by nitrogen with a dinulcear species containing reduced titanium and subsequent reduction of the activated nitrogen by magnesium.

In general, in those cases where the yields of products approach one NH_3 molecule (after hydrolysis) per transition metal atom the formation of a dinuclear complex, in which two transition metal atoms are linked to two nitrogen atoms, is probable. As stated above, the yield of ammonia often approaches two molecules per transition metal atom. As already mentioned, this has been observed for highly reducing systems. These results probably correspond to mononuclear complexes with subsequent reduction by non-transition metal atoms, for example:

$$MN_2 + LiNp \rightarrow M{-}N{=}N{-}Li + Np \xrightarrow{LiNp} N^{3-}.$$

On this hypothesis, it is possible to account for the different results obtained for different orders of mixing of the reactants [38]. If the vanadium compound is added to the reducing agent, i.e. the reaction proceeds in the presence of lithium naphthalide, there is a possibility of the formation of the complex V–N=N–Li and up to one mole of N_2 per mole of the transition element can be reduced. For the reverse order of mixing, the dinuclear complex includes two transition element atoms and the maximum yield corresponds to the reduction of 0.5 mole of N_2 per mole of vanadium.

The study of intermediate complexes with molecular nitrogen. Bearing in mind the very high ionisation potential of the nitrogen molecule (367 kcal mole^{-1}), the negative sign and high absolute magnitude of its electron affinity (−84 kcal mole^{-1}), [7] and the high dissociation energy of the first π-linkage which is ruptured, it might have been possible to conclude long ago that complex formation is essential as the first stage in the activation of nitrogen.

After the discovery by Allen and Senoff of the first complex with bivalent ruthenium [2] and the first proof that such complexes can be obtained directly from molecular nitrogen [3,83], it appeared that the activation of nitrogen by complex formation received direct confirmation. The first studies on the properties of the complexes appeared to support this hypothesis. It has been concluded that [2,84] nitrogen in the complex can be reduced to ammonia on treatment with sodium tetrahydroborate. However, subsequent careful tests using $^{15}N_2$ showed [7,85–87] that the reports concerning the reduction of nitrogen in the complex were incorrect and that in reality nitrogen in the complexes is

not reduced either by sodium tetrahydroborate or by other reducing agents. With increase of the number of known stable mononuclear and dinuclear complexes (see the reviews [7-9]), an increasing number of such complexes were tested to check the possibility of further reactions of the nitrogen bound in them and each time the results proved to be negative. Initially the studies on the complexes with nitrogen and the reduction reactions in the Vol'pin–Shur systems developed in parallel and there were no points of contact between them.

It was not until 1969 that the first reports of complexes with nitrogen in which the nitrogen ligand is capable of further reactions were published. The number of such complexes then began to increase and some of them could be isolated and investigated in detail. These studies in fact yield the most definite conclusions concerning the mechanism of the reduction of nitrogen.

Van Tamelen et al. [79] were the first to report a complex with nitrogen capable of further reduction. According to their data [79], this complex is formed when a benzene solution of dimeric titanocene is stirred for three weeks in an atmosphere of nitrogen. During this period, more than 0.9 mole of nitrogen is absorbed per mole of monomeric titanocene.

The infrared spectrum of a solution of the titanocene complex with nitrogen shows a band at 1960 cm^{-1}, which has been tentatively assigned to the NN vibration in the complex, although experiments with $^{15}N_2$, which would confirm this hypothesis, were evidently not carried out. Nowadays this assignment of the frequency appears doubtful, in particular because the NN frequency in the intermediate complexes is usually much lower. The complex with nitrogen is formed reversibly and decomposes with the evolution of nitrogen when the nitrogen over the solution is replaced by argon. Measurements of the molecular weights showed that the complex is dimeric and the formula $(Cp_2TiN_2)_2$ was attributed to it. On treatment with sodium naphthalide the nitrogen in the complex is reduced quantitatively to ammonia: $(Cp_2TiN_2)_2 \xrightarrow{e} \xrightarrow{H^+} 4NH_3$. We may note that this result is unusual for metallocene systems, which in other cases give rise to at most one mole of ammonia per mole of titanium. More detailed data on this complex were not subsequently published.

Complexes with quite different properties were discovered in the same year in the nitrogen-fixing systems $Cp_2TiCl_2 + RMgX + N_2$ (R = i-Pr or Et).[4] The most definite results were obtained for isopropylmagnesium chloride. On the hypothesis that the intermediate complexes must be unstable, the authors [4] attempted to detect the formation of the complexes on sharp cooling of the solution.

When the reaction of isopropylmagnesium chloride with dicyclopentadienyltitanium dichloride was carried out at −60°C and the solution was cooled further under nitrogen to between −80° and −100°C, an intensely blue complex with nitrogen was formed rapidly and reversibly (λ_{max} = 610 nm). Spectroscopic study of the reversible complex formation reaction with nitrogen subsequently showed that the complex incorporates two titanium atoms per nitrogen molecule and that its heat of formation is only 5 kcal $mole^{-1}$.[88] Evidently this complex can be isolated from solution in the system $Cp_2TiCl + i\text{-}C_3H_7MgCl + N_2$.[89] It is somewhat more stable in the solid state than in solution, but decomposes slowly at a temperature as low as −70°C with liberation of nitrogen. The composition of the complex corresponds to the formula $(Cp_2TiR)_2N_2$. A more stable intermediate complex, formed in the system $Cp_2TiCl_2 + (i\text{-}C_3H_7)MgCl + N_2$ in the presence of triphenylphosphine, has also been reported[4]. The complex with nitrogen is likewise intensely coloured (λ_{max} = 420 and 520 nm). On treatment with alcohol, the complexes evolve nitrogen and on standing in the presence of an excess of a reducing agent the nitrogen bound in the complex is converted into a nitride, which hydrolyses to form ammonia.

A more stable complex, analogous to the blue complex $(Cp_2TiR)_2N_2$ in composition, was isolated by Teuben and de Liefde Meijer in the reaction between Cp_2TiPh and N_2 in toluene at −78°C.[90] In this case the complex slowly evolves nitrogen above 0°C and rapidly at 70°C. Subsequently a number of $(Cp_2TiR)_2N_2$ complexes, where R = *o*-, *m*-, or *p*-tolyl, benzyl, or pentafluorophenyl, were obtained similarly [91,92].

In all cases the complexes are formed reversibly in toluene solution and give rise to the appearance of an intense blue colour (λ_{max} = 600–630 nm). The complexes are diamagnetic. Their infrared spectra do not show appreciable absorption corresponding to the vibration of the NN bond. The complexes with nitrogen exhibit extremely varied thermal stabilities. Thus the *m*-tolyl complex decomposes only at 75°C, the *o*-tolyl complex evolves nitrogen at −20°C, and the 2,6-dimethylphenyl derivative is not formed at all.

The structure of the complexes is still obscure but, according to infrared spectroscopic data, the nitrogen molecule is probably located symmetrically between two titanium atoms or a structure of the π-complex type is formed.

The extremely large extinction coefficient in the region of the visible absorption maximum suggests that the blue adducts with nitrogen are charge-transfer complexes. In accordance with the formula, it is reasonable to assume that the degree of oxidation of the species reacting with nitrogen is three [91,92] and that the structural formula of the complex is, for example,

$$Cp_2Ti\diagdown N \diagup\!\diagdown N \diagup TiCp_2 .$$

However, the nitrogen complexes with metal compounds having the d^1 electronic configuration are at any rate very unusual and the origin of the intense blue absorption band is not clear for this type of structure. In order to retain the earlier hypothesis that bivalent titanium must be active in the relation to nitrogen, one can postulate the structure

$$[Cp_2Ti^{II}] \rightarrow N{\equiv}N \rightarrow [R_2Ti^{IV}Cp_2]$$

or

$$[Cp_2TiR]^- \rightarrow N{\equiv}N \rightarrow [Cp_2TiR]^+$$

and regard these complexes as analogous to the intensely coloured dinuclear complexes with nitrogen containing univalent rhenium, which were first obtained and investigated by Chatt et al.[93] Here nitrogen behaves as a bridge between the donor (Re^I) and the acceptor, which can be a compound incorporating metals with the d^0 electronic configuration, for example:

$$Re^I \rightarrow N{\equiv}N \rightarrow AlR_3 .$$

The dinuclear complexes $(Cp_2TiR)_2N_2$ evidently constitute the first stage in the activation of nitrogen in the system under consideration. Their hydrolysis results in the liberation of molecular nitrogen without appreciable reduction. When $(Cp_2Ti\ i\text{-}C_3H_7)_2N_2$ is treated with an excess of $i\text{-}C_3H_7MgCl$, new complexes are formed which evolve hydrazine on hydrolysis after reduction at low temperatures or ammonia at temperatures above 0°C.

The nitrogen in the complex $(Cp_2TiPh)_2N_2$ can be reduced at −20°C with sodium naphthalide in THF.[91,92] This results in the formation of products, which hydrolyse with liberation of hydrazine and ammonia and also the formation of traces of aniline, the overall yield being quantitative with respect to the nitrogen in the complex. About half the nitrogen is converted into hydrazine. There is evidence that the cyclopentadienyl structure is destroyed on reduction.

In the search for intermediate complexes corresponding to more highly reduced states of nitrogen, the system $Cp_2TiCl + CH_3MgI$ was investigated[94,95] in ether. In this case Cp_2TiCH_3 is evidently formed in solution in the first stage and on cooling to −100°C reacts with nitrogen, forming an intensely blue complex. On standing for about 1 h at −70°C, the blue complex gradually disappears and a dark complex with the composition $(Cp_2Ti)_2N_2$, which is stable at room temperature, is deposited from the solution.

The infrared spectrum of this complex shows a band at 1285 cm^{-1}, shifting to 1235 cm^{-1} when $^{14}N_2$ is replaced by $^{15}N_2$, which shows that it belongs to the NN vibration.

Measurement of the magnetic susceptibility showed that the magnetic moment of the complex decreases reversibly with decrease of temperature, which suggests an equilibrium between the singlet and triplet states of the complex. It can be represented schematically as follows:

$$\underset{\text{triplet}}{Cp_2Ti^{III}-N=N-Ti^{III}Cp_2} \rightleftharpoons \underset{\text{singlet}}{CpTi^{IV}=N-N=Ti^{IV}Cp_2} .$$

The difference between the energies of these two states amounts to only 85 cal $mole^{-1}$ according to the measurements of Ivleva et al.[96]

When the complex is treated with a methanol solution of hydrogen chloride at −60°C, the formation of equal amounts of nitrogen and hydrazine is observed, the sum nitrogen + hydrazine being equivalent to half the amount of titanium, in agreement with the above formula. When the complex is treated with hydrogen chloride in ether, the main products are nitrogen and ammonia (the yield of ammonia is about 30% with respect to titanium) and hydrazine is hardly formed at all. These results can be explained by the fact that in the hydrolysis of the complex the primary product is di-imide, which, depending on the conditions, subsequently disproportionates to nitrogen and hydrazine or to nitrogen and ammonia:

$$(Cp_2Ti)_2N_2 + 2HCl \rightarrow 2Cp_2TiCl + N_2H_2 ,$$
$$2N_2H_2 \rightarrow N_2 + N_2H_4 ,$$
$$3N_2H_2 \rightarrow 2N_2 + 2NH_3 .$$

Thus the complex can be regarded as a derivative of di-imide, although, according to the infrared spectroscopic data, the multiplicity of the NN linkage in the complex is probably less than two.

The complex, which evidently corresponds to the next stage in the reduction of nitrogen in the coordination sphere of titanium, was isolated in the reduction of titanocene by isopropylmagnesium chloride in the presence of nitrogen at −60°C for 3 h in ethereal solution[97]. According to analysis, its composition is $(Cp_2Ti)_2N_2MgCl$. The complex is paramagnetic, its magnetic susceptibility corresponding to one electron for two titanium atoms. According to infrared spectroscopic data, the NN vibration lies at 1260 cm^{-1}, as shown by the isotopic shift of the band to 1220 cm^{-1} when $^{15}N_2$ is used in the synthesis instead of $^{14}N_2$. In accordance with these data, the structure of the complex can be represented in the following form:

$$Cp_2Ti^{III}-N=N \rightarrow Ti^{II}Cp_2 \leftrightarrow Cp_2Ti^{IV}=N-N-Ti^{III}Cp_2 ,$$
$$\qquad\qquad\quad | \qquad\qquad\qquad\qquad\quad \diagdown MgCl$$
$$\qquad\quad MgCl$$

the second formula being preferable. When the complex $(Cp_2Ti)_2B_2MgCl$ is treated with an alcoholic solution of hydrogen chloride at −60°C, more than 80% of nitrogen is converted into hydrazine, evidently via the reaction

$$(Cp_2Ti)_2N_2MgCl + 4HCl \rightarrow Cp_2TiCl_2 + Cp_2TiCl + MgCl_2 + N_2H_4 .$$

The remainder of the bound nitrogen is converted into molecular nitrogen with simultaneous evolution of hydrogen.

When the complex $(Cp_2Ti)_2N_2MgCl$ is allowed to stand with a solution of $i\text{-}C_3H_7MgCl$ in ether at room temperature, the product is $Cp_2TiN(MgCl)_2$, which hydrolyses with formation of ammonia. Thus the sequence of stages in the reduction of nitrogen in the Cp_2TiCl_2 (or Cp_2TiCl) + RMgX systems can be represented as follows:

$$Cp_2TiCl \xrightarrow{RMgX} Cp_2TiR \underset{}{\overset{N_2}{\rightleftharpoons}} 0.5[(Cp_2TiR)_2N_2] \rightarrow 0.5[(Cp_2Ti)_2N_2] \xrightarrow{RMgX} \rightarrow 0.5[(Cp_2Ti)_2N_2MgX] \rightarrow Cp_2TiN(MgX)_2 .$$
$$\downarrow H^+ \qquad\qquad \downarrow H^+ \qquad\qquad \swarrow H^+ \quad \searrow RhLi, H^+ \qquad \downarrow H^+$$
$$N_2 \qquad\qquad N_2H_2 \qquad\qquad N_2H_4 \qquad NH_3, PhNH_2 \qquad NH_3$$

It is interesting that, when the complex $(Cp_2Ti)_2N_2MgCl$ is treated with phenyl-lithium, the hydrolysis of the product results in the formation, together with ammonia, of an appreciable amount of aniline (up to 1% relative to titanium). These data and those of other investigations[91,98] concerning the formation of traces of aniline in the reduction of the complex of $(Cp_2TiR)_2N_2$ by sodium naphthalide indicate the possible mechanism of the formation of aniline in the Vol'pin–Shur systems when phenyl-lithium is employed as the reducing agent. Vol'pin and coworkers[61-64] suggest that the hydrolysis product (aniline) is formed via the insertion of nitrogen in the Ti–Ph bond:

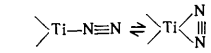
$$Ti-Ph + N_2 \rightarrow Ti-N=N-Ph \rightarrow \text{products.}$$

We now see that the Ph–N linkage can be formed also when phenyl-lithium acts on the intermediate dinuclear complexes formed in the multistage reduction of nitrogen.

Several elegant results concerning the nature and properties of the complexes in the systems containing titanocene were obtained in Brintzinger's studies[98-100]. Titanium compounds interacting with molecular nitrogen were discovered in these investigations: bis(pentamethylcyclopentadienyl)titanium(II), dicyclopentadienyltitanium(II), and its complex with triphenylphosphine. A solution of $[C_5(CH_3)_5]_2Ti$ reacts with carbon monoxide to form the dicarbonyl and with nitrogen at very low temperatures to form a complex which may be an analogue of the dicarbonyl and at a higher temperature to form an intensely coloured blue dinuclear complex containing one nitrogen molecule for two titanium atoms. The complex is in equilibrium with nitrogen and has λ_{max} = 568 nm. Dicyclopentadienyltitanium was obtained in the reactions, discovered by the authors, involving the decomposition of the hydride Cp_2TiH at room temperature. The hydride is formed in the reaction of $Cp_2Ti(CH_3)_2$ with hydrogen. When solutions of titanocene obtained in this way are cooled in the presence of nitrogen, intensely blue solutions of the complex (λ_{max} = 597 nm, $\epsilon \simeq 10^4$) are formed. The complex can be isolated from solution and has the composition $(Cp_2Ti_2)N_2$ according to the data of Bercaw et al.[101] When it is treated with solutions of lithium naphthalide the coordinated nitrogen is reduced and ammonia is evolved on hydrolysis. The complex of titanocene with triphenylphosphine $Cp_2Ti(PPh_3)$ (λ_{max} = 521 nm) interacts with nitrogen. In toluene solution at room temperature 0.33 mole of N_2 is absorbed per mole of titanium. When the resulting adduct is heated to 110°C, approximately

half the nitrogen is converted into an ammonia derivative and the remainder is evolved in the form of free nitrogen.

Bercaw et al. reported recently [101] that at low temperatures in the presence of nitrogen the dinuclear complex $\{[C_5(CH_3)_5]_2Ti\}_2N_2$ is converted into the mononuclear complex $[C_5(CH_3)_5]_2TiN_2$. ^1H, ^{13}C, and ^{15}N NMR data led them to the conclusion that in the last complex there is a reversible rearrangement of the nitrogen in the complex:



It is readily seen that all the properties of the dinuclear nitrogen complexes with titanocene obtained in a number of investigations [98-100] agree with those of the complexes $[Cp_2TiR]_2N_2$ described above, while their compositions are analogous to those of the di-imide complex, which has completely different properties.

Further investigations should show whether the above discrepancies are related to experimental inaccuracies in any of the above investigations or whether these complex nitrogen-fixing systems can indeed contain complexes with nitrogen having the same compositions and different properties and complexes of different compositions and extremely close properties.

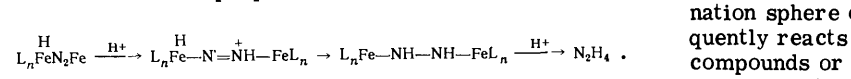
Interesting complexes with nitrogen, capable of undergoing further reduction reactions, were detected in nitrogen-fixing systems containing iron:

$$FeCl_3(PPh_3)_2 + i\text{-}C_3H_7MgCl + N_2\ ^{69,102},$$
$$FeCl_3 + LiPh + N_2\ ^{70}.$$

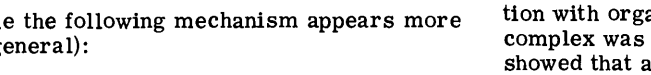
In the first of these systems in ether at −50°C a relatively unstable complex is formed with molecular nitrogen, which slowly decomposes in solution with evolution of nitrogen at a temperature as low as 0°C.

The band at 1760 cm^{-1} (there is an isotopic shift to 1710 cm^{-1} on replacement of $^{14}N_2$ by $^{15}N_2$) in the infrared spectrum corresponds to the NN vibration.

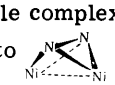
The Raman spectrum contains an exceptionally intense band at 1760 cm^{-1}.[103] This corresponds to the dinuclear fragment FeN_2Fe with high polarisability of the NN bond. Molecular nitrogen is completely evolved from the complex both on heating and on decomposition by carbon monoxide and ethyl alcohol. However, on treatment with hydrogen chloride, hydrazine is formed together with molecular nitrogen. It has been concluded [69,102] that the role of HCl consists in the protonation of the coordinated N_2 molecule, which promotes its partial reduction in accordance with the proposed mechanism:



At the present time the following mechanism appears more likely (and more general):



In the $FeCl_3$–$LiPh$–N_2 system at room temperature and atmospheric nitrogen pressure the reaction also leads to the formation of a complex with nitrogen [70]. Kinetic data (proportionality of the rate of reaction to the square of the concentration of iron, independence of nitrogen pressure above 200 torr and of the concentration of phenyl-lithium) shows that in this case the rate is limited by the formation of a dinuclear complex of the reduced iron compound (without nitrogen), which is followed by rapid coordination of nitrogen. Presumably the intermediate complex with nitrogen is also dinuclear. In this case neither the intermediate complex with nitrogen nor the final product were isolated from solution and the compositions were not determined, but the reduced iron compound is presumably stabilised by phenyl-lithium, since the independence of the rate of reaction of the concentration of phenyl-lithium is observed only in the presence of a large excess of the reducing agent.

When a solution of the product is treated with hydrogen chloride, hydrazine, nitrogen, and ammonia are formed (28, 9, and 15% of the iron content respectively). Possibly the intermediate complex is in this case to some extent analogous to the dinuclear nitrogen complex with zerovalent nickel stabilised by phenyl-lithium [104] and having the composition $\{[(PhLi)_3Ni]_2N_2.2Ft_2O\}_2$. It follows from the X-ray diffraction analysis of this stable complex [105] that the fragment Ni_2N_2 has a structure close to  , the length of the NN bond (1.35 Å) being intermediate between those of single and double bonds. The lithium atoms in the phenyl-lithium molecules in the complex adjoin nitrogen atoms and exhibit electron-accepting properties, enhancing electron transfer from the nickel atom. There have as yet been no reports stating whether or not the nitrogen bound in the complex can be converted into hydrazine or another reduced compound.

In the $FeCl_3$–Mg–N_2 system in tetrahydrofuran a dinuclear complex stable at room temperature is also formed. Its composition corresponds to the formula $[(THF)_{1.5}MgCl_3Fe]_2N_2$. The complex reacts with HCl to form hydrazine [71].

Some of the examples quoted show that the instability of the complex is not a necessary condition for the involvement of nitrogen in the coordination sphere of the metal in further reactions, at least in those cases where powerful reducing agents take part in the formation of the complexes. New attempts to introduce into the reaction the nitrogen in the coordination spheres of known stable complexes are of interest in this connection.

Vol'pin et al. [106] showed that, when the complex $(Ph_3P)_3CoHN_2$ reacts with lithium napthalide in the presence of titanium tetrachloride and other transition metal compounds, the nitrogen bound in a complex with cobalt is reduced to ammonia after hydrolysis. In the absence of added transition metal salts the nitrogen is not reduced.

However, it has been established [107] that under these conditions nitrogen is initially displaced from the coordination sphere of cobalt in the form of free N_2 and subsequently reacts in the usual way with reduced titanium compounds or other additives.

The first successful attempt to introduce into the reaction with organic compounds the nitrogen in a mononuclear complex was made by Chatt et al. [108] These workers showed that acid chlorides RCOCl (R = CH_3, C_2H_5, C_3H_7, or *p*-$CH_3OC_6H_4$) react with *trans*-$W(N_2)_2(dpe)_2$ to form $(dpe)_2W{=}N{-}NHCOR$, where dpe = $PhPCH_2CH_2PPh_2$. The nitrogen in the reaction product is protonated, presumably owing to traces of moisture, which gives rise to hydrogen chloride. The complex can be deprotonated on reaction with triethylamine to form a new series of complexes $WCl(dpe)_2N_2COR$ having a band at 1338 cm^{-1} in the infrared corresponding to a vibration of the complex (there is a shift to 1298 cm^{-1} when the nitrogen is replaced by $^{15}N_2$). An analogous reaction with RCOCl has been discovered for the molybdenum complex of *trans*-$Mo(N_2)_2(dpe)_2$.

Another interesting reaction, discovered by Chatt et al.[109], consists in the protonation of nitrogen in *trans*-$M(N_2)(dpe)_2$ with formation of an N_2H_2 complex:

$$trans\text{-}M(N_2)_2(dpe)_2 \xrightarrow[(THF)]{HX} M(dpe)_2X_2N_2H_2 + N_2$$

(M = W or Mo; HX = HBr or HCl for W and HBr for Mo). It is suggested that the N_2H_2 group is bound to M, giving the structure

$$M\langle^{NH}_{NH}\| \quad \text{or} \quad M{=}N{-}NH_2 .$$

Thus the reduction of nitrogen to a di-imide derivative or hydrazine is caused by protonation (as suggested above for the iron complex). However, in mononuclear complexes protonation has so far precluded the isolation of the reduced products (N_2H_2, N_2H_4, or NH_3) from the coordination sphere of the metal and these results are naturally also consistent with the view that the reduction of nitrogen in a dinuclear complex should in general proceed more readily than in a mononuclear complex.

Sellman and coworkers[110-113] recently obtained new data for mononuclear and dinuclear complexes of manganese, tungsten, and chromium, with di-imide as a possible intermediate in the reduction of nitrogen. In this case the complexes were formed by the oxidation of hydrazine and not directly from molecular nitrogen and their structures and properties should naturally be examined with a certain degree of caution in relation to the mechanism of the reduction of nitrogen in the coordination sphere of the metal.

IV. REDUCTION OF NITROGEN IN PROTIC MEDIA

For a long time the biological fixation of nitrogen achieved by certain micro-organisms and algae constituted the only known nitrogen reduction reaction involving protons derived from water:

$$N_2 + 6e + 6H^+ \rightarrow 2NH_3 .$$

The attempt to carry out this reaction under non-biological conditions was begun a very long time ago. As early as 1916 Zenghelis[114] claimed that, when nitrogen is passed into hydrochloric acid in which metallic zinc dissolves a certain amount of ammonia is formed evidently by the action of hydrogen *in statu nascendi* on nitrogen.

Subsequently analogous attempts were frequently repeated. It was reported in a patent[115] that nitrogen is hydrogenated to ammonia in aqueous solutions of molybdenum hydride derivatives.

Haight and Scott[116] reported in 1964 the formation of small amounts of ammonia in the electrochemical reduction of nitrogen or in its reduction by chemical reducing agents in the presence of molybdate or tungstate. Subsequently similar results were obtained[117] using compounds of a whole series of transition metals.

It is noteworthy that, in view of the low yield of ammonia and the comparatively large amounts of the starting materials, there was always some doubt whether or not molecular nitrogen was the source of the detected ammonia. Small amounts of ammonia can be formed from impurities in the initial reagents, for example, metal nitrides or nitrogen oxides (which are reduced to ammonia under the reaction conditions). The studies by the present author and his coworkers frequently led to the detection of small amounts of ammonia in attempts to reduce nitrogen in protic media, but subsequent careful tests showed that molecular nitrogen was not the source of ammonia.

In testing for the fixation of small amounts of nitrogen one usually employs a technique involving labelled $^{15}N_2$ nitrogen, which was developed previously and was used successfully to investigate the reduction of nitrogen in biological systems. The formation of $^{15}N_2$ and $^{15}N^{14}N$ nitrogen, in amounts appreciably exceeding its natural content, in the hypobromite oxidation of the ammonia formed constitutes qualitative evidence of the fixation of nitrogen and can be used in quantitative measurements of the yield of ammonia. This method has been employed[118] in an attempt to reproduce the data for the fixation of nitrogen described by Haight and Scott[116] and Yatsimirskii and Pavlova[117], but the result was negative. There is also other evidence (see, for example, Hardy and Knight[119]) that the reduction of nitrogen under the conditions employed by the above authors[116,117] does not in fact occur.

Positive results with $^{15}N_2$ constitute an essential criterion of the validity of the results obtained when the amounts of ammonia formed are small (this must be recalled if only because analogous studies without a special test of the results continue to be reported). However, one should note that the excess of mass 29 over its natural abundance in the mass spectrum of nitrogen obtained by the oxidation of the evolved ammonia does not by itself constitute unambiguous evidence for the reduction of nitrogen and has to be tested, since it may be the result of a random contamination of the ionisation chamber of the mass spectrometer by organic substances (for example ether), which yield on ionisation fragments having a mass of 29. Evidently reproducible agreement between the results of chemical analysis (with $^{14}N_2$) and mass spectrometric analysis (with $^{15}N_2$) must be obtained.

Considerable advances have been made recently in the study of nitrogenase—the enzyme which catalyses the biological fixation of nitrogen (see, for example, the reviews of Hardy et al.[19] and Ohmes and Grundemann[20]). It is useful to examine simultaneously biological and non-biological nitrogen fixation, since progress in this field is undoubtedly largely due to the joint efforts of chemists and biologists.

1. Nitrogenase as a Catalyst of the Reduction of Nitrogen

Detailed data on nitrogenase are of course the scope of the present review. Here we shall briefly describe the features of the reduction of nitrogen in the presence of nitrogenase from the chemists' point of view.

The enzyme isolated from micro-organisms is a combination of two proteins, one of which (MoFe-protein) contains molybdenum, iron, sulphide groups, and mercapto-groups, with 1 or 2 molybdenum atoms and 20–30 iron atoms per molecule. The other (Fe-protein) contains 2 iron atoms and also sulphide and mercapto-groups. In the presence of the isolated enzyme nitrogen can be reduced by a specially added reductant—sodium dithionite. The reaction requires the presence of ATP, the reduction of nitrogen to ammonia being accompanied by the coupled hydrolysis of ATP.

In the absence of nitrogen hydrogen is evolved owing to transfer of electrons to water protons. All three nitrogenase reactions (hydrolysis of ATP, evolution of hydrogen, and the reduction of nitrogen) are possible only in the presence of both nitrogenase components—MoFe-protein and Fe-protein.

Apart from nitrogen, in the presence of the nitrogenase component other compounds containing a triple-bond can

be reduced: acetylene, nitrous oxide, isonitriles, and nitriles. Ethylene (*cis*-dideuterioethylene when the reaction is carried out in heavy water) is the product of the reduction of acetylene. Ethylene is not a substrate of nitrogenase and does not undergo further reduction.

When the system is saturated by the substrate, the rates of all the nitrogenase reactions are determined by the transfer of electrons and are thus independent of the nature of the substrate. The activation energy for the reaction amounts to 14 kcal mole^{-1} above 20°C. The presence of magnesium ions is essential for the nitrogenase reaction, possibly in order to carry out the ATPase process.

An important result concerning the structure of the enzyme was obtained by Likhtenshtein (see, for example, Ref. 120). It was found that the iron atoms entering into the composition of the MoFe-protein are combined with one another, forming a cluster of linked atoms.

It is interesting that molybdenum, which is absolutely essential for the catalysis of the reduction of nitrogen by nitrogenase, can nevertheless be replaced by vanadium. The remaining elements proved to be inactive. It proved possible recently to isolate nitrogenase containing vanadium instead of molybdenum [121,122] and showing activity for N_2.

2. Reduction of Nitrogen by Mixed Hydroxides in the Presence of Molybdenum and Vanadium Compounds

Positive and reproducible results in attempts to reduce nitrogen in protic media were obtained for the first time in 1970 and were published in a number of reports [5,6,123,124]. In their search for systems of this kind, the authors began with predictions [7] based on a theoretical treatment [16], taking into account results obtained in the study of the biological fixation of nitrogen. In the first place reagents with a reduction potential close to that of active nitrogenase and sufficient for the formation of hydrazine from nitrogen ($E_0 = -0.23$ V at pH 0) were chosen. These reducing agents must simulate the section of nitrogenase which activates electrons. It follows from theoretical considerations that the activators of molecular nitrogen must have a fully defined set of properties. It was therefore natural to select, by analogy with the biological fixation of nitrogen, compounds of molybdenum (and also vanadium, which can replace molybdenum in nitrogenase), on the hypothesis that at a sufficient reduction potential these compounds form species suitable for the activation of nitrogen.

It was suggested that the intermediates formed (for example, Mo=N–NH–Mo) must be hydrolysed with formation of hydrazine, which appears as the final or intermediate product. This hypothesis was largely responsible for success in the search for nitrogen-fixing systems, since, in contrast to ammonia, the appearance of small amounts of hydrazine from impurities is unlikely, the available analytical tests for hydrazine are very sensitive, and, having detected hydrazine, it was possible to select optimal conditions empirically.

The first system in which the formation of hydrazine from nitrogen in a protic medium was observed was Ti^{3+}–$Mo^{V\text{-}VI}$–N_2 (in aqueous or anhydrous alcohol in an alkaline medium). Subsequently the Cr^{2+}–Mo^{V}–N_2 and V^{2+}–Mo^{V} systems were discovered and it was found that, as in biological systems, vanadium compounds can replace molybdenum with retention of activity in relation to N_2. In this connection vanadium(II) compounds proved to be capable of reducing nitrogen in an aqueous medium without the addition of other transition metal compounds.

The Ti^{3+} – $Mo^{V\text{-}VI}$ – N_2 system [5,6,123–125]. In this case the reduction of nitrogen is observed only in a highly alkaline medium (at pH ≥ 10.5). With increase of the concentration of alkali, the yield of hydrazine passes through a maximum. Without the addition of molybdenum compounds ($MoOCl_3$, MoO_4^{2-}), the reaction hardly occurs.

Small amounts of hydrazine were detected even at room temperature and atmospheric pressure. The yield of hydrazine increases with nitrogen pressure and temperature.

At 90–110°C and a nitrogen pressure of 100–150 atm the system is catalytic with respect to molybdenum: several tens of nitrogen molecules can be reduced to hydrazine and ammonia per molybdenum atom. The reduction of $^{15}N_2$ proved to be consistent with the results obtained using light nitrogen.

The increase of the yield following the addition of other metal (Mg, Ca, or Ba) salts proved to be extremely interesting. Magnesium salts (chloride or sulphate) have a particularly marked effect.

The addition of these salts retards the reaction of titanium(III) hydroxide with water (which results in the evolution of hydrogen) and there is a simultaneous increase of the yield of hydrazine. It proved to be a maximum for the ratio Mg : Ti = 1 : 2.

At low temperatures hydrazine is virtually the only nitrogen reduction product. Above 85°C ammonia appears, its relative yield increasing with temperature. A kinetic study showed [125] that ammonia is a secondary product and is formed on reduction of hydrazine. Carbon monoxide and acetylene inhibit the reaction. In the presence of carbon monoxide a yellow carbonyl compound of molybdenum, in which the oxidation state of molybdenum is three, passes into the solution. Under these conditions, acetylene is reduced to ethylene, the reaction occurring also without molybdenum compounds.

In the absence of nitrogen the system evolves hydrogen from water irreversibly. Under these conditions, hydrogen cannot, of course, reduce nitrogen to hydrazine in an alkaline medium. However, it has been shown [126] that in an acid medium hydrogen can be used as a reducing agent for titanium(IV) (in the presence of platinum) and, after increasing the alkalinity of the solution, the resulting titanium(III) can (in the presence of molybdenum) reduce nitrogen to hydrazine. Thus, under the conditions of alternate increase of the acidity and alkalinity of the solution, hydrogen can reduce nitrogen to hydrazine; the energy deficiency is then in fact made good by the energy of neutralisation of the acid by alkali.

The temperature variation of the rate yields an activation energy for the reduction of nitrogen to hydrazine of 13 kcal mole^{-1}. [125] The attempts to employ instead of molybdenum other transition elements combined with titanium(III) were unsuccessful. Only vanadium compounds (for example $VOCl_2$) proved to be capable of replacing molybdenum with partial retention of activity in relation to nitrogen.

The Cr^{2+} – Mo^{V} – N_2 system [6,126]. Nitrogen is reduced to hydrazine when an aqueous alcoholic suspension of chromium(II) hydroxide is mixed with an $MoOCl_3$ solution in an atmosphere of nitrogen. In this case the reaction proceeds at an appreciable rate even in room temperature and the minimal concentration of alkali at which nitrogen is reduced to hydrazine is appreciably less than in the presence of titanium(III). The catalytic yields in relation to molybdenum were not determined in this system.

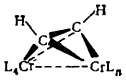
In such systems acetylene is also reduced in the absence of molybdenum, the reaction occurring in acid

solutions of chromium(II) salts as well. In this connection we may note that, in one of the earlier attempts to investigate the reduction of acetylene to ethylene from the standpoint of the simulation of the nitrogenase reaction, a study was made of the process [127]

$$C_2H_2 + 2Cr^{2+} + 2H^+ \rightarrow C_2H_4 + 2Cr^{3+} .$$

This reaction, discovered as early as 1916, [128] is interesting because, as in the case of nitrogenase, acetylene is quantitatively converted into ethylene without further reduction to ethane. The rate of reaction is proportional to the square of the concentration of chromium, which indicates the formation of a dinuclear complex of chromium ions and acetylene. Indeed, on cooling aqueous alcoholic solutions, the reversible formation of a relatively unstable dinuclear complex of acetylene and chromium, the heat of formation of which is only about 2 kcal mole^{-1}, was observed spectroscopically [129].

Further study of the analogous but more stable complex, which is formed in the presence of ammonia and can be isolated from the solution, showed [130] that its structure corresponds most closely to the formula



with a C–C bond close to a single bond and sp^3-hybridised C–H bonds. Thus acetylene in the complex is in fact reduced by a "four-electron" mechanism to an ethane derivative.

The reduction of acetylene in aqueous solution of chromium(II) salts is catalysed by acids and can be represented as follows:

$$2Cr^{2+} + C_2H_2 \rightleftharpoons [CrC_2H_2Cr]^{4+} \xrightarrow{H^+} [CrC_2H_3Cr]^{5+} \xrightarrow{H^+} 2Cr^{3+} + C_2H_4 .$$

Studies [131] on the reduction of other unsaturated compounds in a solution of chromium(II) salts showed that the mechanism involving two chromium ions is general. In acid media nitrogen is not reduced by Cr^{2+} ions, although the reduction potential of chromium(II) $E_0 = -0.40$ V is sufficient to form hydrazine from nitrogen. Admittedly it has been reported [132] that small amounts of ammonia are present in acid solutions in the reduction of nitrogen by zinc in the presence of chromium(VI) compounds, but these results were not confirmed by use of labelled nitrogen and are as usual doubtful.

The formation of small amounts of hydrazine in the electrochemical reduction of nitrogen in acid solutions in the presence of molybdenum complexes has been reported [133]. The yields did not exceed 1% with respect to molybdenum and varied appreciably from experiment to experiment.

The $V^{2+}-N_2$ system [6,124,134,135]. The formation of hydrazine was observed on mixing an aqueous alcoholic suspension, prepared beforehand, of a mixture of vanadium(II) and magnesium hydroxides with an $MoOCl_3$ solution in an atmosphere of nitrogen. In this case appreciable yields of hydrazine were observed at high temperatures and high concentrations of alkali (in excess of 1 M).

Hydrazine is also formed on reduction of nitrogen in aqueous solution by freshly precipitated vanadium(II) hydroxide produced in the presence of added magnesium salts. In this instance the presence of molybdenum compounds is not required.

This, the simplest of the known nitrogen-reducing systems, proved to be the most active. When the optimal conditions are selected, nitrogen is reduced at a high rate in aqueous solutions even at room temperature and under an atmospheric nitrogen pressure. Together with hydrazine, ammonia is formed even at room temperature. The reaction again proceeds only in strongly alkaline media.

In this case magnesium salts proved to be even more important than for other analogous systems: in their absence hydrazine is hardly formed. At room temperature and [atmospheric ?] nitrogen pressure the reaction ceases (the system loses activity) when the yield of reduction products reaches 8–20% relative to the reducing agent, but, on raising the nitrogen pressure to 20–40 atm, the overall yield of hydrazine and ammonia becomes nearly quantitative, i.e. the following reactions take place:

$$4V(OH)_2 + N_2 + 4H_2O \rightarrow 4V(OH)_3 + N_2H_4 ,$$
$$6V(OH)_2 + N_2 + 6H_2O \rightarrow 6V(OH)_3 + 2NH_3 .$$

Vanadium(II) is comparatively readily regenerated by the electrochemical reduction of the vanadium(III) formed. In this connection and bearing in mind that, by selecting appropriate conditions it is possible to drive the reaction solely to the formation of hydrazine, the reaction can be employed as a new method for the synthesis of hydrazine from molecular nitrogen [136].

Kinetic data again show that ammonia is a secondary product formed by the reduction of hydrazine.

The activation energy for the reduction of nitrogen to hydrazine is only 10 kcal mole^{-1}. The vanadium system is also active in the presence of inhibitors of nitrogen fixation [134]. Under these conditions, carbon monoxide hardly retards the reduction of nitrogen. Acetylene competes with nitrogen for active centres (being itself converted into ethylene). Under these conditions, acetylene is only three times more active than nitrogen.

Even the reactivity of oxygen is comparable to that of molecular nitrogen in the reaction in alkaline solutions containing a suspension of vanadium(II) hydroxide in the presence of magnesium hydroxide. Therefore such solutions are capable of fixing nitrogen directly from air. The yield of reduction products is smaller only by a factor of two compared with pure nitrogen [134].

The oxidation-reduction potential of the system was measured and its relation to activity with respect to nitrogen was investigated [137].

3. Reduction of Nitrogen in Homogeneous Solutions of Vanadium Complexes [138,139]

In the search for homogeneous systems capable of fixing N_2 in protic media, Nikonova et al. [138] observed that vanadium(II) complexes with phenols containing two hydroxy-groups in *ortho*-positions relative to one another (catechol, dihydroxynaphthalene, etc.) have this ability. In alcoholic, aqueous alcoholic, and aqueous media the complexes can rapidly reduce nitrogen to ammonia even at room temperature and atmospheric pressure; the yield of ammonia increases with pressure and temperature.

The reaction with nitrogen proceeds in a narrow pH range [139]. The maximum yield in water (about 60% at room temperature, $P_{N_2} \geq 70$ atm) is attained at pH ~ 10. In this case the intermediate formation of hydrazine is not observed, which may be related to its reduction under the experimental conditions. Indeed, it has been shown that hydrazine is rapidly reduced to ammonia by vanadium(II) complexes of catechol.

Simultaneously with the reduction of nitrogen, the complexes decompose water, hydrogen being evolved. Under these conditions acetylene is reduced to ethylene, *cis*-dideuterioethylene being formed from C_2D_2 in H_2O. [140]

4. The Reduction of Nitrogen in Molybdenum–Thiol Systems

Schrauzer and coworkers reported in 1970–1971 the reduction of nitrogen to ammonia by sodium tetrahydroborate in the presence of molybdate and compounds containing mercapto-groups (cysteine, thioglycerol, and glutathione)[141,142]. The authors regard this system as a close model of nitrogenase, although under the optimal conditions the yield of ammonia is extremely small, reaching 0.06–0.1% relative to the initial molybdenum compound after five days at a nitrogen pressure of 140 atm. In later communications[143,144] the authors reported that the results were confirmed with the aid of labelled nitrogen $^{15}N_2$.

Acetylene inhibits the reduction of nitrogen, while carbon monoxide does not affect the yield of ammonia appreciably. In order to account for the absence of the inhibiting capacity of CO (in contrast to the behaviour in the biological fixation of nitrogen), the authors suggest the existence of an additional coordination site at the molybdenum atom (which is occupied by the enzyme in the biological system). However, it is not clear why CO cannot occupy also the second coordination site at the molybdenum atom. It is likewise difficult to imagine that, after its addition to molybdenum, the reactivity of carbon monoxide with respect to N_2 remains unchanged (this is evidently postulated by the authors).

Much higher yields of ammonia (1.5 moles of ammonia per mole of molybdate) have been quoted[145] for the Na_2MoO_4–$FeSO_4$–$NaBH_4$–N_2 system in the presence of 2-aminoethanethiol. However, subsequently the authors[145] were unable to reproduce their results (see Chatt and Leigh[25]). It was found that the system incorporating the pure reactants is virtually inactive with respect to nitrogen and it has been tentatively suggested that the system can begin to reduce nitrogen only after undergoing changes under the influence of certain hitherto unknown factors.

The data reported by Schrauzer and coworkers concerning the activity of molybdenum–thiol systems with respect to nitrogen are also still very contradictory. Thus the role of the added iron salts is obscure. In the first report[141] the authors do not mention iron, while in the next[142] they note that an iron salt is a necessary cocatalyst. Finally, it was stated in a recent communication[144] that an iron salt increases the yield of ammonia only slightly. In the same report[144], it is unexpectedly stated that the primary reaction product is di-imide, which accumulates in the course of 40 min.

It has been reported[146] that nitrogen is not reduced at all by sodium tetrahydroborate in the presence of the molybdenum–glutathione complex. These contradictions are probably related to the low activity of the system with respect to nitrogen.

Much more definite results were obtained for the reduction of other compounds, which can serve as substrates of nitrogenase: acetylene, isonitriles, etc. In particular it has been shown that acetylene[147] yields ethane simultaneously with ethylene, the latter not being an intermediate in the formation of ethane. This distinguishes molybdenum–thiol systems from nitrogenase, in the presence of which the only reduction product is ethylene. The very fact of the formation of ethane in this case constitutes direct confirmation of the possibility of the "four-electron" reduction of acetylene without its emergence from the coordination sphere of the complex.

One of the characteristic features of molybdenum–thiol systems is the activating effect of ATP, which, as stated by Schrauzer et al.[147], simulates the action of ATP on the functioning of nitrogenase. However, it has been established[148,149] that hydrolysis of ATP hardly occurs under the conditions of the operation of molybdenum–thiol system and the accelerating effect of ATP as well as of ADP and other nucleoside phosphates is in fact related to a change in the pH of the medium. Other acids, for example, sulphuric acid, act no less effectively.

Molybdates are not unique catalysts in these systems. For example, in the reduction of isonitriles molybdate can be replaced by compounds of other transition metals (WO_4^{2-}, VO_3^-, Pd^{2+}, Rh^{3+}, Ru^{3+}, Co^{3+}, and Fe^{2+}), some of which are more effective than molybdenum compounds[143].

5. The Cobalt–Porphyrin System

A reduction system containing a soluble porphyrin derivative of cobalt—*meso*-tetra(*p*-phenylsulphonato)-porphinatocobalt(III) (CoTPPS) and sodium tetrahydroborate—was described in a recent study[150]. The authors reported the reduction of nitrogen "on passing pure dry air" through an aqueous solution containing CoTPPS and $NaBH_4$ at pH 10. When the reaction was carried out over a period of one week with a daily addition of sodium tetrahydroborate solution, the authors observed the formation of 0.8–1 mole of ammonia per mole of CoTPPS. However, when these results were tested with the aid of labelled nitrogen[151], it was observed that the entire ammonia detected[150] is not formed from molecular nitrogen but evidently originates from the nitrogen of the porphyrin rings, i.e. the system is not active with respect to N_2. On the other hand, according to these data[150], the system reduces acetylene catalytically to ethylene and partly to ethane. Other unsaturated compounds (azide, cyanide, and acetonitrile) are also reduced catalytically. It is suggested that, under the influence of sodium tetrahydroborate, $Co^{III}TPPS$ is reduced to a cobalt(I) derivative which is involved in the reduction of the substrates. It was established earlier that cobalt(I) derivatives readily reduce nitrous oxide to nitrogen[152,153].

6. Complexes of Iron Compounds

It has been shown[154] that certain nitrogenase substrates can be reduced catalytically in the presence of iron complexes. The reducing agents were sodium tetrahydroborate or sodium dithionite in alcohol, water, or buffer mixtures. In the presence of dichlorotetrapyridineiron(II) as a catalyst sodium azide is reduced by sodium tetrahydroborate to ammonia and nitrogen. Cyanide is reduced to methane and ammonia. On reduction, acetonitrile give rise to ethane and ammonia. Acetylene and methylacetylene are reduced slowly to ethylene and propene and ethylene is reduced fairly rapidly to ethane, the last reaction being strongly inhibited by acetylene, which indicates the formation of stable acetylene complexes. On the basis of their results, the authors conclude that at the present time model experiments do not demonstrate whether molybdenum, iron, or both metals activate nitrogen in the nitrogenase reaction.

It has been noted that low yields of ammonia are formed when molecular nitrogen is reduced by iron complexes. However, without a test using $^{15}N_2$ these results give rise to the usual doubts.

7. The Mechanism of the Reduction of Nitrogen in Protic Media

Since the discovery of systems reducing nitrogen in protic media, only a short time has as yet elapsed and many aspects of the mechanism of the action of these systems still remain obscure.

The isolation of the carbonyl derivative of molybdenum(III) in the Ti^{3+}–Mo^{V}-VI nitrogen-fixing system in the presence of CO permits the conclusion that nitrogen is also activated by species containing molybdenum(III) (d^3 electronic configuration). Vanadium in the bivalent state, i.e. also in the d^3 electronic configuration, is active in relation to nitrogen.

The high pH values at which hydroxides are active with respect to N_2 provide evidence that the transition metal atoms interacting with N_2 have an effective negative charge. This is evidently required primarily to create a higher reduction potential. In homogeneous vanadium systems phenols, which are powerful electron donors, also probably increase the reduction potential of the system and ensure the reduction of N_2.

However, the results show that a high reduction potential is by itself insufficient for the creation of active systems. Vanadium(II) and molybdenum(III) systems exhibit specific activity in relation to nitrogen and their presence is essential. Presumably the d^3 configuration of molybdenum(III) and vanadium(II) makes them fairly powerful one-electron reducing agents and ensures the stability of the intermediate complex of the type

$$M{=}{=}N{=}{=}N{=}{=}M$$

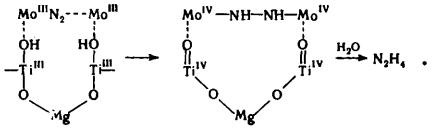
as a result of a dative interaction of the remaining electron pairs at the M atoms with the π-linkage of nitrogen.

The dinuclear structure is indicated particularly by the much higher activity of these systems in relation to acetylene molecules than in relation to ethylene [155]. The role of added metal salts, particularly of magnesium compounds, also confirms the necessity for a polynuclear structure. Data concerning the retardation of the formation of hydrazine in the vanadium system by vanadium(III) ions [156] led to the conclusion that a quartet of four vanadium(II) ions at a short distance from one another is necessary.

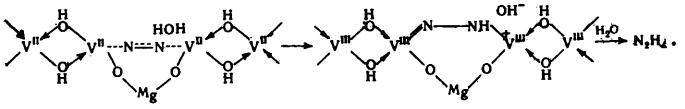
Apparently two vanadium ions form a dinuclear complex with N_2 and two other ions must transfer an additional two electrons to activated nitrogen in order to achieve the four-electron reduction to hydrazine. The magnesium ion (the efficiency of which is related to its small dimensions and the high concentration of charge) evidently forms a suitable structure, moving apart the atoms of the reducing agent to a specific distance with the aid of hydroxo- or oxo-bridging bonds.

These postulates are confirmed by measurements of the magnetic susceptibility of vanadium(II) hydroxide in the presence and absence of magnesium ions [157]. In the presence of magnesium ions the effective magnetic moment per vanadium atom increases, which indicates a decrease of electron exchange between the vanadium atoms.

The following mechanism for the formation of hydrazine in the Ti^{3+}–Mo^{V}-VI–Mg^{2+}–N_2 system has been suggested [124] (bearing in mind that molybdenum takes part in the reaction in the tervalent state):



A similar mechanism can be proposed for systems incorporating vanadium(II) hydroxide, but in this case vanadium ions play the role of all four atoms. One cannot rule out the possibility that a water molecule is involved in the reaction and that the mechanism is heterolytic. For example, the following mechanism can be proposed for the vanadium(II)–magnesium(II) hydroxide:



In homogeneous systems polyoxyaryl ligands also apparently give rise to dinuclear complexes. In all cases it is suggested that a dimolybdenum (or divanadium) structure is created in the intermediate complex and not one with two different metals, for example Mo^{III} and Cr^{II} or Mo^{III} and Ti^{III}.

There is as yet no direct proof of this hypothesis, although in dinuclear complexes in vanadium systems the second atom in the complex cannot of course be other than vanadium. However, bearing in mind that the reducing agent is not specific, it appears more likely that the reducing agents transfer electrons (and hydrogen atoms) to nitrogen activated in the complex containing two molybdenum atoms and in molybdenum systems.

V. COMPARISON OF NITROGENASE AND VARIOUS NITROGEN-FIXING SYSTEMS

The problem of which systems simulate the action of nitrogenase and which cannot be regarded as its models is to some extent academic. It appears that an absolute model cannot exist at all and that each reaction investigated from the standpoint of the simulation of nitrogenase simulates only a property or several properties of the enzyme. In the course of development of our knowledge of the mechanism of the action of nitrogenase, and following the discovery of new nitrogen-fixing systems, the models have improved to an increasing degree.

One can agree with the view of Newton et al. [154] that "the crucial test of a nitrogenase model is its ability to catalyse the reduction of molecular nitrogen at ambient temperature and pressure". However, the most general conclusions are apparently obtained not from a comparison of nitrogenase with any one nitrogen reduction reaction, but by examining the sum total of the information concerning both the reaction of nitrogen and systems which do not reduce nitrogen and can be regarded as models only by convention.

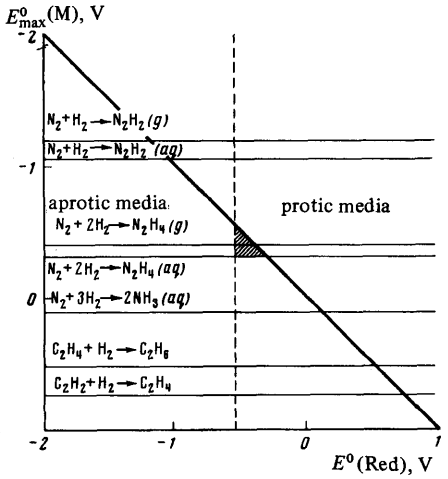
Moreover, the number of nitrogen reduction reactions under the conditions approaching those in which nitrogenase is active is so far small and it is therefore reasonable to consider also the reactions of other nitrogenase substrates. The available results permit the following generalisation. Many transition metals in low valent states can activate and reduce nitrogen to nitrides in aprotic media under the influence of powerful reducing agents. In protic media, including the aqueous medium, moderately strong reducing agents reduce acetylene and other nitrogenase substrates, also in the presence of a large number of various transition metal compounds.

The reduction of nitrogen in protic media (by moderately strong reducing agents) at a fairly high rate has so far been observed only for metals which are effective as part of the active centre of nitrogenase, namely molybdenum and vanadium. This agreement can hardly be fortuitous

and is evidently a consequence of a profound analogy between the mechanism of the action of nitrogenase and of systems reducing nitrogen in protic media.

There is no reason to suppose that in the future systems incorporating other metals in the active centre will not be discovered. However, there is no doubt that molybdenum and vanadium compounds in simple combinations form active nitrogen-fixing systems more readily than other metals.

The explanation of the comparative scarcity of nitrogen-reducing systems is probably related, to a first approximation, to the energetic difficulties which were considered in Section II of the present review.



Schematic representation of the free energy relations of nitrogen-fixing reactions.

The situation is illustrated schematically in the Figure, where the horizontal lines represent the free energies of the corresponding reactions referred to one electron and the inclined line corresponds to the maximum reduction potential of the catalyst M (which must not exceed the potential of the reducing agent Red participating in the reaction). At a given reduction potential, a particular reaction is possible if the corresponding horizontal line is located underneath the inclined straight line. Naturally, the greater the distance between the inclined and horizontal lines the greater the probability of finding a catalyst M for this reaction, other conditions being equal.

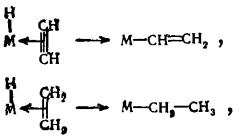
At very high reduction potentials there is a possibility of two-electron reduction of nitrogen. In such instances the rupture of the π-linkage can occur in the mononuclear complex with subsequent formation of the structure M–N=N–M', where M' is a non-transition metal, for example lithium. At even higher potentials there is a possibility of a one-electron mechanism and the transition metal ceases to be necessary for the reduction of nitrogen.

When E^0 is reduced, the formation of a dinuclear complex MN_2M with two transition metals, which is stabilised by the additional interaction of the *d* electrons with the π-linkages of nitrogen, becomes necessary. In this case there is a possibility of further reduction to a hydrazine derivative and then to the nitride with the maximum yield (in catalytic systems) of one nitride molecule per transition metal atom. The majority of the Vol'pin–Shur systems are of this kind. When the difference between E^0 and the value for hydrazine (or its derivative) is large, there is a high probability that the transition metal compound present in the system will be suitable for the activation and reduction of N_2.

On further decrease of E^0 and transition to protic media, the difference between the potentials of the reducing agent and hydrazine falls and the probability of catalytic action by the transition metal is sharply diminished. We have seen that in the presence of reducing agents sufficiently powerful to reduce nitrogen in protic media the transition metal must possess a comparatively rare combination of a specific set of properties. It is not surprising that such systems are encountered rarely and that in the course of evolution nature has chosen the metals which permit the most efficient reduction of nitrogen.

The difference between the potentials of the reducing agent and the acetylene–ethylene pair can remain considerable under these conditions also on further decrease of E^0. Naturally the probability that the transition metal compound will prove suitable is fairly high and many transition metals may be catalytically active.

Here a mononuclear structure of the complex is again possible. The weakness of the π-linkage in acetylene and ethylene permits the reactions



which take place in numerous known catalytic hydrogenation reactions of unsaturated molecules.

From the standpoint of this approach, the structure of the intermediate complex in nitrogenase as well as in nitrogen-fixing systems in protic media must be dinuclear.

Examination of model systems thus confirms the conclusions reached in studies on the mechanism of the activation of nitrogen by nitrogenase, where a dinuclear structure of the intermediate complex is adopted (see, for example, Refs. 19 and 120) and one of the atoms activating the N_2 molecule is definitely molybdenum. It has been by no means clearly shown whether two molybdenum atoms or one molybdenum atom and one iron atom, as suggested in some investigations [19,158], enter into the dinuclear structure of the nitrogenase complex.

As already stated, in model systems the activation of N_2 presumably takes place in dinuclear complexes involving only molybdenum atoms and the reducing agent transfers electrons to the activated nitrogen.

Thus the study of the fixation of nitrogen in model systems currently known suggests that it is more likely that the biological process also involves two molybdenum atoms rather than one molybdenum atom and one iron atom, although this conclusion cannot be regarded as unambiguous.

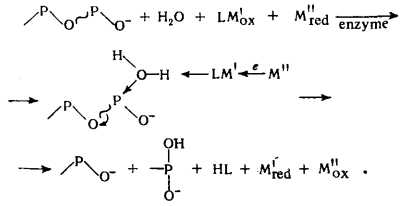
One may note yet another analogy between the nitrogenase and model systems involving hydroxides, which is probably not fortuitous. The metal atoms participating in electron transfer are linked in both cases (in nitrogenase iron ions are linked via bridging sulphide bonds [120] and in the hydroxides Ti^{III}, Cr^{II}, and V^{II} atoms are joined via hydroxo- and oxo-bridges). Presumably this ensures the possibility of many-electron processes involving the nitrogen bound in the complex.

An important characteristic of the biological fixation of nitrogen is the fact that it proceeds as a process coupled with the hydrolysis of ATP. The mechanism of the action of ATP is still obscure.

According to the hypothesis adopted at present[19], the hydrolysis of ATP tends to increase E^0 for the system. Parshall[159] suggests that the phosphorylation of the molybdenum complexes facilitates the formation of molybdenum hydride.

Studies on the changes in the ESR spectra under the influence of ATP have shown[160] that the ATP linked to Fe-protein in nitrogenase does in fact ensure electron transfer from Fe-protein to MoFe-protein. These results are consistent with those of Syrtsova et al.[161] who showed that ATP is not located unduly close to MoFe-protein of nitrogenase, where the nitrogen molecule is evidently activated by combining with the molybdenum atom.

Models of the action of ATP are so far unknown in the reduction of nitrogen in non-biological systems. On the other hand, in many of the examples quoted in the review involving the reduction of both nitrogen and other compounds, an acid which protonates the substrate and facilitates the reduction plays an activating role. In this connection it is possible to suggest[148,149] that an active proton is formed in the hydrolysis of ATP which ensures electron transfer (for example from the iron atom of Fe-protein of nitrogenase to the iron cluster of MoFe-protein). For example, the following chemical mechanism of this coupled process may be suggested:



As a result of the energy of the high-energy bond of ATP the potential of M' (for example of the iron cluster of MoFe-protein) may be sufficiently high to reduce the activated nitrogen molecule.

Naturally the suggested mechanism of the action of ATP requires a definite steric activation by the enzyme molecule, which has not so far been achieved in non-biological studies.

The alkaline medium in model systems creates an effective negative charge on the metal atoms activating molecular nitrogen and increases thereby the reduction potential of the system. In this case there is no need for additional activation by the proton arising in the hydrolysis of ATP and the water proton can prove to be a sufficiently powerful acceptor.

The determination of further details of the relation between the mechanism of the reduction of nitrogen in models systems and its enzymatic reduction would probably require the introduction of a large number of unjustified hypotheses and would not at present be useful for the determination of new and more specific data concerning the mechanism, particularly since the rapid development of this field will evidently make it possible in the near future to employ firmly established experimental facts as a basis.

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During the decade which has elapsed since the discovery of the nitrogen reduction reactions in solutions of transition metal complexes, the chemistry of molecular nitrogen has already required serious revision and considerable expansion. There is no doubt that progress in this field will continue also in the future.

Processes of practical value should presumably be developed in parallel with the discovery of new reactions which are of fundamental interest, particularly reactions which are still closer models of the biological fixation of nitrogen. Although competition with the modern large-scale ammonia synthesis is hardly likely in the immediate future, one may hope that the syntheses of other nitrogen-containing substances will find applications in the laboratory or in industry.

Molecular nitrogen is becoming an increasingly common ligand and reagent in catalytic and non-catalytic reactions.

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Hydrogen Transfer from Organic Compounds Catalysed by Transition Metal Complexes

I.S.Kolomnikov, V.P.Kukolev, and M.E.Vol'pin

The review deals with the new rapidly developing field of homogeneous catalysis and coordination chemistry, namely with reactions involving hydrogen transfer from organic compounds to transition metal complexes accompanied by the dissociation of a C-H bond and the formation of a metal-hydrogen bond. Particular attention has been devoted to catalytic reactions in which transition metal compounds serve as catalysts of hydrogen transfer and of the reduction of organic compounds by the C-H bonds of other organic molecules.
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I. INTRODUCTION

The homogeneous hydrogenation of organic compounds catalysed by transition metal complexes is one of the most thoroughly investigated fields of homogeneous coordination catalysis (see the relevant reviews[1-17]). The most important stage in the mechanism of homogeneous hydrogenation reactions is the activation of the H_2 molecule and the dissociation of the H-H bond. Recently we witnessed the growth of interest in extremely similar processes—the activation and dissociation of a C-H bond by transition metal compounds. Reactions of this kind are being increasingly used to transfer hydrogen and (or) an organic residue to different molecules.

This review deals with the part of the problem concerning hydrogen transfer from one organic molecule to another with the aid of transition metal compounds. These reactions have not so far been reviewed and are only mentioned in studies on homogeneous hydrogenation (see, for example, Ugo[13] and Kwiatek[14]).

Hydrogen transfer reactions are of significant interest both from the standpoint of the search for new methods of activating C-H bonds and in the preparative sense, since they lead to new ways of achieving hydrogenation and dehydrogenation reactions under mild conditions. It should also be noted that reactions of this type have attracted attention from the standpoint of the simulation of biochemical hydrogen and electron transfer processes (cf. Zelenin and Khidekel'[18]).

In the present review we consider only those catalytic hydrogen transfer reactions which are accompanied by the dissociation of C-H bonds. We are not concerned with the large field of reactions accompanied by the oxidation of C-H bonds, which results in electron transfer to a molecule of oxygen or another oxidant. Thus we are dealing primarily with processes where one can speak with greater or lesser certainty of hydrogen transfer from one organic molecule to another, catalysed by transition metal compounds.

Catalytic hydrogen transfer from organic compounds has much in common with homogeneous hydrogenation by molecular hydrogen. Like homogeneous hydrogenation, it includes two fundamental stages.

1. Dissociation of the C-H bond and hydrogen transfer to the metal (M):

$$R{-}H + M \rightarrow R{+}MH \quad \text{or} \quad R\!\!<\!\!\begin{matrix}H\\H\end{matrix} + M \rightarrow MH_2 + R\,.$$

2. Hydrogen transfer from the metal to an unsaturated substrate (S):

$$M{-}H + S \rightarrow S{-}H + M \quad \text{or} \quad MH_2 + S \rightarrow SH_2 + M\,.$$

The second stage is evidently the same as the analogous stage in homogeneous hydrogenation. Thus the specific features of hydrogen transfer processes are fundamentally related to the specific features of the first reaction stage. In this connection we shall consider separately the first, most important reaction stage and shall then return to the problem of the catalysis of hydrogen transfer, which includes the simultaneous occurrence of both processes.

II. DISSOCIATION OF THE C-H BOND AND HYDROGEN TRANSFER TO THE TRANSITION METAL

As in the dissociation of the H-H bond, the dissociation of the C-H bond with the aid of transition metal compounds can occur in principle via several different mechanisms (M is the transition metal atom in the complex).

1. With proton transfer:

$$R{:}H + M \longrightarrow R^- + (M{-}H)^+\,.$$

2. With hydride hydrogen transfer:

$$R{:}H + M \longrightarrow R^+ + (M{-}H)^-\,.$$

3. With homolytic dissociation of the C-H bond:

$$R{:}H + 2M \longrightarrow M{-}H + M{-}R\,.$$

4. Via reactions of the oxidative addition type:

$$R{-}H + M \rightarrow M\!\!<\!\!\begin{matrix}H\\R\end{matrix}\,.$$

The nature of the process occurring will of course depend not only on the transition metal compounds but to

no less an extent on the nature of the C–H bond in the reacting organic compounds, the properties of which can vary within extremely wide limits.

Reactions of Type (1)

These involve the acid dissociation of the C–H bond and protonation of the transition metal compounds. They are not of interest for the present problem, since such hydrogen transfer cannot lead to the reduction of the substrate. However, one should note that the analogous process—the dissociation of the C–H bond as a result of electrophilic substitution,

$$R{-}H + M^+ \longrightarrow RM + H^+ , \qquad (1a)$$

is the first stage of a number of important catalytic processes. The metal–carbon σ bond formed in this reaction can undergo further transformations and in the first place can give rise to oxidative dimerisation products[19]. A reaction of this type is, for example, the first stage of the conversion of benzene into biphenyl under the influence of palladium and platinum compounds[20–23]:

$$ArH + Pd^{2+} \rightarrow ArPd^+ + H^+ ,$$
$$2ArPd^+ \rightarrow ArAr + 2Pd^+ .$$

Possibly the oxidative dimerisation of olefins under the influence of palladium salts takes place analogously[24–27]:

$$2CH_2{=}CR_2 + Pd^{2+} \rightarrow R_2C{=}CHCH{=}CR_2 + 2H^+ + Pd^0 ,$$

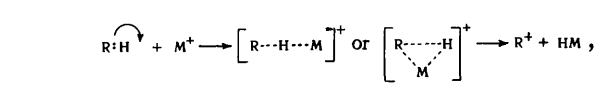
as well as the oxidative coupling of aromatic hydrocarbons to olefins[28]†:

$$ArH + Ar'CH{=}CH_2 + Pd^{2+} \rightarrow Ar'CH{=}CHAr + 2H^+ + Pd .$$

We shall examine in somewhat greater detail reactions of types (2), (3), and (4), which are of greatest interest from the standpoint of hydrogen transfer to unsaturated substrates.

Reaction (2)

This can be regarded as the transfer of the hydride ion H^- from carbon to the metal (the hydride shifts in organic chemistry have been reviewed[29]). Reactions of this type can occur either as a synchronous transfer of hydrogen and an electron pair via a transition state of a linear or π-type,



or as a result of a one-electron transfer followed by the transfer of hydrogen in the form of a proton (or radical):

$$R{:}H + M^+ \rightarrow \begin{matrix}[RH^{+\cdot} + \cdot M] \rightarrow R^+ + HM \\ \searrow [R^+ + H^+ + :M^-] \nearrow\end{matrix} .$$

However, regardless of the nature of these "intimate" mechanisms of the hydride shift, the latter should be favoured by factors such as a positive (not unduly large) charge at the metal atom and the presence of π-ligands, which stabilise the metal–hydrogen bond.

The hydride mobility of the C–H bond in the organic compound which behaves as the donor of the hydride ion is particularly important for the occurrence of such reactions. The ease of the elimination of the hydride ion is paralleled by the stability of the carbonium ion formed as a result—the more stable the carbonium ion under the given conditions the greater the ease with which the hydride ion is split off from the initial C–H bond. The stability of carbonium ions is known to be determined to a considerable degree by the nature of the substituents at the carbonium carbon atom.

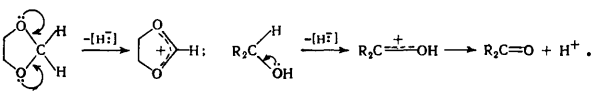
The resulting carbonium ions are stabilised and the hydride shifts via mechanism (2) are thus facilitated by electron-donating substituents of the following kinds.

a. Alkyl groups; the ease of elimination of hydride hydrogen increases in the sequence Me–H < Me_2CH–H < Me_3C–H.

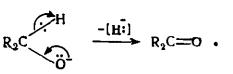
b. Substituents containing multiple bonds (in the first place carbon–carbon bonds) coupled with the carbonium centre and giving rise thereby to the possibility of the delocalisation of the positive charge. The accumulation of such aryl or vinyl substituents at the carbon atom significantly facilitates the elimination of the hydride ion from the latter; an example is provided by triphenylmethane, which is readily converted into the triphenylmethyl cation:

$$Ph_3CH \xrightarrow{-[H^-:]} Ph_3C^+ .$$

c. Substituents containing a free pair of *p* electrons ($-\ddot{N}R_2$, $\ddot{O}R$, $\ddot{S}R$, etc.). Such substituents stabilise the carbonium centre with formation of much more stable conjugate cations:

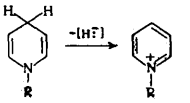


Groups bearing not only an electron pair but also a negative charge facilitate the elimination of the hydride ion even more. In particular this accounts for the high reducing capacity of alkoxides:



d. The hydride ion elimination reaction is significantly facilitated when it results in the formation of molecules with enhanced stability. This factor accounts for the particularly great ease of elimination of the hydride ion from cyclopropene and cycloheptatriene (including cases where the process takes place under the influence of transition metal compounds), leading to the formation of non-benzenoid aromatic cyclopropenylium and tropylium cations:

Another example is provided by the dihydropyridine-nucleotide coenzyme (reduced nicotinamide-adenine dinucleotide NADH), which is an active hydride ion donor (cf. Zelenin and Khidekel'[18]):



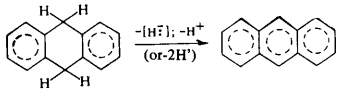
This reaction, which is biochemically important, is facilitated both by the presence of the free electron pair

† However, one cannot rule out the possibility that in the dimerisation of olefins the first stage is the dissociation of the C–H bond via mechanisms (2), (3), or (4). Thus reversible homolytic dissociation of the vinyl C–H bond has been suggested[27] for the oxidative coupling of acrylonitrile under the influence of ruthenium(III) salts:

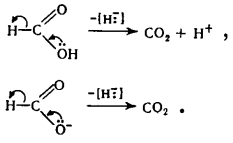
$$2L_nRu + 2CH_2{=}CHCN \rightleftarrows 2L_nRuH(CH{=}CHCN) \rightarrow NCCH{=}CH{-}CH{=}CHCN .$$

of nitrogen and by the formation of the aromatic pyridinium system.

In certain cases the stabilisation of the products of the hydride shift reaction is accompanied by rapid elimination of a proton. The elimination of the hydride ion from dihydroanthracene, which leads to the formation of the aromatic anthracene system, takes place in this way:



The ease of elimination of the hydride ion from formic acid and formates can be explained not only by the influence of the free electron pair of the adjacent oxygen atom but also by the considerable stability of the resulting carbon dioxide molecule:



Reaction (3)

We shall now turn to the mechanism of reactions (3), which involves the homolytic dissociation of the C–H bond. The energy of the homolytic dissociation of the C–H bond ($R-H \rightarrow R\cdot + H\cdot$) is 103 ± 2 kcal mole^{-1} (at 298°K) for the methane molecule and has similar values for other saturated hydrocarbons and for benzene. It differs very little from the dissociation energy of the H–H bond, which is 104.2 kcal mole^{-1} (at 298°K)‡. Thus comparison of reaction (3) with the analogous homolytic dissociation reaction of the H_2 molecule,

$$H_2 + 2M\cdot \rightarrow 2MH ,$$

shows that the differences between the free energies of these two reactions must be determined primarily by the differences between the stabilities of the metal–carbon and metal–hydrogen bonds.

Reaction (4)

The same considerations apply also to the occurrence of the oxidative addition reactions of type (4). As in the analogous reaction of H_2,[30] the energy of this reaction can be deduced from the following qualitative considerations. If in the course of the dissociation of the C–H bond the metal is oxidised as a result of oxidative addition via mechanism (4) and passes from the square d^8 configuration to the octahedral d^3 configuration [d^6 configuration (Ed. of Translation)], the energy of the reaction will be approximately described by the equation

$$\Delta E = E_{M-H} + E_{M-C} - (E_{C-H} + P) ,$$

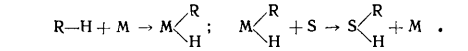
where E_{M-H} is the energy of the hydrogen–metal bond, E_{M-C} the energy of the carbon–metal bond, E_{C-H} the dissociation energy of the C–H bond, and P the promotion energy of electron transfer in the ligand field to a higher orbital (for example from the $5d_{z^2}$ orbital to the $6p_z$ orbital). As stated above, E_{C-H} changes within fairly narrow limits and ΔE will thus depend primarily on P and E_{M-C}. P will decrease (and hence ΔE will increase) following the introduction of electron-donating ligands (promoting the transfer of non-bonding electrons to higher orbitals) and on passing to metals of the lower Periods. On the other hand, electron-accepting ligands should hinder the reaction. One should of course note that, for hydrogen transfer catalysts, P must not be very small either, since otherwise the hydride formed will be unduly stable and will be unable to give up its hydrogen to the substrate.

It is as yet not completely clear how the E_{M-C} depend on different factors. However, one should note that previous ideas concerning the low thermodynamic stability of the transition metal–carbon bond proved to be incorrect and that the role of the ligands in the stabilisation of these bonds is related in the first place to kinetic factors[31,32]. Electron-donating, strongly nucleophilic ligands should probably exhibit a powerful stabilising effect[31]. The available thermodynamic data are very scanty, but they do show that the transition metal–aryl bond is much more stable than the transition metal–alkyl bond. Thus the energy of the Pt–Ph bond in $(Et_3P)_2PtPh_2$ is approximately 250 kJ mole^{-1},[33] while the Pt–Me bond in $CpPtMe_3$ has an energy of only about 164 kJ mole^{-1}.[34] Similarly the energies of the Ti–Ph and Ti–Me bonds in Cp_2TiPh_2 and Cp_2TiMe_2 are respectively 350 and 250 kJ mole^{-1}.[35]

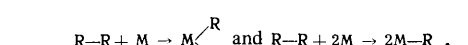
Thus, other conditions being equal, the reactions involving the oxidative addition of the C–H bond to a transition metal atom should occur much more readily for aromatic compounds than for aliphatic compounds. Indeed the experimental data quoted below confirm this conclusion.

Furthermore, in oxidative addition reactions occurring with the formation of a metal–carbon bond the entropy component will presumably make a large contribution to E_{M-C} (in contrast to the M–H bond). For this reason, such reactions should be favoured by a low coordination number of the initial complex (which is frequently associated also with a low oxidation state of the metal) and a small size of the ligands present and of the organic group R introduced.

It is noteworthy that reactions of type (3) and (4) give rise to the possibility not only of hydrogen transfer but also of the transfer of various organic groups R to substrates S with the aid of transition metal complexes, for example:



It has been shown recently that the dissociation of C–C bonds can sometimes take place analogously to the dissociation of C–H bonds with formation of products containing a metal–carbon σ bond[36–39]:



In certain cases these reactions, in which the metal is inserted into the C–C bond, constitute intermediate stages in skeletal rearrangements[40,41]. However, examination of these interesting reactions is outside the scope of the present review.

The data available at present by no means make it always possible to decide which of the mechanisms (1)–(4)

‡ In those cases where the radical R· is stabilised by conjugation, the dissociation energy is appreciably lower: 77 kcal mole^{-1} for the allyl–H bond and 78 kcal mole^{-1} for the benzyl–H bond. This accounts for the greater ease of dissociation of these bonds.

governs the activation of the C–H bond; usually this has to be inferred solely on the basis of the structure of the resulting transition metal hydride complexes.

Fairly extensive experimental data on the use of various organic hydrogen donors for the synthesis of hydride complexes have accumulated in the coordination chemistry of transition metals (see reviews [42-44]). We shall examine these experimental results from the standpoint of the ideas formulated above concerning the dissociation of C–H bonds. We shall consider first reactions where a hydride mechanism of type (2) can be postulated.

The formation of ruthenium, osmium, rhodium, and iridium hydride complexes using alcohols as hydrogen donors has been most widely investigated. This reaction is promoted by alkaline agents, i.e. the C–H bond in alcohols is activated as a result of the formation of the alkoxide ion and in the course of the reaction the alcohols themselves are converted into aldehydes and ketones; reactions of this type probably take place with a hydride ion shift via mechanism (2).

Thus, when the complex $PtCl_2(PEt_3)_2$ is refluxed in an ethanol solution of potassium hydroxide, the hydride complex of platinum and acetaldehyde are obtained [45,46]:

$$PtCl_2(PEt_3)_2 + KOH + EtOH \rightarrow PtHCl(PEt_3)_2 + Me-C\overset{O}{\underset{H}{<}} + KCl + H_2O ,$$

$$Ru_2Cl_5(PEt_2Ph)_6Cl + 2EtOH + 2KOH \rightarrow 2RuHCl(CO)(PEt_2Ph)_3 + 2CH_4 + 2KCl + 2H_2O .$$

The rhodium hydride complex $HRh(PPh_3)_4$ is formed when $(Ph_3P)_3RhCl$ interacts with triphenylphosphine in n-propyl alcohol in the presence of alkaline agents [47]. In certain cases hydride complexes can be obtained from alcohols also in the absence of alkalis. Thus, when $(Ph_3P)_3IrCl$ reacts with ethanol (in the absence of a base), the hydride complex $(Ph_3P)_3IrH_2Cl$ and acetaldehyde are obtained [48]. The question of which hydrogen atom in the alcohol passes to the metal was elucidated for the formation of iridium hydride complexes in the presence of deuteriated alcohols [49]:

$$K_2IrCl_6 + Ph_3P \begin{cases} + CH_3CH_2OH + H_2O \rightarrow IrHCl_2(Ph_3P)_3 , & (1) \\ + CH_3CH_2OH + D_2O \rightarrow IrHCl_2(Ph_3P)_3 , & (2) \\ + CH_3CH_2OD + D_2O \rightarrow IrHCl_2(Ph_3P)_3 , & (3) \\ + CH_3CD_2OH + H_2O \rightarrow IrDCl_2(Ph_3P)_3 . & (4) \end{cases}$$

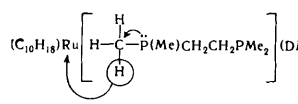
The mechanism shows that the interaction of the iridium salt and triphenylphosphine with both aqueous ethanol and with EtOD in the presence of D_2O [reactions (1)–(3)] leads to the formation of the iridium hydride complex $IrHCl_2(PPh_3)_3$, i.e. neither water nor the hydrogen atom of the alcoholic hydroxy-group behave as hydrogen donors in this reaction. On the other hand, the use of an alcohol with deuterium atoms at the 1-C atom [reaction (4)] leads to the formation of the deuteriated complex $IrDCl_2(Ph_3P)_3$. The experimental data show convincingly that the formation of hydride complexes from alcohols takes place as a result of the elimination of a hydrogen atom from the 1-C carbon atom of the alcohol, which exhibits the greatest hydride mobility. The fact that the addition of a base facilitates the removal of hydrogen from the alcohol as a result of the enhancement of the effect of p, σ conjugation in alkoxides becomes understandable from the same point of view.

One should note that alcohols can behave not only as hydrogen donors but also simultaneously as donors of the carbonyl group. For example, when triphenylphosphine is refluxed with $(NH_4)_2OsCl_6$ in the monomethyl ether of diethylene glycol, the mixed hydridocarbonyl complex $HOsCl(CO)(Ph_3P)_3$ is obtained [50]. When [^{14}C]ethylene glycol was used, it was shown that the glycol in fact behaves as the carbonylating agent in this reaction.

The formation of iridium, ruthenium, rhodium, and osmium hydride complexes in the reaction with alcohols has been described also in a number of other studies [51-58].

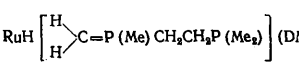
When transition metal complexes react with alcohols, it is not always possible to isolate and identify the hydride complex, although its formation is indirectly confirmed by the identification of the alcohol dehydrogenation products. For example, when allyl alcohol was refluxed with $RuCl_3 \cdot 3H_2O$, propene, acrolein, and propionaldehyde were found in the reaction products, although the hydride complex was not identified [59]. The study of the effect of phosphines on the capacity of rhodium complexes to eliminate hydride hydrogen from alcohols showed that the more basic the phosphine the greater the ease of this reaction [60].

It is noteworthy that the ligands coordinated to the metal atom can themselves behave as hydride donors in the formation of transition metal hydride complexes. In this case the hydride complex is formed as a result of hydrogen transfer from the organic component of the ligand molecule to the metal atom with dissociation of the C–H bond. Thus in the ruthenium complex $(C_{10}H_{18})Ru(DMPE)$, where DMPE = $Me_2P(CH_2)_2PMe_2$, hydrogen transfer from the methyl group of the phosphine ligand leads to the formation of a ruthenium hydride complex [61]:



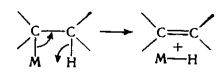
$$\rightarrow C_{10}H_{18} + RuH[CH_2{=}P(Me)CH_2CH_2PMe_2](DMPE) .$$

According to the authors' data, the hydride complex is in tautomeric equilibrium with a zerovalent ruthenium complex:



The dissociation of the C–H bond of the methyl group is observed also for the rhodium complex coordinated to the $(o\text{-tolyl})_3P$ ligand [62].

Reactions involving the intramolecular transfer of hydride hydrogen from the β-position of σ-alkyl ligands, leading to the formation of hydride complexes, are very common in the chemistry of organic derivatives of transition metals (they have been reviewed [63]):



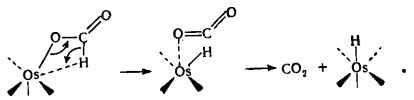
Reactions of this type take place readily when organolithium, organomagnesium, and organoaluminium compounds act on salts and complexes of transition metals. As an example of reactions involving individual σ-alkyl derivatives, we may quote the reaction of the platinum complex $PtCl(Et)(PEt_3)_2$, which eliminates ethylene on heating and forms a hydride complex via the mechanism [64,65]

That β-elimination does in fact take place has been demonstrated, in particular for the n-butylcopper complex [66]:

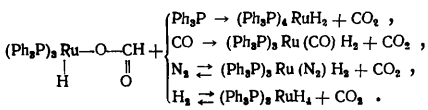
$$(Bu_3P)CuCH_2CD_2CH_2CH_3 \rightarrow (Bu_3P)CuD + CH_2{=}CDCH_2CH_3 .$$

Coordinated formate ligands can also readily give up hydrogen with formation of hydride complexes. For example, the osmium formate complex $Os(OOCH)_2(CO)_2 \cdot (PPh_3)_2$ is converted on refluxing in benzene into the

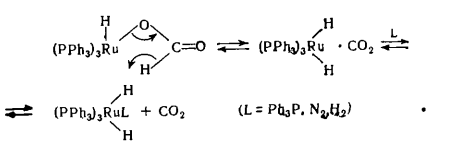
hydride $H_2Os(CO)_2(Ph_3P)_2$ with evolution of carbon dioxide via the mechanism [67]



The migration of hydrogen from carbon to the transition metal was observed very easily in the ruthenium formate complex $(Ph_3P)_3Ru(H)OOCH$. [68-70] This complex eliminates carbon dioxide unusually readily under the influence of various agents with formation of a hydride complex:

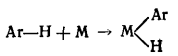


These unusual properties of the ruthenium formate complex can be accounted for by the exceptional ease of the migration of the hydride hydrogen of the formate group to the metal, accompanied by the formation of an unstable ruthenium hydride complex with carbon dioxide via the mechanism

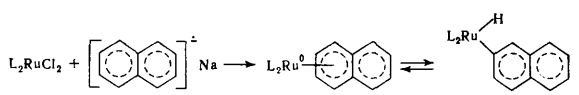


All the examples described above concerned reactions leading to the formation of a metal–hydrogen bond via mechanism (2), i.e. with formal transfer of a hydride ion from the C–H bond. Reactions involving the dissociation of the C–H bond via mechanisms (3) and (4), accompanied by the simultaneous formation of metal–carbon and metal–hydrogen bonds, constitute another group.

In contrast to hydride addition reactions, processes of this type are most typical for the dissociation of aromatic C–H bonds and the majority of examples known at present concern reactions of the type

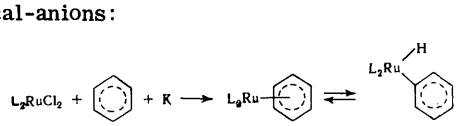


These reactions, which occur under the influence of low-valence transition metal derivatives, are frequently accompanied by the intermediate formation of π-arene complexes and their isomerisation to σ-aryl derivatives. According to the data of Chatt and Davidson [71], dichlorodi-(1,2-bisdimethylphosphinoethane)ruthenium is converted on treatment with sodionaphthalene in tetrahydrofuran (THF) into a π-arene complex of ruthenium which is in equilibrium with the σ-naphthylruthenium hydride complex:

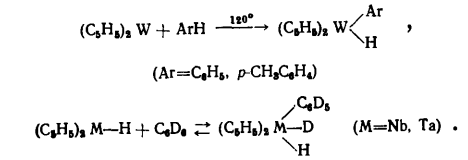


$(L = Me_2PCH_2CH_2PMe_2)$

The radical-anions of other aromatic hydrocarbons react similarly. In the case of benzene one can employ a mixture of benzene and metallic potassium instead of the radical-anions:



Similar reactions with aromatic radical-anions have been observed for cyclopentadienyl complexes of tungsten, tantalum, platinum, and other transition metals [72-75], for example:

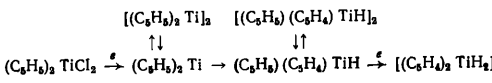


Titanium, vanadium, and chromium complexes give rise to reactions of the same type, with dissociation of the aromatic C–H bond [76,77].

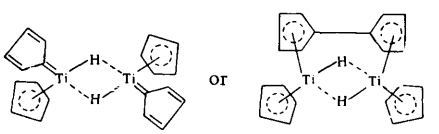
It has been shown by X-ray diffraction [78] that the product of the reaction of naphthalene with the 1,2-bisdimethylphosphinoethane complex of ruthenium is indeed a σ-naphthyl derivative of ruthenium.

It is noteworthy that hydrogen isotope exchange in benzene, catalysed by platinum salts, proceeds via an analogous mechanism with preliminary dissociation of the C–H bond [79,80].

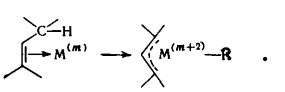
Not only aromatic hydrocarbons of the benzene type but also cyclopentadienyl ligands can serve as a source of hydrogen for the formation of the metal–hydrogen bond. Thus, in the reduction of titanocene derivatives by sodium, magnesium, sodionaphthalene, and other reducing agents, extremely ready migration of hydrogen from the ligand to the metal takes place [81-84]:



These reactions are also accompanied by the π, σ rearrangement of the ligand. Thus the following structural formulae have been proposed for the hydride form of titanocene $[(C_5H_5)(C_5H_4)TiH]_2$:

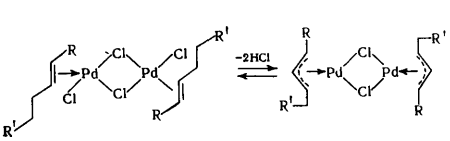


Finally the formation of hydride–allyl complexes from olefinic π complexes can be included among reactions of the type occurring with homolytic dissociation of the C–H bond via a mechanism close to oxidative addition:



(m = degree of oxidation)

Thus ruthenium hydride–allyl complexes $HRu(CO)_9(C_{12}H_{15})$, $HRu_3(CO)_9(C_{12}H_{17})$, and $HRu_3(CO)(C_{24}H_{33})$ are formed when cyclododecatriene reacts with ruthenium carbonyl $Ru_3(CO)_{12}$. [85] In the formation of π-allyl complexes of palladium, allyl hydrogen is also split off with intermediate formation of the Pd–H bond [86-91]:



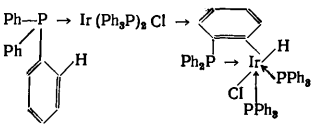
Dienes are formed in the decomposition of allyl complexes at an elevated temperature; a reaction of this

kind in the presence of oxidising agents (for example $CuCl_2$) can be achieved catalytically[92,93]:

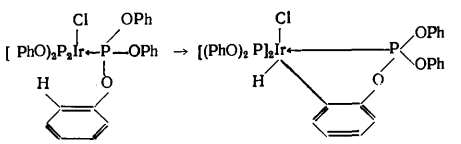
$$ROOCCH_2CH{=}CHCH_2COOR + 2CuCl_2 \xrightarrow{PdCl_2} \rightarrow ROOCCH{=}CHCH{=}CHCOOR + 2CuCl + 2HCl\ .$$

Another group of reactions occurring with insertion of the metal in an aromatic C–H bond comprises intramolecular hydrogen transfer from the *ortho*-position in the aromatic rings of phenylphosphine and phenyl phosphite ligands. Thus, on heating a solution of $(Ph_3P)_3IrCl$ in benzene, a hydride complex is formed[94]. The migration of the hydrogen atom from the phenyl ring was demonstrated using a fully deuteriated initial complex. On heating of $[P(C_6D_5)_3]_3IrCl$ in benzene, the product is a complex whose infrared spectrum indicates the presence of the Ir–D bond and the absence of the Ir–H bond.

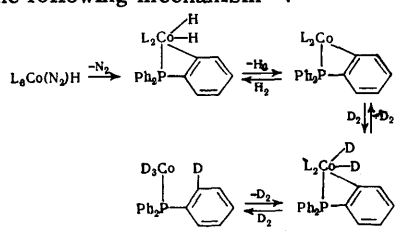
Evidently this reaction is a type of oxidative addition [reaction (4)]:



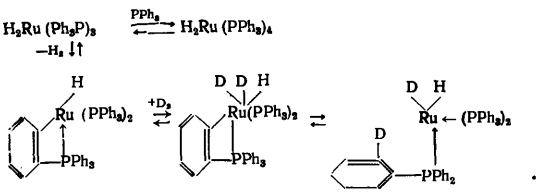
The interaction of IrCl(1,5-cyclo-octadiene) with triphenyl phosphite in acetone also leads to the formation of a hydride complex as a result of the migration of the *ortho*-hydrogen from the ligand[95]:



In many instances reactions of this kind are reversible and lead to the exchange of the *ortho*-hydrogen atoms of the benzene rings with the hydride hydrogen linked to the metal. For example, the exchange of hydrogen for deuterium in the *ortho*-positions of the benzene ring of the triphenylphosphine ligands in the cobalt complex proceeds via the following mechanism[96]:

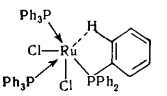


The deuterium exchange reactions take place similarly with the phosphine complexes of ruthenium[97–99]. For example, when the ruthenium complex $H_2Ru(Ph_3P)_4$ was allowed to react with D_2 in benzene and this was followed by the decomposition of the resulting complex with hydrogen peroxide, deuterium was identified in the benzene ring[99]. On the basis of these results, the authors concluded that in the course of the reaction there is a rapid reversible interaction of the ruthenium atom with the *o*-C–H bond:



A similar hydrogen transfer to the ruthenium atom with formation of a hydride complex occurs also in the case of the triphenyl phosphite ligand[100].

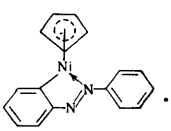
It is noteworthy that the ease of migration of hydrogen from the *ortho*-position of the benzene ring is probably related not only to the nature of the metal but also to the structure of the complex. X-Ray diffraction analysis of the triphenylphosphine complex of ruthenium $(Ph_3P)_3RuCl_2$ showed that the hydrogen atom in the *ortho*-position in the benzene ring is at a very short distance from the ruthenium atom[101]:



This accounts for the ease of migration of the hydrogen atom to ruthenium in such complexes.

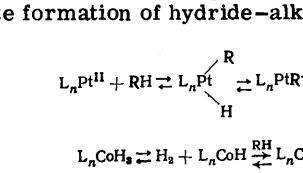
The formation of hydride complexes as a result of hydrogen transfer from the phenyl group and the coordinated phosphine ligand was also observed for cobalt and iron complexes. Thus the interaction of $HCo(N_2)[P(C_6D_5)_3]_3$ with bis-(1,2-diphenylphosphinoethane) results in the formation of a mixture of $HCo(DPPE)_2$ and $DCo(DPPE)_2$, where DPPE is diphenylphosphinoethane[102], while irradiation of $Fe(C_2H_4)(DPPE)_2$ in benzene solution leads to the formation of ethylene and the hydride complex $HFe(o\text{-}C_6H_4)(PC_6H_5)CH_2CH_2P(C_6H_5)_2(DPPE)$, the phosphine ligand behaving as the source of hydrogen in both instances[103,104]. A similar reaction has been observed also for ruthenium complexes with triphenylphosphine[105,106].

It is noteworthy that the cleavage of the *o*-C–H bonds of the benzene ring in the ligands proceeds so readily that in many cases they yield products with a stable transition metal–carbon bond. Certain transition metal complexes of azobenzene[107,108] and Schiff bases[109,110] have this structure, for example:



In the course of formation of such complexes the metal is apparently inserted in the *o*-C–H bond with subsequent elimination of hydrogen (as a proton or a hydrogen atom).

The examples examined above concern the insertion of the metal in an aromatic C–H bond. However, recent findings show that transition metal compounds are capable of being inserted also in an aliphatic C–H bond in saturated hydrocarbons. Shilov, Shteinman, and coworkers[111–113] and then also other workers[114,115] observed deuterium exchange involving methane, ethane, and other saturated hydrocarbons under the influence of platinum and cobalt. The results can be accounted for by reversible oxidative addition with dissociation of an aliphatic C–H bond and the intermediate formation of hydride–alkyl derivatives:



Analysis of kinetic data for deuterium exchange with water in aqueous acetic acid solutions of platinum(II) salts showed that the activity of the platinum compounds decreases in the sequence $PtX_2 > PtX_3^- > PtX_4^{2-}$ and in the

following sequence of the ligands X: Cl > Br > I. However, this reaction can occur also without the formation of a hydride via the elimination of a proton and the formation of an alkylplatinum derivative[116]:

$$PtCl_4^{2-} + RH \rightleftarrows PtCl_3R^{2-} + H^+ + Cl^- .$$

Thus fairly numerous organic substrates can behave as hydrogen donors in reactions with transition metal complexes leading to hydride complexes. However, the formation of hydride complexes alone is insufficient for the reduction of organic substrates. The hydrogen atom in the hydride complex must be sufficiently labile for the complex to be capable of participating in hydrogen transfer reactions. Moreover, as in homogeneous hydrogenation, the resulting hydride complex must be able to coordinate and activate the unsaturated substrate.

III. CATALYTIC HYDROGEN TRANSFER

The range of catalytic reactions involving hydrogen transfer from organic compounds to unsaturated substrates (olefins, aldehydes, ketones, etc.) known at present is much narrower than that of hydrogen reduction reactions. However, the number of known reactions of this kind is rapidly increasing and some of them have already assumed preparative importance.

1. Reduction by Alcohols, Alkoxides, and Ethers

Alcohols and alkoxides are most widely used as hydrogen donors. One of the first studies in this field was carried out by Italian workers[47,117], who found that unsaturated compounds can be reduced in the presence of rhodium, complexes using benzyl alcohol as the hydrogen donor. In the presence of rhodium complexes of the type $L_3Rh(CO)H$, where L = Et_3P, Bu_3P, Ph_2MeP, etc., the reduction of oct-1-ene by benzyl alcohol in the presence of potassium benzyloxide (with formation of PhCOOK) was observed. However, this reaction was fairly slow even at an elevated temperature (130°C), the maximum yield of the hydrogenation product (octane) amounting to only 35% after 4 h (Table 1).

Table 1. Catalytic activities of the phosphine complexes of rhodium in hydrogen transfer from benzyl alcohol to oct-1-ene (0.06 mole of benzyl alcohol, 0.035 mole of oct-1-ene, 0.006 mole of potassium benzyloxide, and 0.0003 mole of the catalyst, 130°C, time 4 h).

Catalyst	Conversion of benzyloxide into benzoate, %	Conversion of oct-1-ene into octane, %
$HRh(CO)(PEt_3)_3$	50	35
$HRh(CO)(PBu_3)_3$	25	6
$HRh(CO)(PEt_2Ph)_3$	15	3
$HRh(CO)(PMePh_2)_3$	2	traces
$HRh(CO)(PEt_3)_3$	4	6

The reduction of unsaturated compounds with hydrogen transfer from alcohols can occur also in the presence of certain transition metal salts[118]. Thus rhodium and ruthenium chlorides catalyse at 100°C the reduction by ethanol of hex-3-yne to hex-3-ene, of cyclopentadiene to cyclopentene, and of 5-vinylbicyclo[2,2,1]hept-2-ene to 2-vinylbicyclo[2,2,1]heptane, the ruthenium salt proving to be more active than the rhodium salt.

The authors of this investigation suggest that in the course of the reduction process an intermediate complex with an Rh–H bond is formed and is responsible for the reduction. The study[119] where it was shown that rhodium salts catalyse the dehydrogenation of 2-propanol is interesting in this connection. It is suggested that the dehydrogenation of the alcohol proceeds via an intermediate hydride according to the mechanism

$$Me_2CHOH + [Rh^{III} - Cl] \rightleftarrows Me_2CO + [Rh^{III} - H] + HCl ,$$

$$[Rh^{III}H] + HCl \rightarrow [Rh^{III}Cl] + H_2 .$$

The alcohol dehydrogenation reaction has also been described in the presence of cobalt carbonyl as a process which is the converse of the hydrogenation of aldehydes in the hydroformylation reaction[120–123].

There are literature data concerning the transfer of hydrogen from alcohols to unsaturated compounds under the influence of transition metal acetylacetonates (for example, nickel acetylacetonate)[124]. The reaction proceeds under fairly severe conditions at a temperature of 200–220°C. Methyl linoleate and methyl octadecadienoate, which have conjugated double bonds, were reduced under these conditions with the aid of different alcohols (isopropyl, n-propyl, ethyl, s-butyl, n-butyl, s-pentyl, and n-tentyl). In the hydrogenation of methyl linoleate the reaction products contain an appreciable proportion of *trans*-octadecenoate. The authors did not observe an appreciable difference between the rates of hydrogenation of *cis*-octadecenoate and its *trans*-isomer, but, owing to steric hindrance, *trans,trans*-octadecadienoate is reduced much more slowly than the *cis,trans*-isomer.

Other examples of hydrogen transfer from alcohols to the unsaturated soya-bean oil esters, to linoleic and linolenic acid esters, and to other polyenes have also been described[125,126]. The reactions proceed at 100°C and lead mainly to the formation of mono-olefins. Complexes of the type $Cl_2M(PPh_3)_2$, where M = Pt or Pd, in combination with $SnCl_2$ behave as catalysts of these hydrogen transfer reactions.

The double bonds activated by functional groups can be selectively reduced by alcohols. Thus a study has been made of the catalytic hydrogen transfer from 2-propanol to $\alpha\beta$-unsaturated ketones in the presence of iridium compounds[127,128]. The reduction of the double bond is catalysed by the complex $H[IrCl_4(Me_2SO)_2].2Me_2SO$, which on refluxing forms the hydride $HIrCl_2(Me_2SO)_3$.

The C=C double bond in benzylideneacetophenone and in other similar compounds has been reduced with the aid of the same catalytic system:

$$PhCOCH{=}CHPh \rightarrow PhCOCH_2CH_2Ph ,$$

$$Me_3CCOCH{=}CHPh \rightarrow Me_3CCOCH_2CH_2Ph ,$$

$$PhCO(CH{=}CH)_2Ph \rightarrow PhCO(CH_2CH_2)_2Ph .$$

The reduction of $\alpha\beta$-unsaturated ketones to saturated ketones by benzyl alcohol is catalysed effectively by the ruthenium complex $(Ph_3P)_3RuCl_2$.[129] For example, when 1-phenylbut-1-en-3-one is heated in benzyl alcohol in the presence of a catalytic amount of the ruthenium complex at 200°C, the product is 92% of 1-phenylbutan-3-one. Together with benzyl alcohol, other alcohols were also employed as hydrogen donors in this reaction: $PhCH_2CH_2OH$, $PhCH(OH)CH_3$, and $CH_3(CH_2)_6CH_2OH$ (Table 2). The same investigators showed that the aromatic aldehydes α-$C_{10}H_7CHO$, β-$C_{10}H_7CHO$, and others can also function as hydrogen donors[130] (Table 3).

Reports have been published recently concerning the reduction of the double bond in cyclo-olefins with the aid of dihydric phenols[131,132]§. Thus when cyclo-octa-1,3-diene and cyclo-octa-1,5-diene react with hydroquinone in dioxane in the presence of triphenylphosphine complexes of iron(II), cobalt(II), and nickel(II) at 200°C the cyclo-octadienes are reduced catalytically to cyclo-octene and cyclo-octane. According to the authors, these reactions take place as a result of an intramolecular hydrogen transfer, since the pressure in the reaction vessel remained unchanged in the course of the reactions, i.e. the evolution of molecular hydrogen was not observed. Apart from cyclo-octene and cyclo-octane, isomerisation products were detected at the end of the reaction: cyclo-octa-1,4-diene and cyclo-octa-1,3-diene. The efficiency of various compounds as reducing agents under the conditions investigated decreases in the sequence pyrogallol > catechol > hydroquinone > n-dodecanethiol > 1-octanol > cyclohexene > 2-octanol > 1-dodecanol > n-dodecylamine.

Table 2. Hydrogen transfer from alcohols to $\alpha\beta$-unsaturated carbonyl compounds in the presence of $(Ph_3P)_3RuCl_2$ (Sasson and Blum[129]).

Hydrogen donor (weight, g)	Hydrogen acceptor (weight, g)	Reaction temp., °C	Yield of saturated carbonyl compound after 4 h, %
$PhCH_2OH$ (1.08)	PhCH = CHCOMe (1.46)	200	94
$PhCH_2CH_2OH$ (1.22)	PhCH = CHCOMe (1.46)	200	94
PhCH(OH)Me (1.22)	PhCH = CHCOMe (1.46)	200	93
$Me(CH_2)_6CH_2OH$ (1.30)	PhCH = CHCOMe (1.46)	190	82
$PhCH_2OH$ (1.08)	PhCH = CHCOPh (2.08)	200	98
$PhCH_2OH$ (1.08)	$CH_2CMe_2CH_2CMe = CHCO$ (1.38)	200	41
$PhCH_2OH$ (1.08)	PhCH = $CHCOCMe_3$ (1.88)	200	89
$PhCH_2OH$ (1.08)	PhCH = CMeCHO (1.46)	200	61
$PhCH_2OH$ (1.08)	PhCH = CHCOOEt (1.76)	200	53

The reduction of the multiple bond in unsaturated compounds with the aid of dihydroxybenzene derivatives can occur also in aqueous solutions[133], for example in aqueous alkaline solutions of vanadium(III) in the presence of a number of di- and trihydroxy-derivatives of benzene and naphthalene (catechol, pyrogallol, and 2,3-dihydroxynaphthalene). Acetylene is reduced to ethylene at room temperature.

Together with alcohols, cyclic ethers can also be used as hydrogen donors for the reduction of unsaturated compounds. For example, when tetrahydrofuran is employed as the solvent in the presence of catalysts of the type $Cl_2M(PPh_3)_2$, where M = Ni, Pd, or Pt, the olefins are reduced[125,126,134]. It is interesting that the nickel catalyst is active also in a benzene medium, but it is not clear what the hydrogen source is in this case.

Japanese workers[135] described the reduction of olefins with the aid of dioxane in the presence of a rhodium catalyst. When cyclopentene is heated at 180°C in dioxane solution in the presence of $(Ph_3P)_3RhCl$, 0.43 mole of dioxene and 0.42 mole of cyclopentane are formed. After the reaction the individual complex $(Ph_3P)_2RhCl(C_4H_8O_2)$, formed as a result of the displacement of one phosphine group from the initial complex by dioxane, was isolated.

§ These reactions proceed with the dissociation of O–H bonds only. However, the similarity of the catalysts and conditions employed make it useful to examine them in this section.

By analogy with hydrogenation by molecular hydrogen and the isomerisation of olefins, the authors suggest the following reaction mechanism:

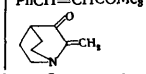
$$RhCl(PPh_3)_2(C_4H_8O_2) \rightleftarrows RhClH(C_4H_7O_2)(PPh_3)_2 \rightleftarrows RhClH_2(PPh_3)_2(C_4H_6O_2) \xrightleftharpoons{+olefin}$$

$$\rightleftarrows RhClH_2(PPh_3)_2(olefin) \rightleftarrows RhClH(alkyl)(PPh_3)_2 \xrightleftharpoons{+dioxane}$$

$$\rightleftarrows RhCl(PPh_3)_2(C_4H_8O_2) + paraffin$$

There is convincing evidence showing that rhodium monohydride complexes are formed via the oxidative addition of dioxane with dissociation of the C–H bond (kinetic data, isotope effect data, etc.). With the aid of organic hydrogen donors, primarily alcohols, it is possible to reduce not only carbon–carbon multiple bonds in unsaturated compounds but also functional groups such as the carbonyl and nitro-groups.

Table 3. Hydrogen transfer to $\alpha\beta$-unsaturated quitones in the presence of ruthenium, rhodium, and iridium complexes[130] (donor : acceptor : catalyst = 1 : [?] : 5×10^{-2} for Nos. 1–8 and 1 : 20 : 5×10^{-3} for Nos. 9–16).

No.	Hydrogen donor	Hydrogen acceptor	Catalyst*	Temp., °C	Reaction time, h	Yield of saturated ketone, %
1	α-$C_{10}H_7CHO$	PhCH=CHCOPh	1	285	2,5	60
2	α-$C_{10}H_7CHO$	PhCH=CHCOPh	2	285	2,5	21
3	α-$C_{10}H_7CHO$	PhCH=CHCOPh	3	285	2.5	34
4	α-$C_{10}H_7CHO$	PhCH=CHCOC(Me_3)	1	285	2.5	60
5	β-$C_{10}H_7CHO$	PhCH=CHCOPh	1	285	2.5	28
6	p-$CH_3C_6H_4CHO$	PhCH=CHCOPh	1	200	14	50
7	p-$CH_3C_6H_4CHO$	p-$MeOC_6H_4CH$=CHCOPh	1	200	14	68
8	p-ClC_6H_4CHO	PhCH=CHCOPh	1	210	14	31
9	HCONHMe	PhCH=CHCOMe	1	180	2.5	25
10	HCONHMe	PhCH=CHCOPh	1	180	2.5	30
11	HCOOH	PhCH=CHCOMe	1	97	24	90
12	HCOOH	PhCH=CHCOMe	2	97	24	16
13	HCOOH	PhCH=CHCOMe	3	97	24	94
14	HCOOH	PhCH=CHCOPh	3	97	24	95
15	HCOOH	PhCH=$CHCOMe_3$	3	97	24	96
16	HCOOH		1	97	24	90

* 1. L_3RuCl_2. 2. L_3RhCl. 3. $L_2Ir(CO)Cl$, L = Ph_3P.

Thus the reaction of substituted cyclic ketones with solutions of chloroiridic acid in aqueous isopropyl alcohol containing different ligands (dimethyl sulphoxide, trimethyl phosphite, or phosphorous acid) leads to the formation of axial alcohols in high yields[127]. For example, 4-t-butylcyclohexanol is formed from 4-t-butylcyclohexanone under these conditions. When the reaction was carried out in the presence of dimethyl sulphoxide, a number of iridium complexes, which catalyse hydrogen transfer reactions, were isolated[128].

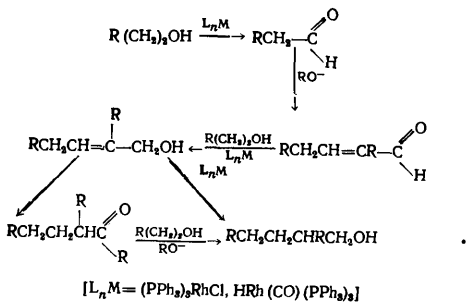
Hydrogen transfer and reduction of carbonyl group are observed also when isopropyl alcohol is refluxed with cyclohexanone in the presence of catalytic amounts of the complexes $IrH_3(PPh_3)_3$, $IrH_3(PPh_3)_2$, $ReH_7(Ph_3P)_2$, and $RuHBr(CO)(PEt_2Ph)_3$.[136] It is interesting that, when 4-substituted cyclohexanones are employed, equatorial alcohols are formed as the main reduction products[137].

An active ruthenium catalyst of hydrogen transfer from primary and secondary alcohols to ketones [$RuCl_2(PPh_3)_3$] was proposed by Freidlin and coworkers[138–141]. The addition of bases accelerates this reaction. The reaction rate depends on the structure of the alkyl substituents in the alcohol molecule and falls sharply following the introduction of bulky tertiary groups. Alkylphenylmethanols reduce ketones at a much higher rate than 2-alkanols. The structure of the ketone has also a significant influence

on the rate of reaction, which decreases in the sequence cyclohexanone > acetophenone > cyclopentanone > 2-hexanone > cycloheptanone > cyclo-octanone.

It is interesting that the univalent rhodium complex $(PPh_3)_3RhCl$, which is an active catalyst of homogeneous hydrogenation, is also active in hydrogen transfer from alcohols[138,139]. Its activity in this reaction is higher approximately by a power of ten than the activity of the ruthenium complex $(PPh_3)_3RhCl_2$ and depends little on the structure of the alcohol and ketone.

Catalytic reduction of aldehydes by alcohols was observed also in the course of the condensation of alcohols catalysed by rhodium compounds[142]. In this reaction the rhodium catalyst dehydrogenates the primary alcohol to the aldehyde with simultaneous formation of a carbonyl–phosphine–hydride complex (in this complex the carbonyl group of the aldehyde formed serves as a source of CO). In an alkaline medium two aldehyde molecules condense with formation of an $\alpha\beta$-unsaturated aldehyde, which is reduced by the rhodium hydride complex to a saturated aldehyde and to a higher alcohol:



$[L_nM = (PPh_3)_3RhCl,\ HRh(CO)(PPh_3)_3]$

Studies on the catalytic reduction of the carbonyl group in complex natural products are interesting. Thus steroid ketones can be reduced by isopropyl alcohol in the presence of tris(triphenylphosphine)rhodium chloride[143]. Under these conditions, the reduction of ketones to axial alcohols is to some extent stereospecific. The rate of reduction in the presence of the rhodium catalyst did not increase appreciably following the addition of alkali.

A study has also been made of the reduction by alcohols of a wide range of steroids in the presence of the $H_2IrCl[P(OMe)_3]_3$ catalyst[144]. This system is fully selective in the reduction of the 3-oxo-group in the presence of oxo-groups in other positions. Thus the oxo-groups in the 6-, 7-, 11-, 12-, 17-, 17α-, and 20-positions are hardly reduced (Table 4).

The reduction of other functional groups, in particular of the nitro-group, by alcohols in the presence of transition metal complexes has been described[145]. Thus a methanol solution of $Fe_3(CO)_{12}$ reduces specifically the aromatic nitro-group to a primary amino-group. The nitro-group is reduced with relatively high yields also in the presence of different substituents in the benzene ring (*p*-Cl, *o*-Cl, *o*-Me, *p*-OMe, *p*-OH, *p*-COOEt, *p*-COMe, *p*-HCOMe, *p*-CH=CH–CH=CH_2, *m*-NO_2, *p*-NH_2, and others).

It is noteworthy that the hydrogen transfer from alcohols to unsaturated substrates occurs under somewhat more severe conditions (temperature 80—130°C) than in homogeneous hydrogenation under the influence of analogous catalysts (usually at room temperature). This can be accounted for by the greater difficulty of the dissociation of the C–H bond compared with the H–H bond.

2. Reduction by Formic Acid and Formates

One of the interesting and extremely effective hydrogen donors for the reduction of organic compounds is formic acid and its derivatives. It is well known that formic acid and its salts are powerful reducing agents. This is usually attributed to the presence of the "aldehyde-like" hydrogen at the carbon atom which exhibits an appreciable hydride mobility (see above). In 1967 Coffey reported that, in the presence of phosphine complexes of platinum, ruthenium, and iridium, formic acid undergoes catalytic decomposition with formation of hydrogen and carbon dioxide[146]. He also stated that, following the introduction into this catalytic system [in the presence of the complex $H_3Ir(PPh_3)_3$] of butyraldehyde, the latter is reduced to the corresponding alcohol. Further results obtained in the reduction of the carbonyl group by formic acid were published by the same author in a patent[147].

Table 4. Reduction of 3-oxosteroids in the presence of the Henbest reagent [H_2IrCl_6, $(MeO)_3P$, and 90% aqueous 2-propanol]*.

Steroid	Amount of initial ketone after 24 h, %	Reaction time [h ?]	Yield of axial 3-OH, %	Yield of equatorial 3-OH, %	Yield of other products, %
5α-Series					
5α-Androstan-3-one	74	131	90	10	–
17β-Hydroxy-5α-androstan-3-one	45	128	95	2	–
5α-Androstane-3,17-dione	71	94	94	2	3-oxo-derivative (3%)
5α-Androstane, 3,11,17-trione	40	72	94	5	–
5α-Cholestane-3,6-dione	73	175	68	29	3-oxo-derivative (3%)
5α-Pregnane-3,20-dione	67	94	78	6-7	3-oxo-derivative (3%), 17-isoproducts (11%)
20α-Hydroxy-5α-pregnan-3-one	88	131	59	4	3-oxo-derivative (34%)
20β-Hydroxy-5α-pregnan-3-one	87	131	15	5	3-oxo-derivative (75%), unidentified products (5%)
5α-Pregnane-3,11,20-trione	61	92	63	9	3-oxo-derivative (3%), 17-isoproducts (24%)
5β-Series					
5β-Androstane-3,17-dione	42	72	98	2	–
17β-Hydroxy-5β-androstan-3-one	78	209	98	2	–
5β-Pregnane-3,2-dione	76	94	72	1	3-oxo-derivative (2%), 17-isoproducts (25%)
20α-Hydroxy-5β-pregnan-3-one	90	232	98	2	–
5β-Pregnane-3,11,20-trione	33	94	72	1	17-isoproducts (27%)
5β-Pregnane-3,12,20-trione	21	72	88	4	17-isoproducts (8%)

* The reaction is carried out in boiling isopropyl alcohol.

It was found recently that formic acid can readily reduce carbon–carbon multiple bonds in the presence of various transition metal complexes as catalysts[148-151].

The study of a wide range of phosphine complexes in this reaction showed that the principal relations observed in hydrogenation by molecular hydrogen are retained also in the reduction of olefins by formic acid. The influence of ligands, the valence of the transition metal, the nature of the substrate, etc. is similar. However, in contrast to hydrogenation by hydrogen, the reduction of olefins by formic acid is significantly affected by the solvent. The reduction hardly occurs in non-polar solvents (benzene, toluene, etc.) even under severe conditions, but proceeds extremely readily in dimethylformamide (DMF) and

dimethylacetamide. It is extremely significant that molecular hydrogen does not hydrogenate olefins in these solvents and under these conditions, which is evidence of intramolecular hydrogen transfer from HCOOH. That the hydride hydrogen from formic acid is involved in the reduction of the olefins has been demonstrated by separate experiments with DCOOH.

Olefins are reduced by formic acid usually at a higher temperature (60–100 °C) than in the hydrogenation by molecular hydrogen in the presence of the same complexes. This is due in all probability to the greater difficulty of the dissociation of the C–H bond in formic acid. There are several ways of increasing the catalytic activity of the systems in which formic acid functions as a source of hydrogen.

1. By employing a combination of catalysts instead of individual complexes. Thus combination of the catalysts $(PPh_3)_2Rh(CO)Cl$ and $(PPh_3)_2Ir(CO)Cl$ is more active than each complex separately.

2. By employing a combination of transition metal complexes one of which is incapable of reducing the olefin but behaves under mild conditions as a catalyst of the decomposition of formic acid and the other can transfer hydrogen to the olefin. Such a system can be achieved, for example, by combining the complex $(Ph_3P)_3Co(N_2)H$, which can catalyse the decomposition of formic acid at room temperature, and any catalyst of homogeneous hydrogenation which can give rise to hydrogen transfer [for example, $(PPh_3)_3RhCl$].

3. By adding formate salts. In this case the formate anion presumably serves as an efficient donor of the hydride ion and formic acid behaves as a proton donor:

$$H\text{—}COO^- + M \longrightarrow (MH)^- + CO_2 ,$$

$$(MH)^- + HCOOH \longrightarrow MH_2 + HCOO^- ,$$

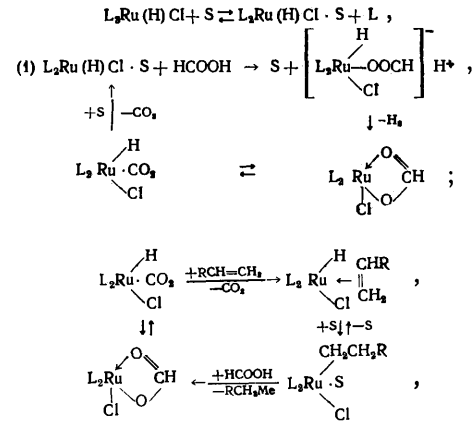
$$MH_2 + RCH{=}CH_2 \longrightarrow M + RCH_2CH_3 .$$

Indeed the employment of a mixture of formic acid and its salt made it possible in a number of cases to increase appreciably the degree of reduction and to lower the reaction temperature. For example, a mixture of formic acid with its salt in the presence of the complex $(Ph_3P)_3RhCl$ reduces quantitatively oct-1-ene and oct-4-ene, while the degree of their reduction by formic acid alone under the same conditions does not exceed 15%. In many instances a mixture of formates and formic acid reduces olefins even at room temperature.

It is interesting that formates themselves are also capable of reducing olefins and acetylenes in the presence of transition metals and in some cases the reduction by alkali metal formates proceeds more readily than by formic acid. Water behaves as the source of protons in such systems. The nature of the cation linked to the formate has hardly any effect on the activity of the reducing agent.

Comparison of the catalytic activities of various transition metal complexes in the reduction of olefins by formic acid showed that ruthenium complexes are the most active and among these the highest activity is shown by $(Ph_3P)_3Ru(H)Cl$. This complex catalyses the reduction of terminal olefins at room temperature in high yields. This behaviour of the ruthenium complex can be explained by the exceptional ease of the dissociation of the C–H bond of the formate group at the ruthenium atom with transfer of the hydride ion to ruthenium (see above). It is noteworthy that the ruthenium formate complex $(PPh_3)_3RuH(OOCH)$ is itself an effective catalyst of the decomposition of formic acid and of the reduction of olefins by formic acid at room temperature.

Kinetic studies and studies on model reactions suggest the following general mechanism of the decomposition of formic acid and the reduction of olefins [in the presence of the complex $(Ph_3P)_3Ru(H)Cl$]:



where S is a solvent molecule.

The decomposition of formic acid under the influence of transition metals can probably proceed not only via the formation of a formate complex with subsequent hydride transfer from the C–H bond to the metal in accordance with the mechanism

$$M + HCOOH \rightarrow HCOOM^- + H^+ \rightarrow HM^- + CO_2 + H^+ \rightarrow MH_2 + CO_2 ,$$

but also by the insertion of the metal in the carbon–hydrogen bond with the initial formation of the hydride of the metallocarboxylic acid:

$$M + HCOOH \rightarrow \overset{H}{\underset{COOH}{M}} \rightarrow MH_2 + CO_2 .$$

Indeed, when formic acid is refluxed with iridium complexes of the type L_3IrCl_3 (where L = Me_2PhP or Et_2PhP), the product is a complex, which has the structure $L_2Ir(CO)H(COOH)Cl$ according to infrared spectroscopic data and its chemical properties[152]. This reaction is of interest not only from the standpoint of the understanding of the mechanism of the decomposition of formic acid but also from the standpoint of the possible transfer of fragments of the metallocarboxylic acid to olefins via a mechanism involving a kind of reductive carboxylation[153]:

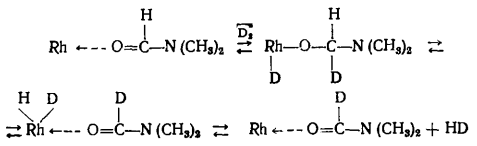
$$M + HCOOH \rightarrow \overset{H}{\underset{COOH}{M}} \xrightarrow{C=C} H\text{—}C\text{—}C\text{—}COOH .$$

The possibility of such addition of the elements of formic acid and also of its esters to cyclohexene and other olefins has been demonstrated in catalysis by rhodium, ruthenium, osmium, and platinum complexes[68]. The complexes $(PPh_3)_3RhCl$, $(PPh_2)_3RhCl$, $(PPh_3)_2Ir(CO)Cl$, and $(PPh_3)Rh(CO)_2Cl$ proved to be the most active catalysts. However, the yields of the carboxylic acid are low and do not exceed 40 mole per mole of the catalyst; the process is complicated by side reactions involving the decomposition of formic acid, the reduction of the olefin, etc.

This reaction is an example of an interesting type of C–H bond dissociation and of the transfer of both hydrogen and of an organic group to the substrate. Such reactions can in many instances lead to new ways of obtaining valuable substances.

In conclusion of the section devoted to formic acid as a reducing agent, mention should be made of the fact that in

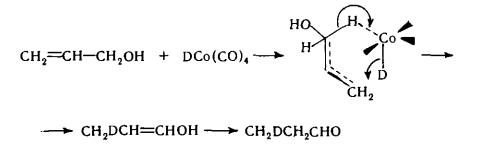
the presence of ruthenium and rhodium complexes the acid is capable of the selective reduction of $\alpha\beta$-unsaturated ketones to saturated ketones[130] (Table 3). It is interesting that, when the complex $(PPh_3)_3RuCl_2$ is used as a catalyst, not only formic acid but also DMF can serve as a source of hydride hydrogen. The study on the exchange of hydrogen in the C–H bond in DMF with molecular deuterium catalysed by rhodium complexes[154,155] is interesting in this connection. The authors propose the following possible mechanism for the exchange process:



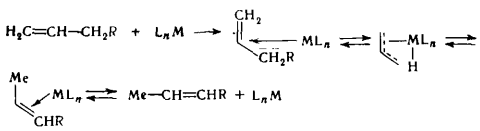
3. Disproportionation Reactions

Catalytic reactions where the same substrate molecule can behave both as a donor and as an acceptor of hydrogen are of great interest. This results either in the isomerisation of the initial molecule (with intramolecular hydrogen migration) or disproportionation (with intermolecular hydrogen migration).

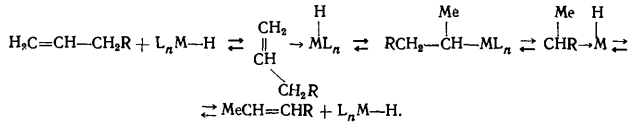
The isomerisation of allyl alcohol to propionaldehyde catalysed by cobalt hydrocarbonyl[156], iron[157], ruthenium[158], and palladium[159] complexes can serve as an example of such intramolecular hydrogen transfer. When allyl alcohol is acted upon by deuteriated cobalt hydrocarbonyl, the entire deuterium is bound in the methyl group of propionaldehyde, which suggests the following mechanism for this reaction[156]:



Numerous olefin isomerisation reactions under the influence of transition metal compounds also constitute essentially intramolecular hydrogen migrations. They occur either with activation of the allylic C–H bond of the olefin (which is most readily dissociated):

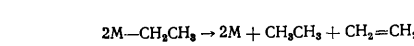


or they involve the metal–hydrogen hydridic bond already present via an intermediate σ-alkyl derivative:

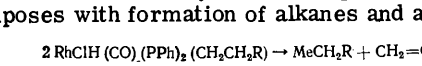


The isomerisation reactions have been discussed in greater detail in numerous reviews, for example that of Orchin[89].

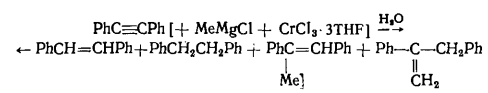
σ-Alkyl derivatives of transition metals, which are in many instances intermediates in the catalytic migration of hydrogen in olefins, are also capable of undergoing very readily intermolecular hydrogen exchange in the course of the dissociation of the metal–carbon bond via the mechanism



For example, the decomposition of pentacyano(2-butenyl)-cobaltate(III) results in the formation of butenes and butadienes[160]. The alkylcarbonylrhodium hydride complex (formed in the decarbonylation of aliphatic aldehydes) decomposes with formation of alkanes and alkenes[161–163]:

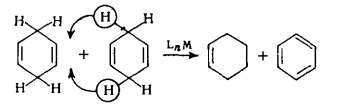


The number of examples of this kind could be greatly extended. It is noteworthy that σ-alkyl groups can behave also as reductants for an "external" substrate (an unsaturated compound), but this reaction does not have preparative value. For example, when tolane reacts at room temperature with σ-methyl derivatives of chromium, tolane reduction products were identified after hydrolysis[164]:

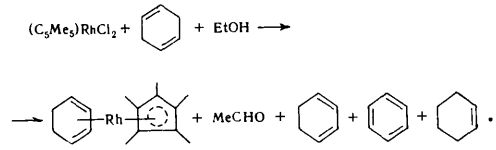


When a deuteriated Grignard reagent was employed it was shown that the methyl group is in fact the hydrogen donor[165].

The olefin disproportionation reactions in the presence of complex catalysts discovered recently are interesting. It was found that cyclohexe-1,4-diene can disproportionate in a homogeneous medium in the presence of $(Ph_3P)_2Ir(CO)Cl$ with formation of benzene and cyclohexane[166]. In this case, as in N.D. Zelinskii's classical irreversible catalysis, one cyclohexadiene molecule behaves as the donor and the other as the acceptor of hydrogen:



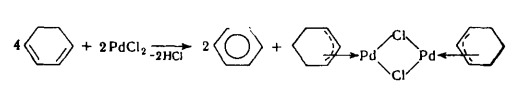
The complex $Ph(\pi\text{-}C_5Me_5)C_6H_8$ also catalyses the disproportionation of cyclohexa-1,3-diene and cyclohexa-1,4-diene to cyclohexene and benzene[167]. This involves the formation of a rhodium complex accompanied by the isomerisation of the 1,4-diene to the 1,3-diene with subsequent disproportionation:



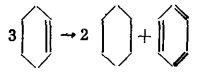
The formation of the rhodium complex from the 1,3-diene is accompanied only by disproportionation without isomerisation.

The reaction of cyclohexa-1,3-diene with $RuCl_3$ in ethanol results in the formation of a π-benzene complex of ruthenium[168]. This reaction probably proceeds via the catalytic disproportionation of cyclohexadiene.

In the presence of palladium salts cyclohexa-1,3-diene is converted into benzene and an allyl complex of palladium[169]:

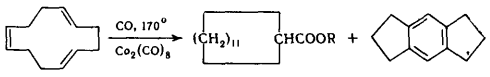


The disproportionation reactions of cyclohexene catalysed by palladium salts[170,171] probably belong to the same type. For example, on heating with $Pd(CN)_2$ at 130°C, cyclohexene gives rise to a mixture of cyclohexanes and benzene [yields of 479 and 212% relative to $Pd(CN)_2$][170]:



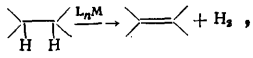
When acted upon by $PdCl_2$, 1-methylcyclohex-1-ene forms similarly methylcyclohexane and toluene even at room temperature[170]; this entails the simultaneous oxidation of the olefin and the formation of metallic palladium. However, the authors believe that palladium complexes and not metallic palladium catalyse this reaction.

An interesting disproportionation reaction was discovered by Rüll[172], who established that, in the presence of $Co_2(CO)_8$ under the conditions of the Reppe synthesis, cyclododeca-1,5,9-triene is converted into the methyl ester of cyclododecanecarboxylic acid. In addition it was found that the corresponding aldehyde is formed in the course of the reaction. Hydrogen required for this reaction is formed as a result of the conversion of cyclododeca-1,5,9-triene into the symmetrical hydrindacene, which was detected in the reaction products:

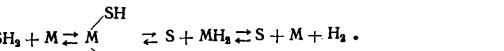


4. Direct Dehydrogenation Reactions

The problem of the possible occurrence of direct dehydrogenation reactions under the influence of complex catalysts, i.e. reactions which are the converse of hydrogenation, for example

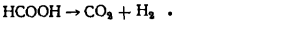


has attracted particular attention. Such reactions could in principle be catalysed by the same complexes as hydrogenation and the reaction mechanism might include the activation of the C–H bond:



However, under mild conditions all these reactions are as a rule thermodynamically unfavourable and the equilibrium is displaced wholly towards the formation of the hydrogenation products.

The few examples in which processes of this kind are known involve the formation of products which are thermodynamically the most stable. Thus, as already stated above, formic acid decomposes extremely readily when acted upon by various transition metal complexes via the mechanism

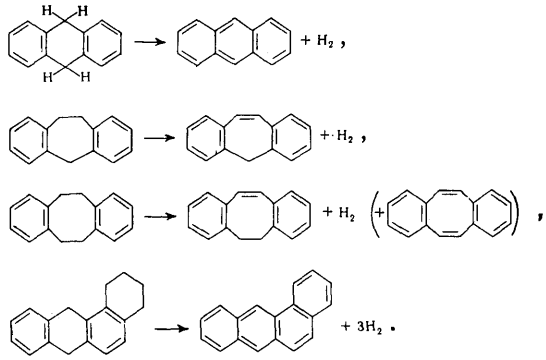


Here the "driving force" of the reaction, which is completely displaced to the right, is the high thermodynamic stability of the CO_2 molecule ($\Delta H_{298} \simeq 264$ kcal mole^{-1}).

Direct dehydrogenation with formation of a C=C double bond was observed in a few instances and only for compounds where the double bond is stabilised by conjugation. Thus it has been stated[173] that cyclohexane is dehydrogenated to benzene on interaction with $IrCl(PPh_3)_3$. However, the yield of benzene was small and it was not clear whether hydrogen was evolved or an iridium hydride complex was formed. (Experiments with a deuteriated substrate showed that hydrogen is transferred to iridium from the phosphine ligands and not from the substrate.) There are also data for the dehydrogenation of cyclohexane by palladium(II) salts[174].

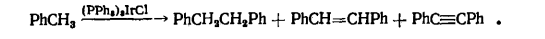
Extremely interesting examples of catalytic dehydrogenation were observed by Blum and Biger[175] for compounds whose dehydrogenation results in the formation of a double bond between two benzene rings. For example, on heating with a catalytic amount of $(Ph_3P)_3RhCl$, $(AsPh_3)_3RhCl$, $(Ph_3P)_2Ir(CO)Cl$, or $(PPh_3)_3RuCl_2$ at 260°C, bibenzyl gives rise to *trans*-stilbene:

Other dehydrogenation reactions proceed similarly:

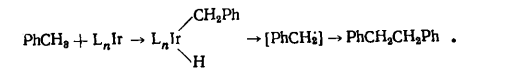


It is interesting that the rates of these reactions are close to those of dehydrogenation at a heterogeneous palladium catalyst, but the reactions in the presence of the complexes are more selective. Thus, on heating with $(Ph_3P)_3RhCl$ (at 225°C for 15 h), 9,10-dihydroanthracene gives a quantitative yield of anthracene (without the formation of tetrahydroanthracenes). Transition metal hydride complexes are probably formed as intermediates in this reaction. Indeed the hydride was isolated in the case of the ruthenium complex.

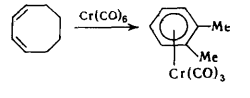
There has been a brief communication[176] concerning the catalytic dehydrogenation of toluene in the presence of $(PPh_3)_3IrCl$:



Presumably the occurrence of this reaction is related primarily to the great ease of the dissociation of the benzyl–hydrogen bond and subsequent dimerisation of the benzyl radicals:



Finally mention may be made of the reaction in the course of which cyclo-octa-1,3-diene is dehydrogenated under the influence of chromium carbonyl with simultaneous ring contraction and aromatisation. The chromium carbonyl complex of *o*-xylene was isolated in a low yield[177]:



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The present review has dealt with a wide variety of reactions involving the dissociation of C–H bonds with subsequent hydrogen transfer to unsaturated compounds. Transition metal complexes are effective catalysts of these reactions and make it possible to carry them out under comparatively mild conditions and fairly selectively.

Alcohols, alkoxides, aldehydes, dihydric phenols, cyclic ethers, etc. can be used as hydrogen donors. Formic acid and formates are particularly convenient reducing agents.

Carbon–carbon double and triple bonds, the carbonyl group, and the nitro-group have been hydrogenated with the aid of these reducing agents. In many instances it proved possible to demonstrate the high selectivity of the reactions and their stereospecificity. It is noteworthy that the ease and selectivity of the hydrogen transfer processes and the availability of the reducing agents and catalysts used make the reactions very convenient in many instances on a preparative scale.

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Cyclic Oxyphosphoranes

B.A.Arbuzov and N.A.Polezhaeva

The review deals with a new interesting field in the chemistry of organophosphorus compounds—cyclic derivatives of pentacoordinate phosphorus containing at least one endocyclic P-O bond and not containing halogens.
The principal types of cyclic oxyphosphoranes with four-, five-, and six-membered rings, spirophosphoranes, and phosphoranes of the condensed and prismatic types have been examined. The methods of synthesis and chemical reactions of cyclic phosphoranes are described: condensation with carbonyl compounds, hydrolysis, alcoholysis, thermal stability, etc. Physicochemical studies on phosphoranes have been undertaken to establish their structures and to investigate their stereochemistry. X-ray diffraction, infrared spectroscopy, ^{1}H NMR, and ^{31}P NMR have been used for these purposes. The groups linked to phosphorus are capable of permutational isomerisation which can occur via the mechanism of the Berry pseudorotation or via turnstile rotation.
The bibliography includes 264 references.

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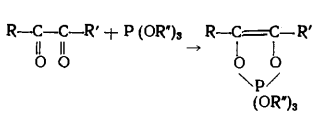
I. INTRODUCTION

Organic derivatives of the hypothetical phosphorus hydride PH_5 (phosphorane) are called phosphoranes. Derivatives of hydroxyl-containing substances with the general formula $R_nP(OH)_{5-n}$ ($n = 0-4$) are regarded as oxyphosphoranes; when $n = 0-3$, they can be treated as derivatives of the ortho-forms of the corresponding phosphoryl compounds $R_nP(O)(OH)_{3-n}$, where $n = 0-3$. The stability of phosphoranes increases on passing from a cyclic to monocyclic and bicyclic compounds.

The present review deals with cyclic phosphoranes containing at least one endocyclic P–O bond. Halogen-containing phosphoranes are excluded.

Cyclic phosphoranes have been vigorously investigated in the last 15 years. The formation of 1 : 1 adducts of α-dicarbonyl compounds with trialkyl phosphites was discovered independently in 1958–1960 by three groups of investigators: Kukhtin[1,2], Birum and Dever[3,4], and Ramirez and coworkers[5,6].



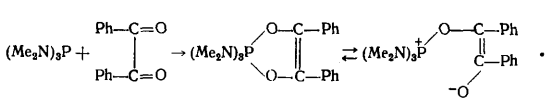
These adducts possess a set of interesting chemical and physical properties, lacked by the classes of organophosphorus compounds known previously, which led to their vigorous investigation by chemical and spectroscopic methods[7,8]. These studies showed that the adducts were unsaturated cyclic oxyphosphoranes. The relative ease of formation of such compounds and the wide variety of reactions which they undergo suggest that cyclic phosphoranes have a very promising future as chemical intermediates. Moreover, cyclic phosphoranes are ideal systems for the investigation of the stereochemistry of pentacoordinate phosphorus[9-13]

II. SYNTHESIS OF CYCLIC PHOSPHORANES

1. Synthesis of Phosphoranes by the Reaction of Phosphorus(III) Acid Derivatives with Carbonyl Compounds

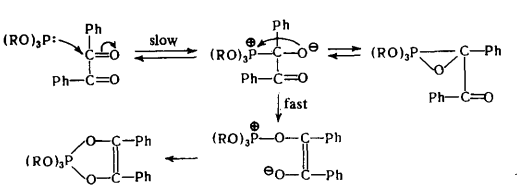
1,3,2-Dioxaphospholens are formed when trialkyl phosphites react with α-dicarbonyl compounds of the aliphatic[14-19], alicyclic[20,21], and aromatic[22-27] series. Phosphonites, phosphinites[19,28], dialkyl phosphoramidites[29-32], and dialkyl phosphonamidites[29,33,34] also form phosphoranes on interaction with α-dicarbonyl compounds. Cyclic phosphites and phosphoramidites react with α-diketones to form spirophosphoranes: 1,3,2-dioxaphospholen-spiro-1,3,2-dioxaphospholans[8,35,36], 1,3,2-dioxaphospholen-spiro-1,3,2-diazaphospholans[35,37], and 1,3,2-dioxaphospholen-spiro-1,3,2-dioxaphosphorinanes[36].

On reaction with certain α-dicarbonyl compounds tris(dimethylamino)phosphine gives rise to an equilibrium mixture of a phosphorane and a dipolar ion[9,37,38]:

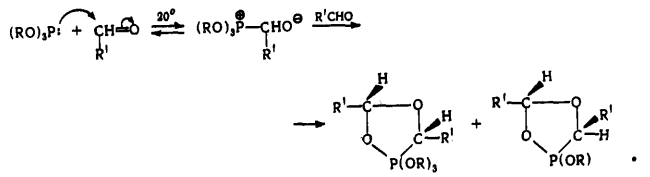


A similar equilibrium has been observed for the phenanthrenequinone–tertiary phosphine adduct[9,39].

The following mechanism has been proposed on the basis of a kinetic study of the reactions of trialkyl phosphites with benzil[40-42] and acyclic[43] and cyclic[21] α-diketones:

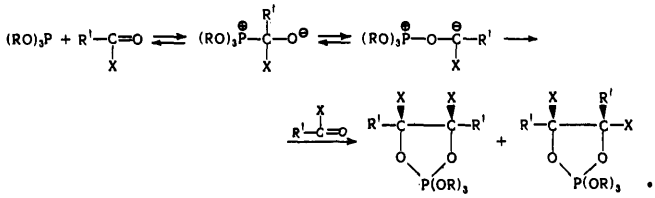


Under mild conditions, aliphatic aldehydes react with trialkyl phosphites to form diastereomeric 1,4,2-dioxaphospholans[44]:

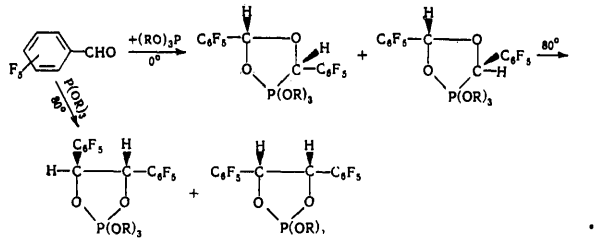


1,4,2-Dioxaphospholans are formed when dimethylketen[45] reacts with esters and ester-amides of tervalent phosphorus.

Aromatic aldehydes and ketones activated by electron-accepting groups[8,32,39,46-55], hexafluoroacetone[28,56,57], fluorenone[58,59], and indantrione[60] react with trialkyl phosphites to form 1,3,2-dioxaphospholans:

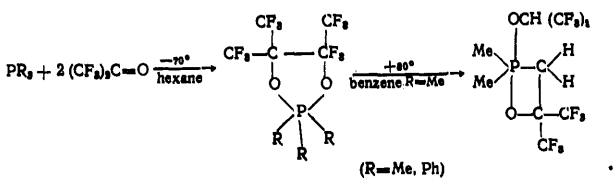


The rearrangement of the adduct with a P–C–O linkage formed initially into one with a P–O–C linkage was demonstrated for pentafluorobenzaldehyde[9,39]:



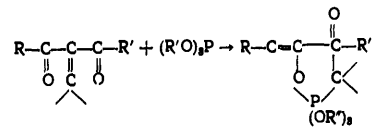
When cyclic phosphites and phosphorous triamides are employed, the products are 1,3,2-dioxaphospholan-spiro-1,3,2-dioxaphospholans[61] and 1,3,2-dioxaphospholan-spiro-1,3,2-diazaphospholans[62,63]. 1,3,2-Dioxaphospholans can also be obtained by the oxyphosphorane condensation of 1,3,2-dioxaphospholens with carbonyl compounds (see the Section on chemical properties).

Aromatic phosphines react with hexafluoroacetone to form 1,3,2-dioxaphospholans[39], while phosphines containing a fairly mobile hydrogen atom in the α-position relative to the phosphorus atom react with hexafluoroacetone to form 1,3,2-dioxaphospholans at −70° and 1,2-oxaphosphetans[64,65] at +80°C (see the Section on the thermal decomposition of phosphoranes):



(R=Me, Ph)

The reactions of trialkyl phosphites with certain $\alpha\beta$-unsaturated carbonyl compounds lead to the formation of 1,2-oxaphospholens; the reactions with methyl vinyl ketone[66], acrolein[67,68], and dibenzylidenecyclohexanone[69,70] take place in this way. Trialkyl phosphites react more readily with $\alpha\beta$-unsaturated carbonyl compounds in which the conjugated system is activated by electron-accepting groups. 1,2-Oxaphospholens have been obtained by the reaction of trialkyl phosphites with alkylidene derivatives of acetylacetone[66,71-73], acetoacetic[72-75] and benzoylacetic[76] esters, benzylidenephenylsulphonylacetophenone[77], and acetyl-*p*-quinone[78]:



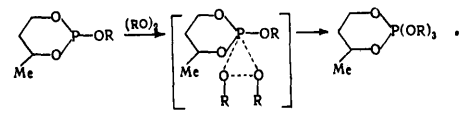
Stable 1,2-oxaphospholens are also obtained when phenylphosphonite and diphenylphosphinite are employed[66,79]. Allenic α-ketones[80] react with phosphites, phosphonites, and phosphinites and the products are also 1,2-oxaphospholens.

The $-N=N-\underset{|}{C}=O$, $-N=\underset{|}{C}-\underset{|}{C}=O$, and $\diagdown C=N-\underset{|}{C}=O$ conjugated systems can be involved in the formation of cyclic phosphoranes: phenylbenzoyldi-imide and azodiformic ester form 1,3,4,2-oxadiazaphospholens[81-83], α-ketoimine gives rise to 1,3,2-oxazaphospholen[84], and 1,1,1,3,3,3-hexafluoro-*N*-acyliminopropane yields 1,4,2-oxazaphospholen[85].

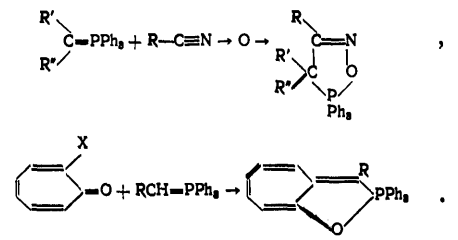
The synthesis of phosphoranes by the reaction of tervalent phosphorus acid derivatives with carbonyl compounds is described in greater detail in the literature[86,87].

2. Other Methods of the Synthesis of Phosphoranes

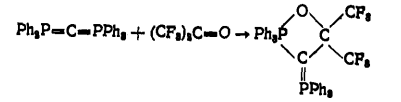
Cyclic phosphoranes of different types can be obtained with the aid of the so called peroxide method. It consists in the treatment of cyclic phosphites[88,89], phosphonites, phosphinites, and amidoesters[90] with alkyl peroxides. The method is general:



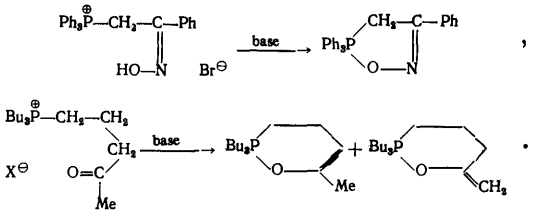
1,3-Dipolar addition to methylenephosphoranes leads to the formation of oxaphospholens. Such reactions take place with nitrones[91,92], nitrile oxides[93-96], epoxides[97], and 2-halogenotropones[98,99]:



In the reaction with phosphorus ylides, hexafluoroacetone yields 1,2-oxaphosphetan[100-103]:

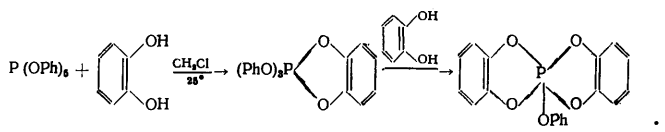


Phosphonium salts containing a hydroxy-group in the γ- or δ-position form phosphoranes on treatment with bases[104-109]:



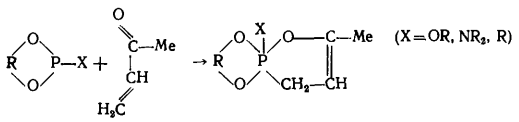
Oxazaphospholens have been obtained by the reaction of trialkyl phosphites with $\alpha\beta$-unsaturated β-nitroacid esters[110] and with 2,6-dimethylaryl 2-nitrophenyl ethers[111].

Cyclic phosphoranes can be obtained by an exchange reaction[112-115] from acyclic phosphoranes and bicyclic phosphoranes can be synthesised from monocyclic phosphoranes (see also the reactions of phosphoranes with glycols):

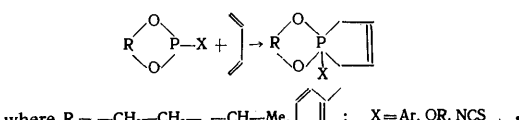


3. Synthesis of Spirophosphoranes and Phosphoranes of the Condensed and Cage Types

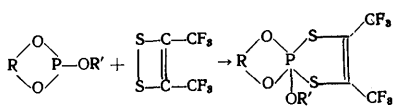
As already mentioned above, spirophosphoranes can be obtained by the interaction of five- and six-membered cyclic phosphites, phosphoramidites, and amides with α-dicarbonyl[8,35-37] and monocarbonyl[61-63] compounds. The reaction of cyclic derivatives of phosphorus(III) with $\alpha\beta$-unsaturated carbonyl compounds takes place similarly[84,116-120]:



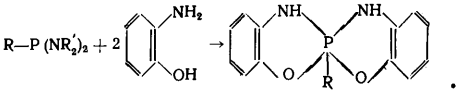
The condensation of the glycol and catechol esters of alkylphosphonous[121] and arylphosphonous acids[122-124] and of the methyl ether and isocyanate of catecholphosphorous [(*OO'*-phenylene)phosphorous] acid[125,126] with 1,3-diene hydrocarbons leads to 1,3,2-dioxaphospholan-spiro-2-phospholens:



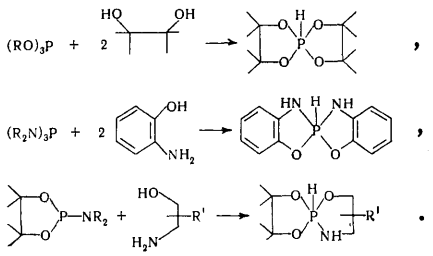
The condensation of cyclic phosphites with 3,4-bis(trifluoromethyl)-1,2-dithietans leads to stable phosphoranes containing sulphur[127]:



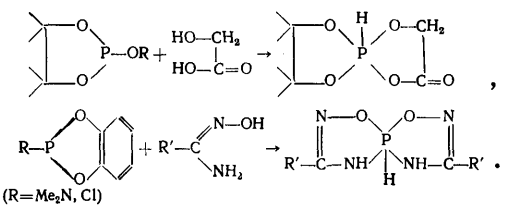
Certain derivatives of tervalent phosphorus form with *o*-aminophenols 1:2 adducts containing a pentacoordinate phosphorus atom[128]:



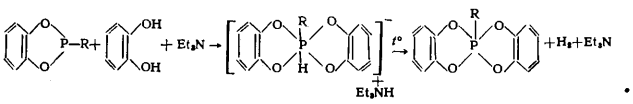
Spirophosphoranes with a P–H bond constitute an interesting group of compounds. They are formed when β-glycols and β-aminoalcohols react with phosphites[129-133] phosphorochloridites[129,134], phosphorus trichloride[129,135,136], tris(dimethylamino)phosphine[135,136,138-142], and cyclic phosphoramidites[143-145]:



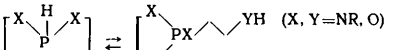
Analogous spirophosphoranes are obtained from derivatives of cyclic phosphites and α-hydroxyacids[146] or amidoximes[147-149]:



The reactions of cyclic phosphorus(III) derivatives with β-glycols and β-aminoalcohols, leading to the formation of spirophosphoranes, takes place only in a neutral or acid medium. In the presence of amines, ammonium salts with a hexacoordinate phosphorus atom are formed[148,150,151], from which spirophosphoranes can be obtained by treatment with acid or on heating:

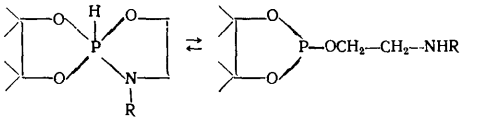


A tautomeric phosphite $\rightleftharpoons$ spirophosphorane equilibrium is characteristic[137,152,155,156] of spirophosphoranes with a P–H bond derived from glycols[131,137,152] or aminoalcohols[140,153,154]:



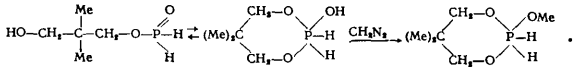
The equilibrium position depends on the temperature and the nature of the substituent in the ring and at the nitrogen atom. When X=Y=O, the equilibrium at room temperature is almost completely displaced towards spirophosphoranes[141,146]. The form with a pentacoordinate phosphorus atom is more characteristic of unsaturated or aromatic systems than of saturated rings or rings with alkyl substituents[154,157]. In asymmetric spirophosphoranes the less substituted ring is opened preferentially[157].

The dependence of the equilibrium position on the substituent at the nitrogen atom can be seen from the following example:

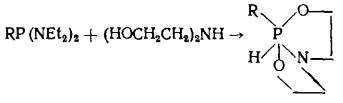


R	H	Me	Et	Ph
Spirophosphorane, %	90	25	3	0

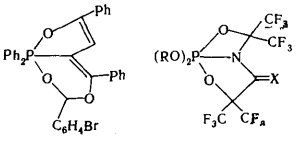
A report has been published[158] on the synthesis of a phosphorane with two P–H bonds:



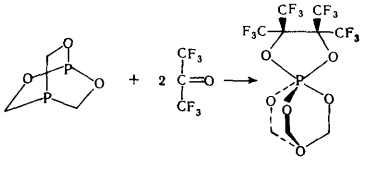
A phosphorane of the condensed type with a P–H bond is formed when aminophosphine reacts with diethanolamine[159]:



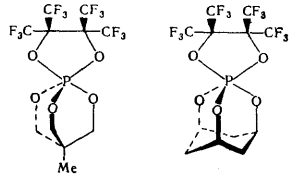
Condensed phosphoranes of the analogous type without P–H bonds have also been described[114,160,161]:



A cage phosphorane[12], which does not react further at the phosphine phosphorus atom, has been obtained by the reaction of a bicyclic phosphite–phosphine with hexafluoroacetone:



Another cage and adamantanoid phosphoranes have been obtained similarly[12,162].



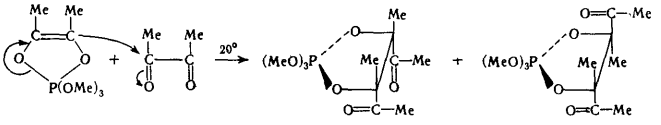
Cage phosphoranes are less stable owing to ring strain and intramolecular twisting in the trigonal bipyramid than the corresponding monocyclic and bicyclic phosphoranes. For this reason the above cage phosphoranes were obtained only with hexafluoroacetone and analogous compounds from, for example, diacetyl could not be synthesised.

III. CHEMICAL PROPERTIES

1. The Oxyphosphorane Condensation

1,3,2-Dioxaphospholens are very reactive. They can condense with carbonyl compounds to form 1,3,2-dioxaphospholans. This new method for the formation of carbon–carbon bonds has been called the oxyphosphorane condensation[7,8,46,163–166].

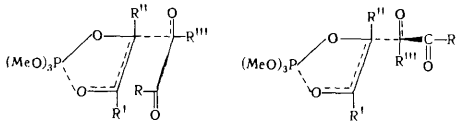
The reaction is nucleophilic addition of the unsaturated carbon atom to the carbonyl group. The condensation can proceed both stereoselectively (with formation of two isomers) and stereospecifically (with formation of one isomer only). For example, 2,2,2-trimethoxy-4,5-dimethyl-1,3,2-dioxaphospholen reacts smoothly with diacetyl to form two diastereomeric 1,3,2-dioxaphospholans[167]:



meso (80%) $\delta^{31}P = +54{,}8$ p.p.m. racemate (20%) $\delta^{31}P = +52{,}8$ p.p.m.

These two forms differ in their ^{31}P and ^{1}H spectra. The nucleus of the phosphorus atom is more effectively screened in the meso-form than in the racemate.

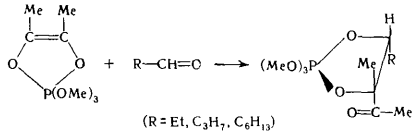
The reaction may proceed[23,168] via the transition states



in which the P–O bond of the phospholen is ruptured and new P–O and C–C bonds of the phospholan are formed.

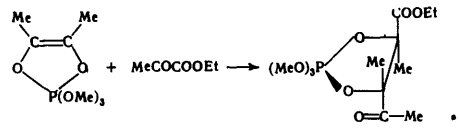
Two factors determine the proportions of the isomers formed: (1) the steric factor, according to which the least bulky groups are closest to one another and (2) the electronic factor associated with the favourable dipole–dipole interaction between the carbonyl groups when these are present.

The following compounds undergo the oxyphosphorane condensation with 1,3,2-dioxaphospholens: benzil, 1-phenylpropanedione (the benzoyl group is attacked exclusively), and phenylglyoxal (the reaction involves the aldehyde group)[168]. Propionaldehyde, butyraldehyde, and heptanal[7] react stereospecifically with formation of only one distereomer, in which the methyl and alkyl groups are in the *trans*-positions relative to one another, i.e. the stereochemistry of the products is determined by steric factors:



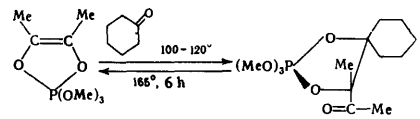
The following compounds undergo condensation with phospholens: benzaldehyde, phthalic and terephthalic aldehydes[169], and others[170,171]. Methyl pyruvate gives rise to two isomers, the product in which the two methyl groups are in the *trans*-positions relative to one another predominating, i.e. the steric repulsion between these two

groups exceeds the dipole–dipole attraction of the acetyl and methoxycarbonyl groups:

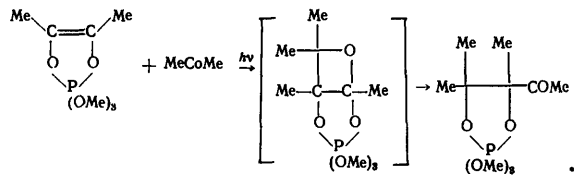


Acenaphthenequinone[7], *p*-benzoquinone[38,172,173], and hexafluoroacetone[174] readily condense with 1,3,2-dioxaphospholens.

Monoketones (cyclobutanone, cyclohexanone, acetophenone, *p*-nitroacetophenone, and $\alpha\alpha\alpha$-trifluoroacetophenone[174]) are less reactive than monoaldehydes and the reaction requires relatively high temperatures (100–120°C), which makes it unsuitable, since under these conditions the thermal decomposition of 1,3,2-dioxaphospholans begins:

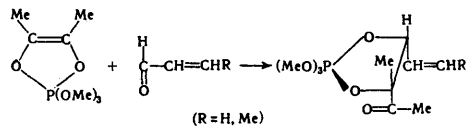


Cyclopentanone, acetone, butanone, 3-hexanone, and benzophenone do not enter into the oxyphosphorane condensation. Acetone can undergo photocondensation[175] with 1,3,2-dioxaphospholens. It has been established[176] that the reaction proceeds via the intermediate formation of oxetans:



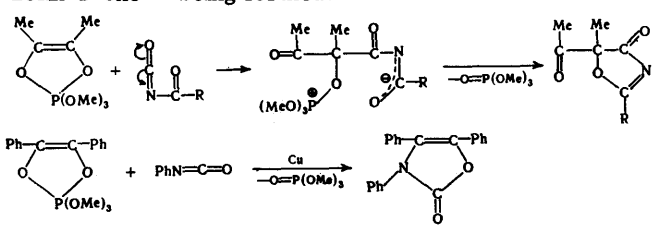
The reactivity of 1,3,2-dioxaphospholens in the oxyphosphorane condensation decreases on passing from dicarbonyl compounds to monoaldehydes and then to ketones. Electron-accepting substituents accelerate this reaction.

$\alpha\beta$-Unsaturated aldehydes[177,178] add to phospholens via the C=O group, and not in the 1,4-positions, with formation of only one stereoisomer:



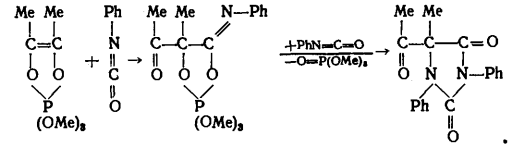
The attempts to condense a phospholen with $\alpha\beta$-unsaturated ketones were unsuccessful.

Systems with cumulative double bonds such as acyl or aryl isocyanates react with phospholenes, a trialkyl phosphate being eliminated and 2-oxazolin-4-one[179] or 4-oxazolin-2-one[180] being formed:

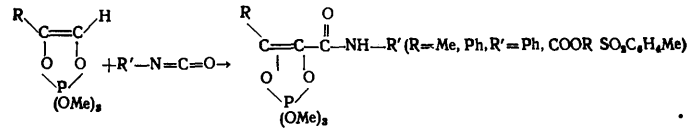


The latter reaction is catalysed by copper and probably proceeds via the intermediate formation of benzoylphenylcarbene, which reacts further with phenyl isocyanate.

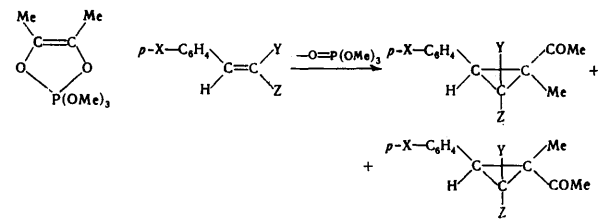
When aryl isocyanate adds to a phospholen without a catalyst, a dioxaphospholan is formed initially and then reacts further with a second molecule of phenyl isocyanate to form a hydantoin derivative[181,182]:



When there is a hydrogen atom at the double bond of the phospholen, the reaction with isocyanates takes place with retention of the phospholen ring[183]:



1,3,2-Dioxaphospholens can condense with olefins containing an electrophilic double bond. The reaction products are substituted cyclopropanes[184,185]:

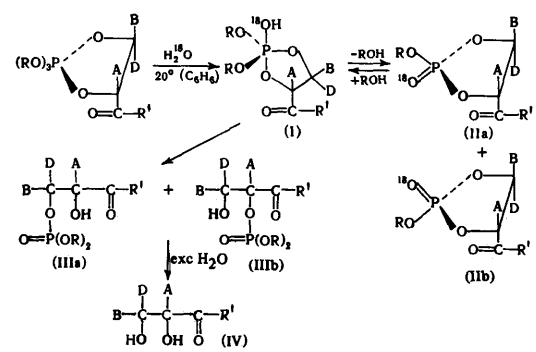


Keten[186] and carbon suboxide[187] react with phospholens at the C=O group. 1,2-Oxaphospholens do not undergo phosphorane condensation with carbonyl compounds[44].

The synthetic possibilities of the oxyphosphorane condensation are very great. Apart from the synthesis of new derivatives with a pentacoordinate phosphorus atom and certain cyclic compounds without a phosphorus atom (as stated above), this reaction leads to a series of new cyclic phosphates, open-chain phosphate esters, and hydroxycarbonyl compounds without phosphorus. All these compounds can be obtained from phosphoranes via hydrolysis.

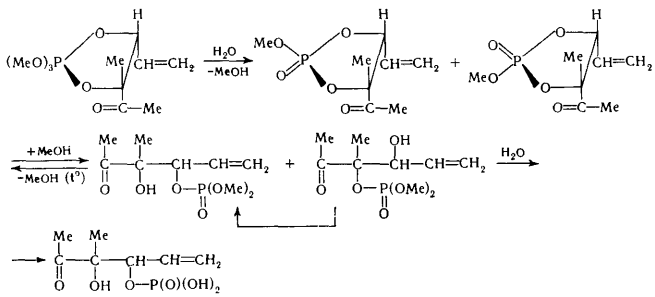
2. Hydrolysis of Phosphoranes

All 1,3,2-dioxaphospholans are extremely sensitive to hydrolysis. There is a possibility of the formation of three types of products: cyclic phosphates, open-chain phosphates, and diols without phosphorus:

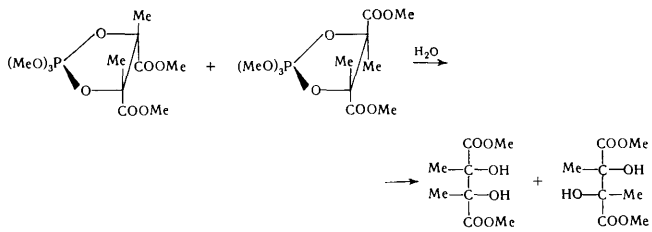


The first stage in the hydrolysis of 1,3,2-dioxaphospholans involves one equivalent of water and the nucleophilic substitution of a methoxy-group by a hydroxy-group[177]. The axial methoxy-group is apparently the first to be exchanged. The intermediate cyclic phosphorane (I) yields the cyclic phosphates (IIa) and (IIb)[165,170,188], which are diastereoisomers at the phosphorus atom. By employing heavy water, it has been shown that ^{18}O enters the phosphoryl group. The methanol formed in the hydrolysis reacts with the cyclic phosphates, yielding the acyclic phosphates (IIIa) and (IIIb) via the same intermediate (I). An excess of water leads to the formation of the corresponding diol (IV)[168,189,190]. The ease of removal of phosphorus from cyclic products depends on the nature of the groups linked to the five-membered ring.

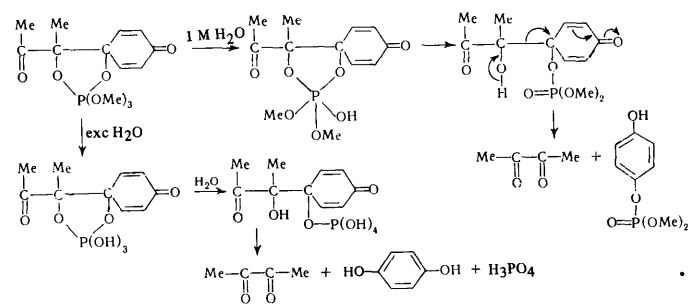
For example, the hydrolysis of 4α-acetyl-2,2,2-trimethoxy-4β-methyl-5α-vinyl-1,3,2-dioxaphospholan[177,178] leads to diastereomeric cyclic phosphates and further to acyclic phosphates. Phosphorus cannot be removed from the molecule even by an excess of water in the presence of an acid: the final hydrolysis product is a phosphate monoester:



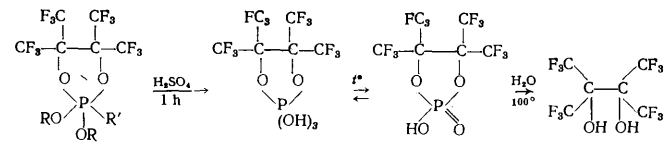
Diastereomeric 1,3,2-dioxaphospholans[46], obtained by the interaction of pyruvate ester with trimethyl phosphite, yield tartaric acid derivatives on hydrolysis[166]:



Thus hydrolysis of 1,3,2-dioxaphospholans makes it possible to obtain various polyhydroxycarbonyl compounds which are difficult to obtain by other procedures. In certain cases the hydrolysis of phospholans results in the cleavage of the C–C bond[172,173]:

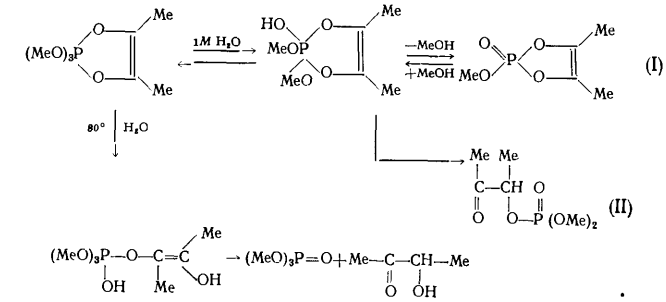


The mechanisms of the hydrolysis by 1 M water and an excess of water are different. The presence in the 1,3,2-dioxaphospholan ring of powerful electron-accepting substituents such as CF_3 makes them chemically inert and their hydrolysis proceeds only when they are acted upon by concentrated sulphuric acid[31,56]:



(R′=OR, NEt_2)

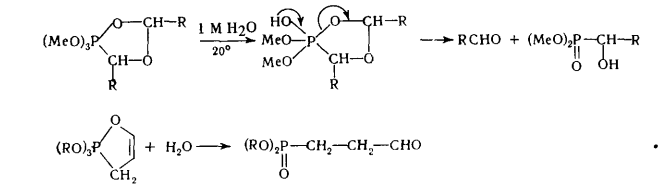
The hydrolysis of 1,3,2-dioxaphospholens proceeds similarly to that of 1,3,2-dioxaphospholans with formation of intermediates of the same type. For example, 2,2,2-trimethoxy-4,5-dimethyl-1,3,2-dioxaphospholen[191] is hydrolysed by one equivalent of water to a cyclic or acyclic phosphate (I or II):



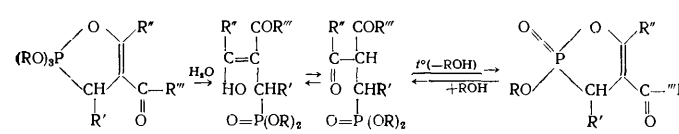
Trimethyl phosphate and acetoin are formed (at 80°C) via a different mechanism, since the phosphates (I) and (II) are not hydrolysed to acetoin under these conditions.

One of the most interesting aspects of the chemistry of cyclic oxyphosphoranes is their hydrolysis and alcoholysis. There is a striking similarity between these reactions and the analogous reactions of cyclic phosphates. The study of the hydrolysis of five-membered cyclic phosphates has shown[192,193] that compounds with a pentacoordinate phosphorus atom are involved in these reactions as intermediates. The hydrolysis of five-membered cyclic dioxyphosphoranes and the hydrolysis and alcoholysis of cyclic phosphates proceed via the formation of the same intermediates.

Phosphoranes containing a P–C bond in the ring are hydrolysed to the corresponding acyclic phosphonates[44,67,68]:

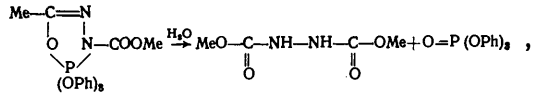


Certain 1,2-oxaphospholens undergo very rapid hydrolysis (sometimes even by atmospheric moisture) with formation of the corresponding ketophosphonates; in certain cases it is possible to isolate the labile enolic phosphonate[44,69,70]. When the products of the hydrolysis of 1,2-oxaphospholens are distilled, the alcohol is split off with formation of a cyclic phosphonate[73–75]:

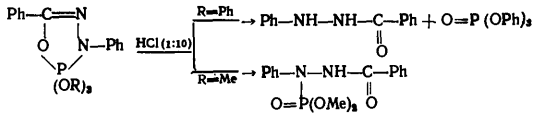


(R=Me, Et; R′, R″=Me, Ph; R‴=Me, OEt)

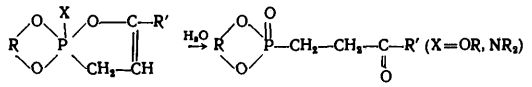
The sensitivity of 1,2-oxaphospholens to hydrolysis can vary within wide limits. While the adduct of triphenyl phosphite with azodiformic ester[83] is more hygroscopic than P_2O_5, the adducts of trialkyl phosphites with phenylbenzoyldi-imide[82,83] are hydrolysed,



only in the presence of hydrochloric acid:



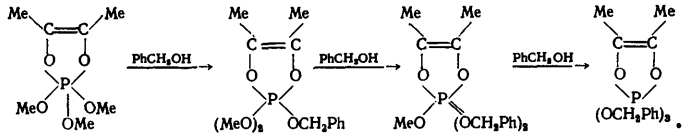
The 1,2-oxaphospholen ring is more sensitive to hydrolysis than the 1,3,2-dioxaphospholan or 1,3,2-dioxaphosphorinane rings. This is clearly seen for spirophosphoranes as an example[116,118]:



When spirophosphoranes obtained by the condensation of cyclic phosphonites with 1,3-dienes are hydrolysed, the ester linkage is broken[123,126].

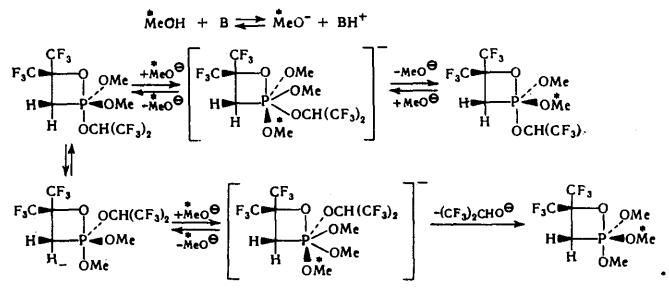
3. Alcoholysis of Phosphoranes

Phosphoranes are capable of undergoing nucleophilic substitution at the pentacoordinate phosphorus atom; the reaction proceeds with the retention of the phospholen ring. It is assumed that in a basic medium the process proceeds via a transition state with a hexacoordinate phosphorus atom[194,195]:



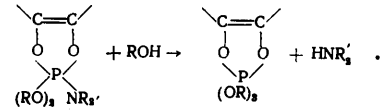
The reaction takes place in steps and the proportions of the products depend on the amount of the initial alcohol and the duration of heating. The rate of substitution depends on the concentration of the base.

The study of this substitution in 1,2-oxaphosphetans showed[115,198] that the nucleophilic RO^- species approaches the phosphorus atom from the equatorial side opposite the equatorial group being removed; the transition state has an octahedral symmetry with a linear distribution of the entering and leaving groups:

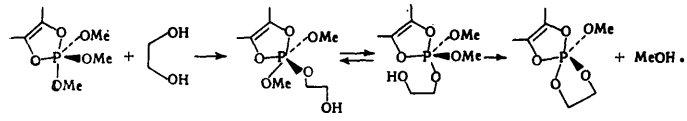


Hexafluoroisopropyl alcohol is more acid than methanol and therefore its anion is more suitable as the leaving group. The relative rates of substitution and of permutational isomerisation[10,12] of phosphoranes (see below) determine the course of this reaction.

When an alcohol is allowed to react with an aminophosphorane, the dialkylamine group is exchanged[30]:

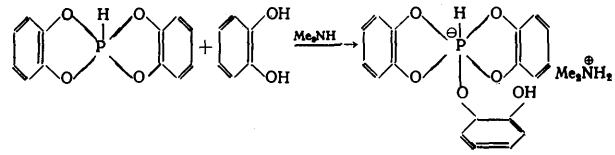


The reaction of ethylene glycol with phosphoranes is exothermic[115]. After the substitution of one equatorial group and subsequent permutation isomerisation, a second equatorial methoxy-group is substituted with formation of a spirophosphorane in which there is an axial-equatorial distribution of the two rings:

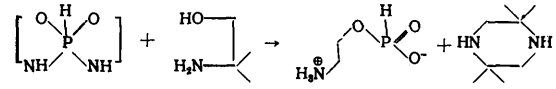


The driving force of this reaction is the appreciable increase of the stability of the resulting spirophosphorane (compared with 1,3,2-oxaphospholen) as a result of the decrease of intramolecular tension, which is smaller in bicyclic phosphoranes.

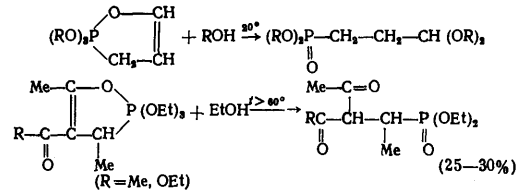
On reaction with β-aminoalcohols or β-glycols in the presence of bases, spirophosphoranes with a P–H bond form compounds with a hexacoordinate phosphorus atom[151]:



Salts of another type can be formed[197]:

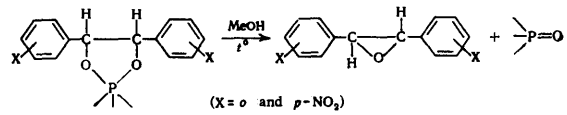


1,2-Oxaphospholen rings are opened by an alcohol[67,68,73]:

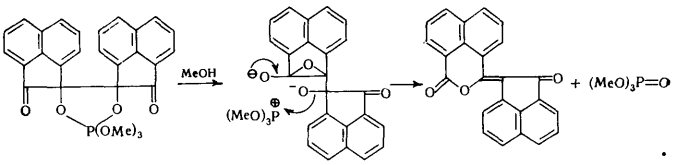


The thermal alcoholysis of 1,3,2-dioxaphospholans leads to the disruption of the phospholan ring. The reactions proceed with the formation of trialkyl phosphates and are frequently accompanied by molecular rearrangements.

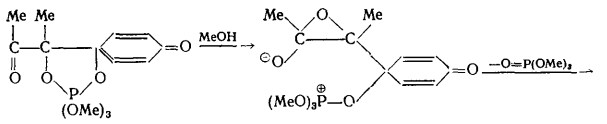
Methanolysis of phosphoranes with two hydrogen atoms and two phenyl groups in the phospholan ring leads to the formation of *trans*-epoxides[63,198]:



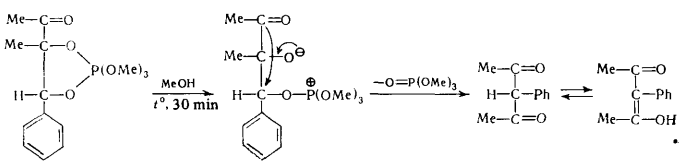
Methanolysis proceeds in a different manner when there are acyl substituents in the phospholan ring[163,164]:



The enol acetate formed on solvolysis can react with the alcohol[172]:



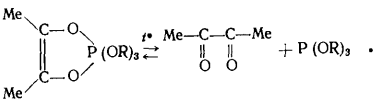
On treatment with hot methanol, 4-acetyl-2,2,2-trimethoxy-4-methyl-5-phenyl-1,3,2-dioxaphospholan loses trimethyl phosphate with a simultaneous skeletal carbon rearrangement, leading to a 1,2-shift of the acetyl group[169]:



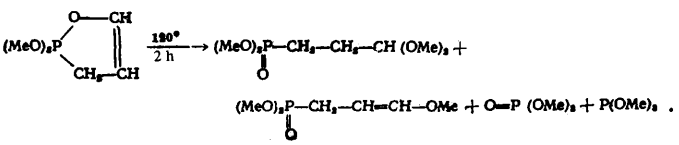
Possibly the high dielectric constant of the solvent (methanol) plays a decisive role in the thermal alcoholysis reactions.

4. Thermal and Photochemical Decomposition of Phosphoranes

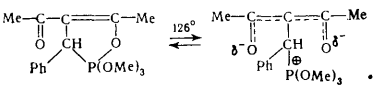
The majority of cyclic phosphoranes are thermally stable up to 100–120°C in an atmosphere of nitrogen[15] and many can be distilled *in vacuo*[5-7]. When certain 1,3,2-dioxaphospholens[14,77,199] and 1,2-oxaphospholens[73] are distilled, their partial dissociation into the initial compounds is observed:



When the simplest 1,2-oxaphospholen is heated, a complex mixture of substances is obtained[68], from which trimethyl phosphite, trimethyl phosphate, the dimethyl acetal of phosphonopropionaldehyde, and a small amount of an enol ether have been isolated; the latter is formed as a result of the thermal decomposition of the acetal[200] during distillation:

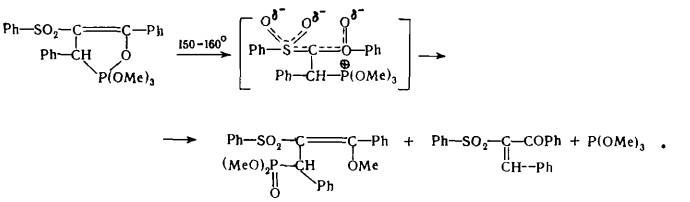


In the course of a study of the stereochemistry of cyclic phosphoranes in solution by ^{1}H NMR it was found[9,11,66] that above 110°C the ring P–O bond in 1,2-oxaphospholens is dissociated. The phosphorane ring is converted into a dipolar ion; the signals of the Me–C= and Me–C(O)– groups in the ^{1}H NMR spectrum merge at 126°C.

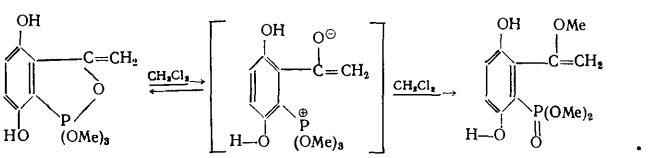


This process is reversible when it occurs below the decomposition and isomerisation temperatures. The temperature at which the Me–C= and Me–C(O)– peaks merge can serve as a measure of the stability of this phospholen system. In the spectrum of the analogous 1,2-oxaphospholen with ethoxy-groups at the phosphorus atom instead of the methoxy-groups the peaks merge at a temperature 15 deg lower. This can serve as an illustration of the importance of steric effects and intramolecular [packing? (Ed. of Translation)] density in the determination of the relative stabilities of compounds with pentacoordinate and tetracoordinate phosphorus. The adduct with EtO groups, which is more sterically strained, is less stable than the MeO adduct.

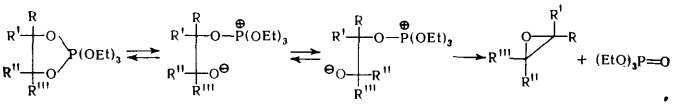
The dissociation of 1,2-oxaphospholen into a dipolar ion has been demonstrated by ^{31}P NMR spectroscopy[77]. The dipolar ion formed isomerises to an enol ether; the reaction is accompanied by the dissociation of the phosphorane (or the dipolar ion) into the initial compounds:



The isomerisation to an enol ether proceeds in the dipolar ion stage, while cyclic phosphoranes do not show a tendency to undergo this reaction; this has been demonstrated in a large number of instances[201]. Cases have been described where phosphoranes in polar solvents are in equilibrium with the dipolar form, the latter undergoing a rapid rearrangement as a result of dealkylation[58,78]:



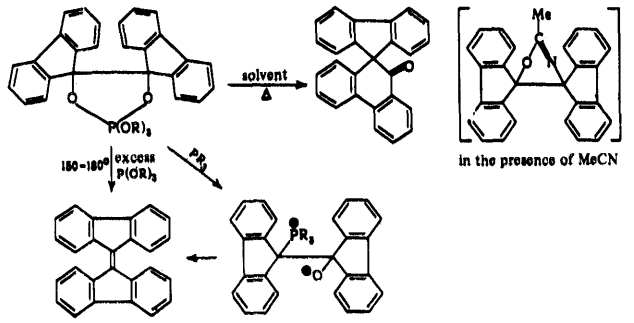
1,3,2-Dioxaphospholans undergo stereospecific thermolysis with formation of *trans*-epoxides. The temperature at which phospholans are decomposed depends on the ring substituents[49,54,89,169]:



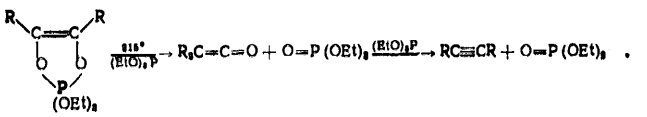
A similar course of the reaction, leading to the formation of epoxides, has been suggested for the highly exothermic interaction of tris(dimethylamino)phosphine with

aromatic aldehydes having electron-accepting substituents [83,203]. Such thermal decomposition of the phosphorane into an epoxide and a phosphate is analogous to the second stage of the Wittig reaction.

The 2 : 1 fluorenone–trialkyl phosphite adducts split off the trialkyl phosphate with a simultaneous rearrangement of the pinacol type on heating in different solvents [58,59,203-206]. The same rearrangement occurs when phospholan is dissolved in anhydrous acetonitrile with formation of an oxazoline in 17% yield [205]. On heating with an excess of the phosphite or phosphine, deoxygenation takes place [206]. The thermal stability of this 1,3,2-dioxaphospholan depends on the nature of the alkoxy-group linked to the phosphorus atom.

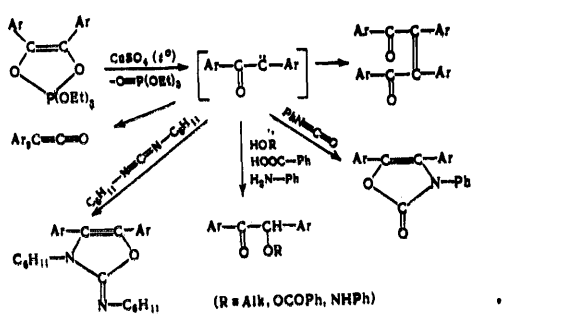


When 1,3,2-dioxaphospholens are heated in the presence of an excess of phosphite, deoxygenation with formation of a trialkyl phosphate and a diaryl- or alkylaryl-acetylene is also observed [207,208]. The intermediate formation of a disubstituted keten in this reaction has been demonstrated:

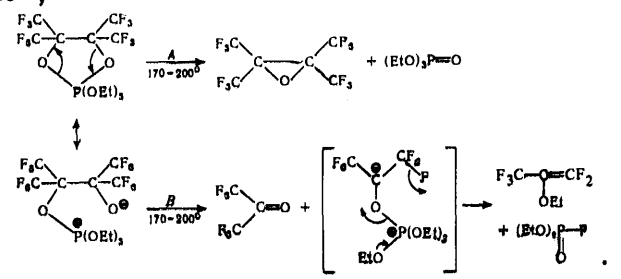


Dialkylacetylenes have not been obtained in the analogous reaction, although the corresponding phosphates are formed.

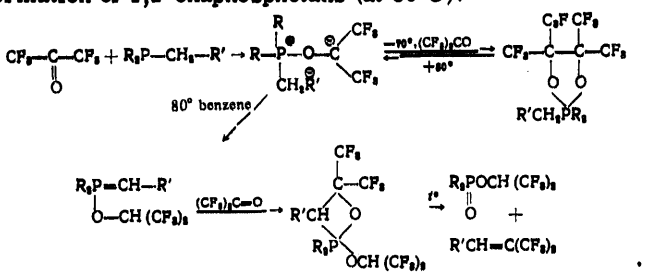
In the presence of copper or its salts 1,3,2-dioxaphospholen is decomposed at a lower temperature. The course of this reaction can be satisfactorily accounted for [180] on the assumption that a carbene is formed initially:



The thermal stability of the 2 : 1 adducts of hexafluoroacetone with various phosphorus(III) derivatives depends on the nature of the groups linked to the phosphorus atom. While 1,3,2-dioxaphospholans having alkoxy-groups at the phosphorus atom decompose at about 170°C into epoxyperfluorotetramethylethane and 2-ethoxyperfluoropropene [57],

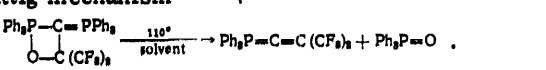


the adducts of hexafluoroacetone with phosphines containing active hydrogen in the α-position relative to the phosphorus atom undergo a rearrangement [64] with the formation of 1,2-oxaphosphetans (at 80°C):

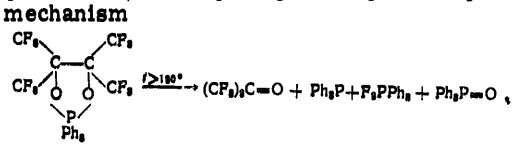


The process includes the cleavage of the 1,3,2-dioxaphospholan formed at a low temperature into a dipolar ion and hexafluoroacetone. The 1,2-oxaphosphetan formed decomposes at a higher temperature into an olefin and phosphinate in accordance with the second stage of the Wittig reaction.

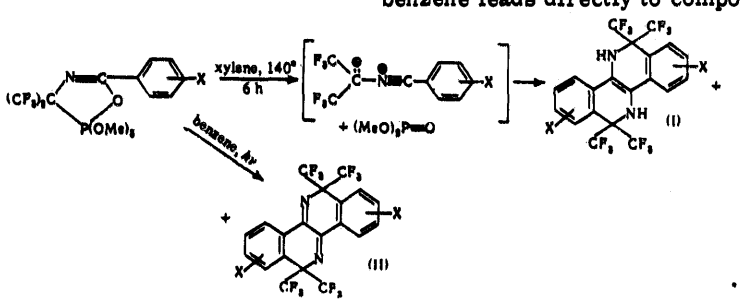
The decomposition of the 1,2-oxaphosphetan proceeds via the Wittig mechanism [101,102]:



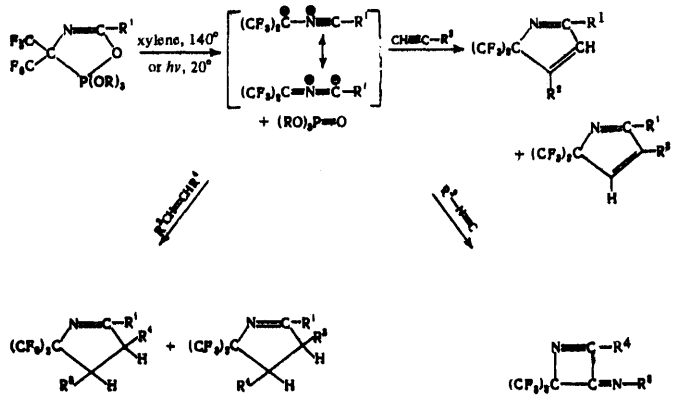
The adduct of hexafluoroacetone and triphenylphosphine is stable up to 120°C, decomposing at a higher temperature via the mechanism



The thermal elimination of phosphate is observed when 1,4,2-oxazaphospholen is refluxed in xylene [209]. The dimer (I) formed under these conditions is readily oxidised to compound (II). Photolysis of the oxazaphospholen in benzene leads directly to compound (II):

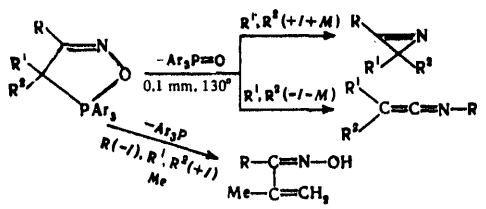


The nitrile imides formed on thermal and photochemical[210] decomposition of 1,4,2-oxazaphospholen can be detected with the aid of dipolarophiles; this results in the formation of products of 3 + 2 and 3 + 1 cycloadditions[210-215]:

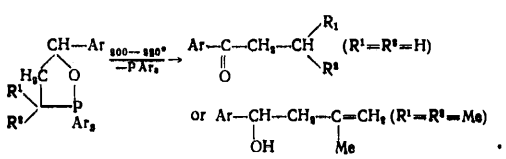


When asymmetric alkenes and alkynes were used, products with both orientations of the dipolarophile relative to the 1,3-dipole were obtained. Interaction with fumarate and maleate esters leads to identical products (epimerisation).

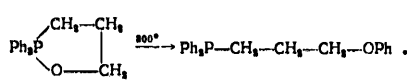
1,5,2-Oxazaphospholens having three phenyl substituents at the phosphorus atom undergo thermal decomposition with formation of either triphenylphosphine or its oxide[95]. The mode of reaction depends on the inductive ($\pm I$) and mesomeric ($\pm M$) effects of the substituents in the phospholen ring[95]:



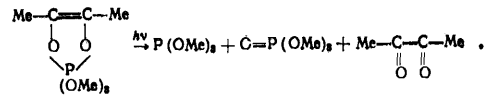
Pyrolysis of certain 1,2-oxaphospholans leads to the elimination of triphenylphosphine[97]:



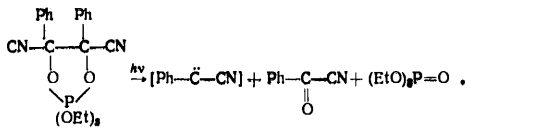
Phospholans of similar structure do not split off triphenylphosphine even at 300°C; a rearrangement, probably via an intramolecular mechanism, to 3-phenoxypropionyldiphenylphosphine takes place on heating[105]:



Photolysis of 1,3,2-dioxaphospholens leads to the formation of a trialkyl phosphite, a trialkyl phosphate, and an α-diketone. The phosphite/phosphate ratio depends on the wavelength of the irradiating light[216]:

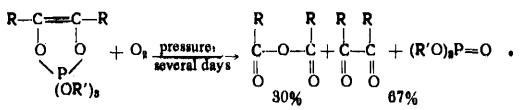


1,3,2-Dioxaphospholans can undergo photocycloelimination[54] (5 → 2 + 2 + 1):

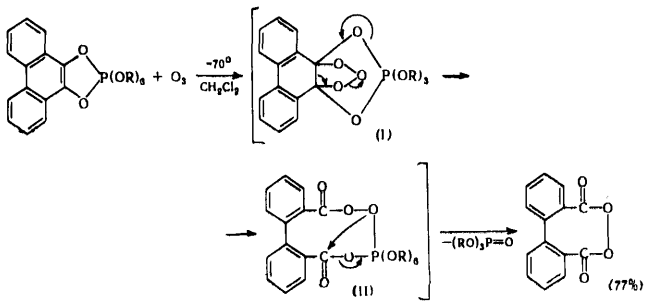


5. Oxidation of 1,3,2-Dioxaphospholens

When acted upon by molecular oxygen, the phospholen ring undergoes a rearrangement of its carbon skeleton with simultaneous dephosphorylation[5,217]:



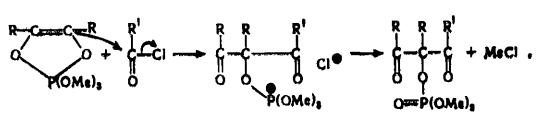
When a phospholen is treated with ozone at a low temperature, peroxide compounds are formed together with phosphates[217,218]:



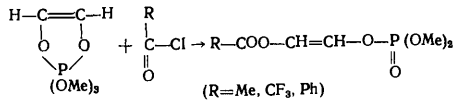
The authors believe that the process proceeds via the intermediate formation of an ozonide (I), which subsequently rearranges to the product (II); the latter splits off phosphate with formation of a peroxide.

6. Interaction of Phosphoranes with Electrophilic Reagents

The interaction of 1,3,2-dioxaphospholens with electrophilic reagents is one of the reactions leading to the opening of the phosphorane ring. The interaction of phospholens with carboxylic acid chlorides[189] can yield polyfunctional carbonyl-containing phosphates, which are of biological interest. Various α-hydroxy-β-dicarbonyl compounds can be obtained by the hydrolysis of the phosphates formed; this is the reason for the synthetic possibilities of the reaction:

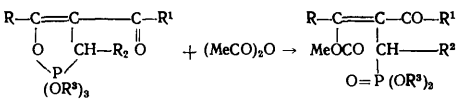


While phospholens with alkyl substituents at the unsaturated carbon atoms undergo *C*-acylation, phospholens with a labile hydrogen atom undergo *O*-acylation[219]:

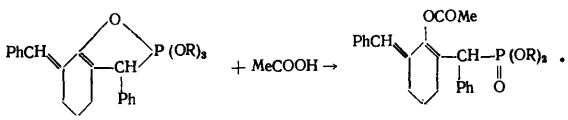


(R=Me, CF_3, Ph)

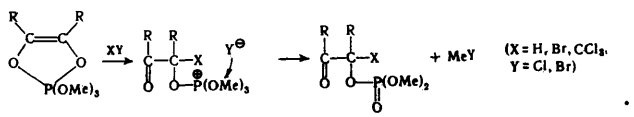
O-Acylation products are obtained when carboxylic acid anhydrides interact with 1,3,2-dioxaphospholens[220] and 1,2-oxaphospholens[68-70,73-76,118]:



The formation of an enol acetate when a 1,2-oxaphospholen was acted upon by acetic acid was noted in one instance[69,70]:

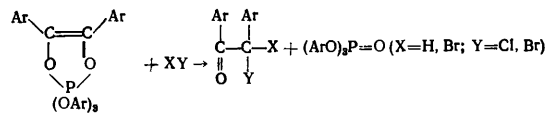


1,3,2-Dioxaphospholens interact with dry HCl,[6,26,186,219] with bromine[6,186,221], and with $CBrCl_3$ (photolysis in the presence of $CBrCl_3$).[222] Under these conditions, phosphates are formed when there are alkoxy-groups attached to the phosphorus atom:

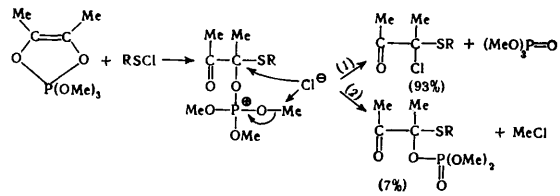


(X = H, Br, CCl_3, Y = Cl, Br)

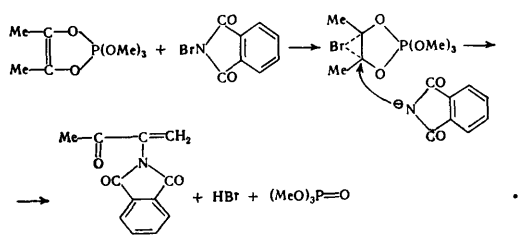
When phenoxy-groups, which are incapable of forming ArY are attached to the phosphorus atom, the intermediate phosphonium product decomposes with elimination of triphenyl phosphate:



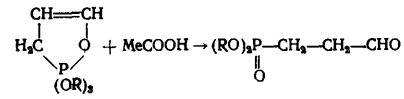
The interaction of phospholens with sulphenyl chloride takes place similarly[223-225], but the authors believe that an anionic attack is more likely:



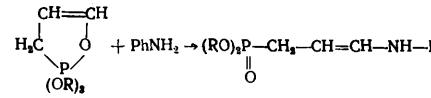
When 1,3,2-dioxaphospholen reacts with *N*-bromophthalimide, trimethyl phosphate is also split off[226]:



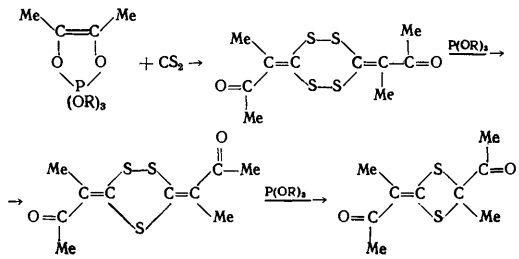
The interaction of certain 1,2-oxaphospholens with acetic acid has been investigated[68,77]:



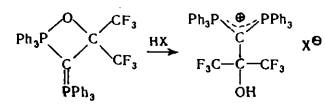
as well as the interaction with aniline[227]:



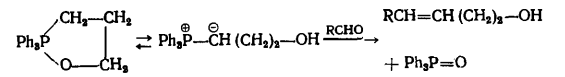
The phospholen ring is disrupted when acted upon by carbon disulphide[228]. The sulphur can be removed from the resulting tetrathi-ine by an excess of phosphite:



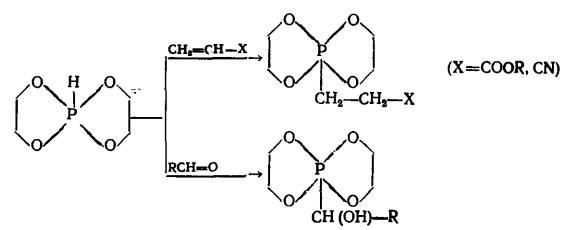
Phosphoranes with three phenyl substituents at the phosphorus atom differ in their chemical properties from phosphoranes with alkoxy-groups. For example, on interaction with HX, 1,2-oxaphosphetans give rise to salts[101]:



1,2-Oxaphospholans can react as ylides with aldehydes, yielding γδ-unsaturated alcohols[229]:

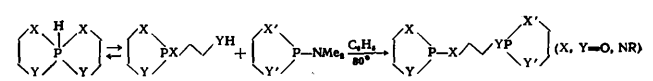


Spirophosphoranes with a P–H bond add to electrophilic multiple bonds[230] and interact with aldehydes[231] like dialkylphosphorous acids:



(X=COOR, CN)

The chemical properties of spirophosphoranes containing a P–H bond are in many ways determined by the phosphorane ⇌ phosphite equilibrium. Intermolecular isomerisation takes place when asymmetric phosphoranes are heated[131,132,143]. The formation of a diphosphite in the subsequent reaction constitutes chemical proof of the existence of the phosphite ⇌ phosphorane equilibrium[232]:



(X, Y=O, NR)

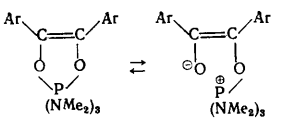
IV. PHYSICAL PROPERTIES. STEREOCHEMISTRY OF PENTACOORDINATE PHOSPHORUS COMPOUNDS

All the physicochemical studies on phosphoranes were undertaken to establish their structures and stereochemistry. Cyclic phosphoranes are ideal systems for the investigation of the stereochemistry of pentacoordinate phosphoranes. The problem of valence in compounds for which a phosphorane structure is proposed can be solved by combination of X-ray diffraction, ^{1}H and ^{31}P NMR, and infrared spectroscopic methods.

1. ^{31}P NMR Spectra

The principal argument in support of the pentacovalence of phosphorus is the high positive chemical shift ($\delta^{31}P$) of these compounds in ^{31}P NMR spectra relative to 85% orthophosphoric acid[7,15]. This implies that the phosphorus nucleus in phosphoranes is more screened than in the standard. In compounds with a dipolar structure and a positive charge on the phosphorus nucleus the phosphorus atom is highly descreened and $\delta^{31}P$ has a high negative value[233]. In those cases where phosphorane $\rightleftharpoons$ dipolar ion equilibrium obtains $\delta^{31}P$ has an intermediate value, since the equilibrium is attained rapidly relative to the NMR time scale. In such cases $\delta^{31}P$ depends on the polarity of the solvent: in non-polar solvents the equilibrium is displaced towards the phosphorane structure and $\delta^{31}P$ becomes more positive; in polar solvents the equilibrium is displaced towards the dipolar form and the chemical shift is displaced towards lower fields.

The benzil–tris(dimethylamino)phosphine adduct has been isolated in two crystalline forms[9,37,38], one of which corresponded to a phosphorane and the other to a dipolar ion. In solution the two forms exist in equilibrium:



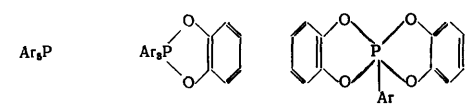
$\delta^{31}P$ = + 29.9 p.p.m. (1 M in hexane)
+13.1 p.p.m. (1 M in CH_2Cl_2)

A similar dependence of $\delta^{31}P$ on the solvent has been noted for adducts of phenanthrenequinone with diethylphenylphosphine and ethyldiphenylphosphine[9,39].

The ^{31}P NMR spectra of phosphoranes have fine structure owing to the interaction of phosphorus with adjacent protons: $^{3}J_{P\text{-}O\text{-}C\text{-}H} \simeq 10\text{–}13$ Hz and $^{2}J_{P\text{-}C\text{-}H} \simeq 20\text{–}24$ Hz.

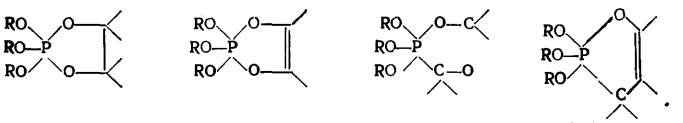
Most of the cyclic oxyphosphoranes have $\delta^{31}P$ in the range +50 ± 30 p.p.m. The dependence of this quantity on the structure of the ring and on the electronegativity of the substituents is not very pronounced. As a rule, the replacement of methoxy-groups at the phosphorus atoms by phenoxy-groups greatly increases $\delta^{31}P$.[36,83]

On passing from acyclic phosphoranes to monocyclic and bicyclic phosphoranes, $\delta^{31}P$ falls[9]:



+ 85.6 p.p.m. + 60.8 p.p.m. + 29.8 p.p.m.

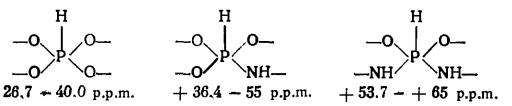
2,2,2-Trialkoxy-1,3,2-dioxaphospholans have $\delta^{31}P$ ranging from +44 to +62 p.p.m.[23] The replacement of one P–O bond in the phosphorane ring by P–C decreases $\delta^{31}P$.



+ 54.8 p.p.m. + 48.9 p.p.m. + 34.1 p.p.m. + 27.8 p.p.m.

The introduction of a second 1,3,2-dioxaphospholen or a 1,3,2-dioxaphospholan ring reduces $\delta^{31}P$, while the introduction of the 1,3,2-dioxaphosphorinane ring does not appreciably alter the chemical shift. The substitution of an endocyclic oxygen atom by nitrogen leads to a slight increase of $\delta^{31}P$ (about 5 p.p.m.), while the replacement of an exocyclic oxygen atom by nitrogen reduces $\delta^{31}P$ by 2–4 p.p.m.[36]

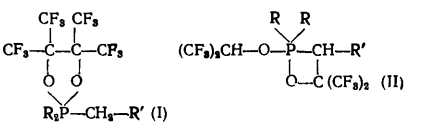
The majority of spirophosphoranes with a P–H bond have $\delta^{31}P$ = +26 – +55 p.p.m.; the values of $\delta^{31}P$ increase when O in the ring is replaced by N:



+ 26.7 – 40.0 p.p.m. + 36.4 – 55 p.p.m. + 53.7 – + 65 p.p.m.

If the molecule contains phenyl substituents, $\delta^{31}P$ decrease. In certain spirophosphoranes containing substituted nitrogen in the ring $\delta^{31}P$ may be between +60 and +100 p.p.m.[143,156] The differences between the chemical shifts of diastereomers are between 1 and 5 p.p.m.[7]

A high positive value of $\delta^{31}P$ constitutes important but not unique evidence of the pentacovalence of phosphorus in cyclic phosphoranes. The chemical shifts of certain phosphoranes are negative. For example $\delta^{31}P$ of 1,3,2-dioxaphospholans obtained by the condensation of hexafluoroacetone with tertiary phosphines[10,11,39,64] vary from −11.7 p.p.m. (for R = Et) to +53.2 p.p.m. (for R = OEt).



Chemical shifts for the phosphorus nucleus in 1,3,2-dioxaphospholans (I) and 1,2-oxaphosphetans (II).

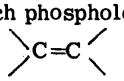
R	$\delta^{31}P$ R_3P	$\delta^{31}P$ (I)	$\delta^{31}P$ (II)	R	$\delta^{31}P$ R_3P	$\delta^{31}P$(I)	$\delta^{31}P$ (II)
Me	+62	+3.2	+23.7	Ph	+5.7	+21.6	—
Et	+19.1	−11.7	+15.7	OEt	−138.5	+53.2	—
n-Bu	+32.6	−7.3	+17.2	OMe	−140.0	+50.1	—

The following observation has been made (see Table): if the signal of the initial phosphorus(III) compound is in the high field region, then $\delta^{31}P$ for the 1,3,2-dioxaphospholan (I) obtained from it is displaced towards lower fields and conversely[11]. In 1,2-oxaphosphetans (II) $\delta^{31}P$ are more positive than in the corresponding 1,3,2-dioxaphospholans (I). Low values of $\delta^{31}P$ have been reported for

certain spirophosphoranes obtained by the condensation of cyclic derivatives of tervalent phosphorus with acrolein[118] (+2 p.p.m.), methyl vinyl ketone[119] (+0.62 p.p.m.), and 3,4-bis(trifluoromethyl)-1,2-dithietan[127] (between −16.5 and −17.5 p.p.m.).

2. Infrared, Raman, and Ultraviolet Spectra

A characteristic feature of compounds with pentacoordinate phosphorus atom is a shift of the stretching vibration band of the P–O–R group towards higher wavenumbers (1090–1075 cm^{-1})[15] compared with the analogous band in compounds with a tetracoordinate phosphorus atom. In the spectra of phosphoranes with aryloxy-groups at the phosphorus atom the P–O–Ar stretching vibration bands are at 1215–1200 cm^{-1}.

The position of the olefin band in the spectra of phospholens depends strongly on the substituents at the double bond and varies from 1664–1645 cm^{-1} [23,27] to 1740 cm^{-1}.[15] In controversial cases the problem of whether or not the band belongs to the stretching vibrations of the double bond can be solved by Raman spectroscopy[15,73]. If a carbonyl group is present in the α-position relative to the double bond in phospholens, there is an interaction between the vibrations and the wave-numbers ν(C=O) and ν(C=C) are markedly distorted[71]. The infrared and Raman spectra indicate the presence of two forms of such phospholens with different mutual orientations of the  and C=O groups[73].

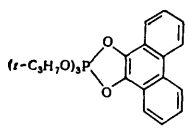
Spirophosphoranes with a P–H bond have a broad band at 2380 ± 30 cm^{-1}.[141,234,235]

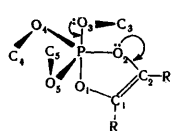
The ultraviolet spectra of 1,3,2-dioxaphospholens[23] and 1,2-oxaphospholens[73,74,76] with a carbonyl or alkoxycarbonyl group in the α-position relative to the double bond are characterised by an intense absorption over a broad section of the spectrum from 220 to 340 nm. The positions of the maxima depend on the substituent in the phospholen ring.

The dipole moments of oxaphospholens are 2–4 D.[6,14,67] The atomic refraction of the phosphorus in phospholen is 3.95.[236]

3. X-Ray Diffraction Analysis

The X-ray diffraction analysis of the two allotropic forms of the 1,3,2-dioxaphospholen obtained by the interaction of phenanthrenequinone with tri-isopropyl phosphite showed that the molecule has a slightly distorted trigonal bipyramidal structure with an axial-equatorial placement of the 1,3,2-dioxaphospholen ring[25,65,160,237,238]. The axial P–O bonds in the ring are longer by 0.1 Å than the equatorial P–O bonds. The exocyclic P–O bonds are somewhat shorter than the endocyclic bonds. This is related to the more intense $p_\pi - d_\pi$ interaction of phosphorus with the exocyclic oxygen atoms. The axial P–O bonds are weaker and more polarisable than the equatorial bonds and are therefore preferred by electronegative substituents.



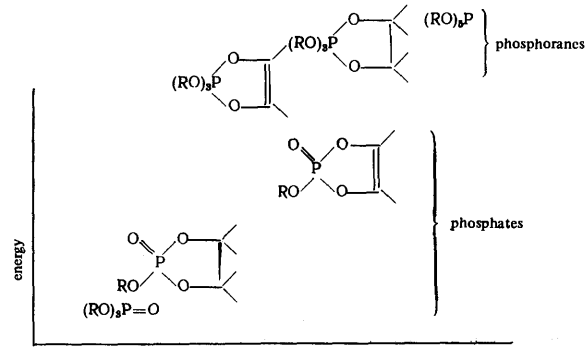


Certain bond lengths and angles in the phenanthrenequinone–tri-isopropyl phosphite adduct[9,11].

Bond length, Å		Angle in degrees			
$P-O_1$	1.753	O_1-P-O_2	89.3	$P-O_1-C_1$	111.9
$P-O_2$	1.649	O_2-P-O_3	88.6	$P-O_2-C_2$	114.2
$P-O_3$	1.641	O_3-P-O_4	91.3	$P-O_3-C_3$	121.8
$P-O_4$	1.601	O_4-P-O_5	93.1	$P-O_4-C_4$	129.8
$P-O_5$	1.586	O_5-P-O_1	117.2	$P-O_5-C_5$	127.5
O_1-C_1	1.347	O_4-P-O_1	117.2		
O_2-C_2	1.433	O_3-P-O_2	125.5		
C_1-C_2	1.333	$O_1-C_1-C_2$	113.9		
O_3-C_3	1.463	$O_2-C_2-C_1$	110.3		

The fact that α-dicarbonyl compounds form 1,3,2-dioxaphospholens with trialkyl phosphites but not with tris(dimethylamino)phosphine can be accounted for by the lower electronegativity of nitrogen (less favourable for the axial position) and the more stringent steric requirements of the dimethylamino-group compared with alkoxy-groups.

The O–P–O and P–O–C angles are capable of undergoing considerable distortion. The trigonal bipyramid is very tightly packed owing to the very short distances between certain non-bonded atoms (down to 2.63 Å). The contraction of the trigonal bipyramid can explain the higher stability of five-membered cyclic phosphoranes compared with acyclic phosphoranes, in contrast to the higher stability of acyclic phosphates compared with five-membered cyclic phosphates, although on the whole phosphoranes have a higher energy than the corresponding phosphates. This is clearly illustrated in the figure below[9,11].



This phenomenon plays a major role in the chemistry of biologically active compounds. Nucleophilic reagents (water, alcohol) add to the P=O group of five-membered cyclic phosphates (but not acyclic phosphates) with formation of intermediate unstable compounds containing a pentacoordinate phosphorus atom[177,178,188,191,192,239–245].

The existence of stable oxyphosphoranes supports the hypothesis that metastable oxyphosphoranes are intermediates in the reaction of tetracoordinate phosphorus[246]. The entering and leaving groups are then located in the axial positions.

4. Permutational Isomerisation

The ligands in the trigonal bipyramid can undergo intramolecular shifts (permutational isomerisation) more or less readily, which occur either via bond deformation (regular process) or via bond dissociation and recombination (irregular process)[162,247].

As a result of permutational isomerisation, the groups occupying the axial and equatorial positions change places, which leads to the formation of a new bipyramid. If all the five groups linked to the phosphorus atom are different, we have twenty chiral isomers, i.e. ten pairs of enantiomers in relation to the configuration at the phosphorus atom. If two ligands are equivalent, the number of isomers decreases to ten, namely six chiral and four achiral isomers. If three ligands are equivalent, we have four achiral isomers.

However, virtually all the ligands linked to the phosphorus atom occupy a definite position in the trigonal bipyramid, which is determined by the electronegativity, steric requirements, and the involvement of the *d* orbitals of phosphorus in the formation of the bonds. All this can be expressed in terms of the general polarity rule[162,247-250].

If any one group cannot occupy an axial position owing to steric or electronic factors, the number of isomers is reduced to twelve. A similar situation obtains if the substituent cannot occupy an equatorial position. Four- and five-membered rings occupy an axial-equatorial position in the trigonal bipyramid[9,25,65,160], while both axial-equatorial and diequatorial positions are possible for a six-membered ring.

Regular permutational isomerisation of acyclic phosphoranes can occur via six different mechanisms[250,251]. It has been shown theoretically[252] and by calculations based on infrared and Raman spectra[253] that the Berry pseudorotation mechanism is the most probable[254]. In a pseudorotation two pairs of axial and equatorial ligands change places via an intermolecular process consisting of the bending of the bonds with deformation of the angles at the central atom. This mechanism is consistent with the experimental data and has undoubted advantages over other mechanisms proposed as alternatives (pseudorotation is discussed in Refs. 248, 253, and 255).

In order to account for permutational isomerisation in cage phosphoranes, a new process called turnstile rotation has been proposed[256]. In turnstile rotation one axial and one equatorial ligand constitute a "pair" and the remaining ligands constitute a "trio". The process consists of a slight deformation of angles at the central atom and in the rotation of the "pair" in relation to the "trio" in opposite directions. On rotation by 60°, a single turnstile rotation (TR) is executed; it can be continued for a further 60° whereupon double turnstile rotation $(TR)^2$ takes place, etc. Ramirez and coworkers[13,246] give preference to this mechanism in the interpretation of the permutational isomerisation of all cyclic phosphoranes.

In turnstile rotation four- and five-membered rings play only the role of the "pair", the remaining ligands playing the role of the "trio", while six-membered rings can play the role of both the "pair" and the "trio". (Turnstile rotation is considered in greater detail in the literature[12,162,247].)

In both pseudorotation and turnstile rotation the axial and equatorial ligands are exchanged in pairs with retention of the position of the third. In turnstile rotation the ligand whose position is retained always forms part of the "trio". For each pseudorotation, there are four equivalent turnstile rotations. However, there are fundamental differences between these mechanisms. Only in turnstile rotation are all the ligands involved in internal motion about the axis passing through the central atom. The geometries, skeletal symmetries, and potential energies of these processes are different[162].

There is no unanimous view in the literature concerning the mechanism of permutational isomerisation in phosphoranes in general and in cyclic phosphoranes in particular. The pseudorotation and turnstile rotation mechanisms must be regarded as the most probable. It is impossible to give preference[257] to either on the basis of experimental data.

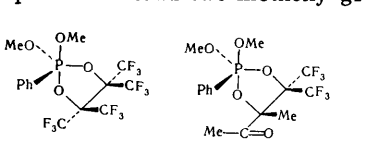
Both these processes presuppose a unimolecular mechanism. A bimolecular process including the formation of either the phosphorane dimer or a complex of the phosphorane with the solvent as the transition state or a metastable excited state has been proposed recently[258] for compounds of the type RPF_4.

5. ^{1}H NMR Spectra. Stereochemistry of Cyclic Phosphoranes

Much information about the structures of phosphoranes and their stereochemistry has been obtained from ^{1}H NMR spectra. The ^{1}H NMR spectra of many 2,2,2-trimethoxy-1,3,2-dioxaphospholens, investigated in the temperature range from +30° to −60°C, contain only one doublet due to the methoxy-groups linked to the phosphorus atoms with $^3J_{P\text{-}O\text{-}C\text{-}H} \simeq 10\text{–}13$ Hz. These results show that the methoxy-groups in the axial and equatorial positions change places, i.e. they are equivalent relative to the NMR time scale. This exchange of ligand positions cannot be inhibited even at fairly low temperatures (−90°C)[7-9,79].

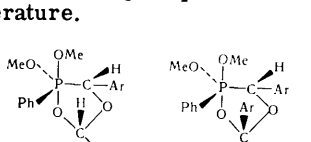
When there are different substituents at the phosphorus atom, the exchange of ligand position is retarded at a higher temperature, as demonstrated by ^{19}F NMR.[259]

A similar phenomenon occurs in 2,2,2-trimethoxy-1,3,2-dioxaphospholans, which give rise to only one doublet due to the methoxy-groups in the ^{1}H NMR spectra at all the temperatures investigated, regardless of molecular symmetry. When there are two methoxy-groups at the phosphorus atom, the ^{1}H NMR spectrum of the phospholan shows a single methoxy-group doublet, provided that the phospholan ring (but not the molecule as a whole) has a plane of symmetry. If there is no plane of symmetry, the ^{1}H NMR spectrum shows two methoxy-group doublets[11]:



one MeO group doublet — two MeO group doublets

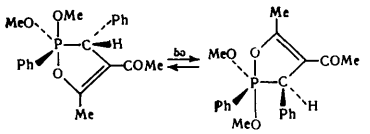
The exchange of ligand positions in 2,2,2-trimethoxy-1,4,2-dioxaphospholans is inhibited at −140°C. At this temperature three methoxy-group doublets appear in the ^{1}H NMR spectrum: the equatorial groups give rise to signals in a lower magnetic field than the axial groups; the $^3J_{PH}$ are higher for the equatorial groups than for the axial groups[44,260]. The *cis*-H/H isomers of 1,4,2-dioxaphospholans with two methoxy-groups at the phosphorus atom are "frozen" at a higher temperature (−42°C), while in the *trans*-H/H isomer the "freezing" occurs at −90°C,[10,11] i.e. the *cis*-isomer is more "rigid" in the sense that the exchange of ligand positions in it is inhibited at a higher temperature.



cis-H/H — *trans*-H/H

The ^{1}H NMR spectra of the diastereomeric 1,3,2-dioxaphospholans and 1,4,2-dioxaphospholans do not differ only in the region of the methoxy-groups. When the molecule contains phenyl substituents, the hydrogen or the methyl group in the *cis*-position relative to such a substituent absorbs in higher fields than the same groups in the *trans*-position[11,51,63,174].

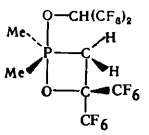
1,2-Oxaphospholens are frozen at −65°C[9-11,66,79,261,262]. 1,2-Oxaphospholens with two methoxy groups at the phosphorus atom exist in solution in the form of two diastereomers. They have different δ^{31}P values in solution at +30°C and for this reason do not undergo stereomutation under these conditions. Each of the two forms has two methoxy-group signals.



$\delta^{31}P = +16.7$ p.p.m. $\delta^{31}P = +13.3$ p.p.m.

The analogous 1,2-oxaphospholen with two phenyl groups at the phosphorus atom is "frozen" at +25°C. It exists in only one configuration[79].

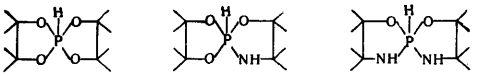
The relative rigidity of the 1,2-oxaphosphetan system was demonstrated by the fact that the ^{1}H NMR spectrum of this phosphorane does not change in the temperature range from −60° to +80°C.[10,39,64]



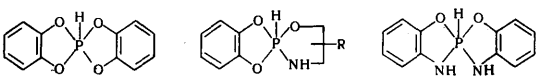
The isomer illustrated here is most stable, i.e. here the two oxygen atoms occupy the axial positions. The ^{19}F and ^{1}H NMR spectra are consistent with this structure: there is a singlet with $\delta^{19}F = +0.4$ p.p.m. relative to CF_3COOH and a doublet with $\delta^{19}F = -3.9$ p.p.m. and $I_{HF} = 5.8$ Hz. The two equatorial methyl groups give rise to a doublet with $\delta = 1.98$ p.p.m. and $^2J_{PH} = 15$ Hz and the protons of the phosphetan ring give rise to a doublet with $\delta = 4.04$ p.p.m. and $^2J_{PH} = 20.7$ Hz.

Spirophosphoranes obey the same rules as other cyclic phosphoranes. The rings assume the axial-equatorial position in the trigonal bipyramid[144,234]. Depending on the ring substituents, there are different numbers of diastereomers[153]. The diastereomers differ in their ^{31}P and ^{1}H NMR spectra at room temperature. At elevated temperatures the rate of interconversion of the diastereomeric forms increases and they cannot be distinguished on the basis of their NMR spectra[157]. The situation simplifies when there is nitrogen in the ring, since the more electronegative oxygen always occupies the axial position. Such molecules are "frozen" even at room temperature[234]. Spirophosphoranes with four oxygen atoms in the ring undergo permutational isomerisation even at −70°C.[263]

The ^{1}H NMR spectra of all spirophosphoranes with a P–H bond show the chemical shift of the P–H proton in the region 6.5–8.5 p.p.m. When the ring oxygen is replaced by the less electronegative nitrogen, the δH shift to higher fields; the position is reversed when there are benzene rings in the molecule[141,143,144,234,264]. J_{PH} increases when the ring is condensed with an aromatic nucleus[235]:



δ_H 7.1-6.8 p.p.m. 7.13-6.66 p.p.m. 6.76-6.4 p.p.m.
I_{PH} 830-802 Hz 800-760 Hz 770-730 Hz



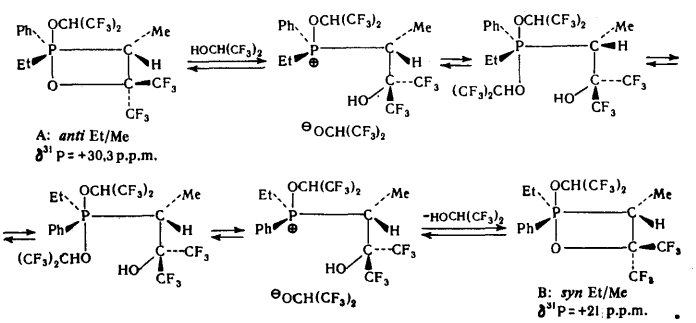
δ_H 8.6 p.p.m. 7.73-7.91 p.p.m. 8.62 p.p.m.
I_{PH} 918 Hz 826-839 Hz 835 Hz

It decreases when oxygen in the ring is replaced by nitrogen. The substitution of H at the nitrogen atom by Me increases I_{PH} and shifts δH to lower fields[154].

6. Irregular Permutational Isomerisation

The base-catalysed irregular permutational isomerisation of oxyphosphoranes can proceed via the intermediate formation of compounds with a hexacoordinate phosphorus atom (see the alcoholysis of phosphoranes described above). An acid-catalysed irregular permutational isomerisation process[12,162,247], proceeding via the formation of a tetracoordinate intermediate, was discovered recently.

The 1,2-Oxaphosphetans A and B are diastereomers differing in the configuration at the phosphorus atom. They are stable in the absence of moisture and are not interconverted at a temperature below that of the Wittig reaction. Their interconversion via the regular process is forbidden, since it requires either the placement of the four-membered ring in the diequatorial position or the location of the P–C bond in the axial position. In the presence of hexafluoroisopropyl alcohol as the catalyst they undergo stereomutation, which proceeds via an irregular process associated with ring opening.



A: *anti* Et/Me
$\delta^{31}P = +30,3$ p.p.m.

B: *syn* Et/Me
$\delta^{31}P = +21$ p.p.m.

The following general rules can be formulated on the basis of the stereochemical study of cyclic oxyphosphoranes: (1) the more electronegative substituents occupy axial positions in the trigonal bipyramid; (2) four- and five-membered rings occupy the axial-equatorial position.

When these requirements are met, phosphoranes are obtained in which there is fairly rapid exchange of ligand positions, provided that the above rules hold for all the intermediate positions in the trigonal bipyramid. The exchange of ligand positions in cyclic oxyphosphoranes can be "frozen" at certain temperatures; 1,2-oxaphospholens constitute a more rigid system than 1,3,2-dioxaphospholans and 1,4,2-dioxaphospholans. In the latter

case some of the diastereomers (*cis*-H/H conformation) are more rigid than others (*trans*-H/H conformation). Certain four-membered cyclic phosphoranes are more stable than the corresponding five-membered phosphoranes. The steric effects and the electronegativities constitute important factors in determining the relative stabilities of pentacoordinate and tetracoordinate phosphorus. The importance of the static and dynamic stereochemistry of phosphoranes is great, since the compounds with pentacoordinate phosphorus are intermediates in the reactions of many derivatives of tetracoordinate phosphorus and can be used in the interpretation of the biochemistry of phosphorus.

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Specific Activity of Metallic Catalysts

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This review deals with published work on the influence of chemical composition, degree of dispersion, and method of preparation on the specific activity of metallic catalysts. In most cases the specific activity is determined by the nature of the metal, and is independent of the degree of dispersion or other parameters. This behaviour is probably due to interaction between the catalyst surface and the surrounding medium, which converts the initial catalyst surface into a state which is relatively unaffected by variations introduced during the preparation of the catalyst. 131 references.

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I. INTRODUCTION

The catalytic activity of unit surface area of solid catalysts, usually termed the "specific activity"†, is the most characteristic parameter of the catalytic properties of the material, and it can be used, together with a knowledge of the accessible surface area, to predict the activity of the catalyst.

The specific activity of a catalyst can be influenced by various factors: 1) the chemical composition; 2) the degree of dispersion of the active component, i.e. its crystallite size, which determines the relative proportions of atoms on the corners, edges, and faces of the crystallite; 3) the method of preparation, and some other factors. The relative importance of chemical composition and of the structural factors listed above in determining the specific activity is one of the most important problems facing the development of an effective theory of catalyst preparation.

During the first phase of the development of catalyst theory, before the advent of effective methods of measuring surface areas, most workers believed that catalytic activity was associated with non-equilibrium structures possessing a large amount of excess free energy, and therefore that the method of preparation of the catalyst could be the predominant factor in determining the specific activity[4-13]. These *a-priori* views were put to the test when methods of measuring surface areas were developed and generally adopted. The results of specific activity studies on one-component oxide catalysts have been discussed[14] by the present writer. The general conclusion was that the specific activity of catalysts of a given composition, measured in the activation-controlled regime

† Some ambiguity exists in the concept of "specific activity": some workers refer the term to the activity of 1 g of the catalyst[1], others to the activity of 1 m^2 of total surface area[2], yet others to the activity of unit "working" surface, by which they understand the "true" surface accessible to the catalytic reaction[3]. The most rational characterisation of the catalyst is to relate the activity to unit surface area of the active component.

with the catalyst and the reacting medium under steady state conditions, is approximately constant and independent of the method of preparation and of the thermal history of the catalyst.

The present review is concerned with the influence of chemical composition, degree of dispersion, and method of preparation on the specific activity of metallic catalysts‡. In Sections II–IV we shall discuss the results of experimental studies available at the time of writing. A discussion of the results obtained by different workers and of possible explanations of the discrepancies observed will be found in the concluding Section. The selection of publications relevant to the present review was limited by the following conditions: 1) we shall consider only those papers in which the reported activities can be compared with the surface area or the degree of dispersion of the active component; 2) we shall confine our discussion to gas-phase reactions, because reactions at a liquid–solid interface or in three-phase gas–liquid–solid systems often involve diffusional limitations which could obscure the effects of interest to us; 3) although the most precise characteristic of the specific catalytic activity is the rate constant of the reaction, related to unit surface area [18,19], we shall also include (for the sake of a balanced presentation of relevant work) those papers in which the activity is characterised by the extent of reaction.

II. EFFECT OF CHEMICAL COMPOSITION ON THE SPECIFIC ACTIVITY OF METALLIC CATALYSTS

The relationship between the specific catalytic activity and the nature of the non-reducible oxide support and the concentration of metal is an important aspect of the study of metal–oxide catalysts.

Table 1. Effect of chemical composition on the activity of cyclohexane dehydrogenation catalysts (Ref. 21).

Catalyst	Carrier	Concn. of metal in catalyst, %	Surface area of metal in catalyst, $m^2\ g^{-1}$	Specific activity (% conversion $m^{-2}\ h^{-1}$)
Pt	η-Al_2O_3	0.4	0.9	97.1
Pt	η-Al_2O_3	0.78	2.3	36.1
Pt	γ-Al_2O_3	0.4	1.1	74.5
Pt	γ-Al_2O_3	0.82	2.33	35.2
Ni	η-Al_2O_3	2.57	—	—
Ni	η-Al_2O_3	6.0	1.46	18.4
Ni	η-Al_2O_3	6.48	0.58	27.6
Ni	γ-Al_2O_3	2.56	—	—
Ni	γ-Al_2O_3	6.0	1.24	20.2–21.0
Ni	Al_2O_3-SiO_2	6.0	1.11	22.3
Ni	SiO_2	6.0	1.29	10.3

Platinum and the platinum metals. Cusumano and coworkers [20] studied the effect of the nature of the carrier on the specific activity of platinum towards the dehydrogenation of cyclohexane. Aluminium oxide and alumina–silicas were used as carriers; the Pt content of the catalysts was 2%. The size of the platinum crystallites, calculated from H_2 adsorption measurements, was less than 10 Å on alumina and 85 Å on Al_2O_3–SiO_2. Measurements in a flow reactor showed that Pt is approximately 6 times more active on Al_2O_3 than on alumina–silica gel, as a result of differences in surface area. The specific activity of the platinum, referred to 1 m^2 of Pt, was found to be independent of the nature of the carrier and of the degree of dispersion of the metal.

Swift and coworkers [21], who studied the same reaction on nickel and platinum supported on γ- and η-Al_2O_3, came to a similar conclusion. Table 1, which is a compilation of their results, shows that samples prepared from γ- and η-Al_2O_3 have practically the same specific activity for equal concentrations of Pt. When the Pt concentration in the catalyst is raised from 0.4 to 0.8% the specific activity falls by a factor of 2–2.5.

Hightower and Kemball [22] have compared the activity and selectivity of platinum catalysts supported on silica gel and on γ- and α-alumina with the activity of a platinum foil towards the more complex deuteration and H exchange reaction in *p*-xylene. No significant difference was found in the specific activity and selectivity of samples deposited on the same carrier and differing only in Pt concentration. Catalysts prepared by depositing Pt on different carriers, on the other hand, differed in selectivity among themselves as well as from the platinum foil. The authors suggest that the water adsorbed on the carrier may have a poisoning effect on the catalyst.

Table 2. Effect of carrier on the activity of Ru, Pt, Tc, Pd, and Re in the hydrogenation and hydrogenolysis of benzene (Ref. 23).

Catalyst composition*		Specific activity, mol. $cm^{-2}\ s^{-1}$, $\times 10^{-12}$		Catalyst composition*		Specific activity, mol. $cm^{-2}\ s^{-1}$, $\times 10^{-12}$	
metal	carrier	hydrogenation	hydrogenolysis	metal	carrier	hydrogenation	hydrogenolysis
Ru	SiO_2	395	300	Tc	γ-Al_2O_3	20	16
Ru	γ-Al_2O_3	350	390	Pd	SiO_2	16	—
Pt	SiO_2	175	—	Pd	γ-Al_2O_3	8.4	—
Pt	γ-Al_2O_3	142	—	Re	SiO_2	1.2	3.4
Tc	SiO_2	4.6	8.9	Re	γ-Al_2O_3	0.5	1.1

*The catalysts contained 1% of metal.

Kubicka showed [23] that the nature of the carrier does not significantly influence the specific activity of ruthenium, platinum, palladium, and rhenium supported on γ-Al_2O_3 and on silica gel (see Table 2) towards the hydrogenation and the hydrogenolysis of benzene. Differences in specific activity for any one metal were less than a factor of 2, and differences in activation energy less than 1 kcal $mole^{-1}$. Only technetium was exceptional its activity towards the hydrogenation of benzene being 4 times greater on Al_2O_3 than on SiO_2. Also rhenium was 3 times more active towards both reactions on SiO_2 than on Al_2O_3.

Witekowa and Matyjewski [24] studied the effect of the nature of the carrier on the specific activity of platinum (on metallic aluminium and on Al_2O_3) and of Pt black towards the oxidation of hydrogen, and found that the total activity is slightly increased, but the specific activity is greatly decreased, by increasing the coverage of aluminium by platinum.

‡ Recent publications by Boudart [15] and Slinkin [16,17] include brief reviews of the specific activity of metallic catalysts, but comprehensive coverage is not claimed.

Nickel and cobalt. The influence of chemical composition on the specific activity of nickel towards the hydrogenation of benzene was investigated [25-29] by examining a large number of catalysts with difference non-reducible components and covering a range of nickel concentrations. Chromium oxide, alumina, magnesia, silica gel, and carbon were used as carriers. The catalysts were prepared both by impregnation and by coprecipitation. Samples of nickel black, prepared by decomposing nickel salts, were also investigated. The catalytic activity was measured by circulating-flow [25-28] and by flow [29] methods. The results of this work are summarised in Tables 3 and 4 and in Fig. 1. It is evident that, in spite of the large difference in chemical composition, the activity of all the catalysts (except the Raney-nickel) is proportional to the surface area of Ni in the catalyst; the specific activity is constant and independent of the nature of the non-reducible oxide and of the Ni content.

Table 3. Effect of carrier on the specific activity of nickel in the hydrogenation of benzene (refs. 25-27).

Carrier and method of preparation	Ni content, wt.%	Area of metallic nickel, $m^2 g^{-1}$	Crystal size, A	Specific activity at 100°, mmole $h^{-1} m^{-2}$ Ni
Nickel black (decomposition of formate)	100	4	1250	0.46
Chromic oxide	50	60	94	0.58
Magnesium oxide	65	65	86	0.65
Carbon	9.4	203	28	0.58
Raney nickel	75	87	65	3.30

Table 4. Effect of Ni content on the activity of $Ni-Al_2O_3$ catalysts in the hydrogenation of benzene (Ref. 29).

Nickel concentration	%	5.4	16.9	29.5	53.0	75.0
Ni surface area	$m^2 g^{-1}$	1.3	14.3	24.5	51.7	43.0
Apparent activation energy	kcal $mole^{-1}$	41.03	39.77	39.35	41.03	37.26
Rate at 35°	mole $h^{-1} g^{-1} \times 10^5$	3.7	48	68.1	138	123
Specific activity at 35°	mol. $s^{-1} cm^{-2} \times 10^{-11}$	4.78	5.62	4.66	4.48	4.8

Taylor and Staffin [30], who studied the effect of carrier on the specific activity of dilute nickel catalysts in the same reaction, obtained rather different results. Their measurements were made under pulsed conditions, in 5-minute experiments. It can be seen from Table 5 that the specific activity increases as the amount of nickel in the catalyst is increased, the effect being slight on SiO_2 but very marked on alumina-silica gel. The nature of the carrier is significant only at low nickel concentrations, samples containing 10% Ni show only marginal differences in activity.

The role of nickel content in nickel-magnesia catalysts has been studied [31] in the particular case of the dehydration of cyclohexane (Fig. 2). The activity was measured in a flow apparatus at 250°, and it was found that the catalytic activity and the H_2 adsorption give similar plots at low nickel concentrations. The plots begin to diverge at Ni concentrations greater than 15%: the adsorption increases monotonically, but the catalytic activity goes through a maximum at 36.5 wt.% Ni. Hence, the specific activity (expressed in relative units) varies in the range 1 ± 0.5 as the nickel content of the catalyst is varied. The authors [31] explain this observation by assuming that the catalytic activity of the nickel is determined by the "coordination of the surface atoms", which is apparently an optimum at a Ni content of 36.5%.

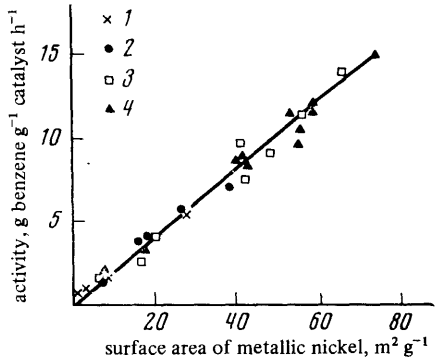

Figure 1. Surface area of nickel against activity of benzene dehydrogenation catalysts of different composition (Ref. 28): *1*) Ni black, *2*) $Ni-Cr_2O_3$, *3*) $Ni-Al_2O_3$, *4*) $Ni-Al_2O_3.Cr_2O_3$.

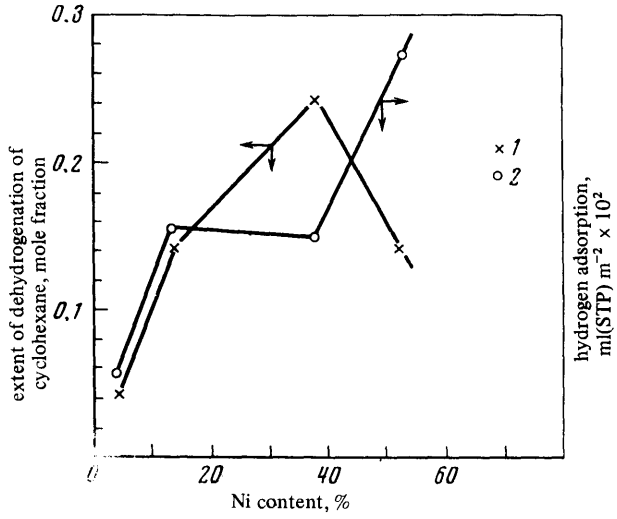

Figure 2. Effect of chemical composition on the activity of catalysts towards *1*) the dehydrogenation of cyclohexane and *2*) hydrogen adsorption (Ref. 31).

Swift and coworkers [21] also studied the effect of the nature of the carrier and of nickel content on the specific activity of nickel towards the dehydrogenation of cyclohexane. They found that samples containing ~2.5% of

nickel were catalytically inactive, and they suggested as an explanation that the nickel in these samples is chemically combined with the carrier and cannot be reduced. Samples containing 6–6.5% Ni on γ- and η-Al_2O_3 and on Al_2O_3–SiO_2 have almost identical specific activities (see Table 1), but the activity of nickel on silica gel is lower by about a factor of 2. The authors ascribe the enhanced activity of the catalysts containing Al_2O_3 to compound formation between the nickel and the aluminium oxide, the nickel being converted into an ionic form. The role of the nickel ions is to capture electrons and transfer them to the metallic nickel, thus modifying its catalytic activity.

Table 5. Effect of chemical composition of the catalyst on the specific activity of Ni in the hydrogenation of benzene (Ref. 30).

Carrier	SiO_2			$SiO_2 - Al_2O_3$		
Ni content, %	1	5	10	1	5	10
Ni crystallite size, Å	12	—	24	26	—	29
Ni surface area, $m^2 g^{-1}$	0.7	5.9	13.6	0.1	3.1	6.8
Specific activity, mole m^{-2} Ni $h^{-1} \times 10^4$	17.9	19.9	22.1	<1	3.84	17.2

Slinkin and coworkers [32] have reported an extensive investigation of the activity of Ni towards the dehydrogenation of cyclohexane as a function of the concentration of nickel in nickel–chromium catalysts. The reaction was studied in a flow reactor; it was found to follow the same kinetic law on all the samples examined. The surface area of metallic nickel was calculated from the concentration of metallic nickel and from its degree of dispersion, determined from X-ray diffraction and from magnetic measurements. The specific activity of the catalysts was found to vary by not more than a factor of 4 as the nickel content was varied from 2.4 to 34.8%: only the sample containing 70.5% Ni had an activity 46 times lower than the maximum. This behaviour is ascribed to incomplete removal of oxygen from the nickel surface.

An approximately constant specific activity was observed also in a study [33] of the influence of composition and degree of dispersion on the activity towards the hydrogenation and hydrogenolysis of cyclopropane of Ni catalysts deposited on kieselguhr, Al_2O_3, and alumina–silica gel.

It is evident from Table 6 that the hydrogenation rate constants for the various catalysts differ by not more than a factor of 2, and the hydrogenolysis rate constants by a factor of 4. According to a more recent study [34], the overall reaction rate varies only within the range ±25% (last column of Table 6).

Taylor and coworkers [35] also studied the hydrogenation and hydrogenolysis of cyclopropane on nickel catalysts, using pulsed conditions in 3-minute experiments. The nickel content of the catalysts was 10 wt.%. The nature of the carrier was found to have a marked influence, the specific activity of nickel being approximately 2 orders of magnitude higher on silica gel than on Al_2O_3–SiO_2.

The same group of workers [36–38] found that the nature of the carrier has a strong effect also on the specific activity of nickel and cobalt towards the hydrogenolysis of ethane: the specific activity of nickel on silica gel was higher than on Al_2O_3 by about a factor of 2, and almost 50 times higher than on Al_2O_3–SiO_2.

Similar results were obtained in the work on cobalt [37], samples based on silica gel and aluminium oxide having the highest activity, and samples based on Al_2O_3–SiO_2 and carbon the lowest. The specific activity of the former was about 20 times greater than the specific activity of the latter, even though the degree of dispersion of the catalysts differed only by a factor of 3.

Table 6. Specific activity of nickel in the hydrogenation and hydrogenolysis of cyclopropane at 60° (Refs. 33, 34).

Ni content, %	Carrier	Nickel surface, $m^2 g^{-1}$	Ni disperseness, (fraction of atoms on surface)	Specific activity, mole $h^{-1} m^{-2} \times 10^3$			
				hydrogenation k_1 (Ref.33)	hydrogenolysis k_2 (Ref.33)	total $k_1 + k_2$ (Ref.33)	total $k_1 + k_2$ (Ref.34)
58	Kieselguhr	63	0.163	5.8	1.28	7.0	7.9
5	$SiO_2 - Al_2O_3$	0.2	0.006	4.0	0.45	4.4	5.0
40	Al_2O_3	5.7	0.022	3.1	1.6	4.7	6.3
14	Al_2O_3	2.8	0.03	2.58	2.0	4.58	6.1

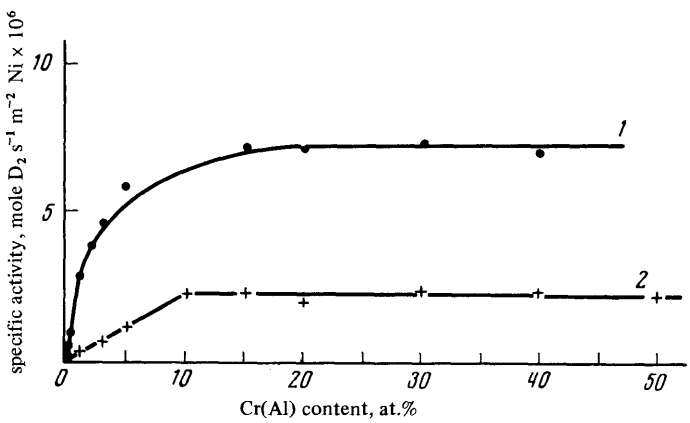

Figure 3. Effect of Cr_2O_3 and Al_2O_3 content on the specific activity of nickel catalysts in the reaction $HDO + H_2 \rightarrow H_2O + HD$: [39–41] *1*) Ni–$Cr_2O_3$; *2*) Ni–$Al_2O_3$.

When the nickel concentration in silica gel and alumina–silica catalysts was changed from 1 to 10% it was found [38] that the specific activity of the nickel varied in the same sense as the nickel content. This observation was explained by postulating an interaction between the nickel and the carrier, which can be expected to be stronger when the nickel content is low. However, the nature of this interaction is not clear.

Margineanu and Olariu [39,40], who studied the reaction $HDO + H_2 \rightarrow H_2O + HD$, found a relationship between the specific activity and the chemical composition of a nickel–chromium catalyst. The concentration of chromium oxide

in the binary system was varied from 0.1 to 40 mole %. With pure nickel, both the surface area and the specific activity were found to be very low. As the concentration of chromic oxide was increased to 5% the activity of the nickel increased 100-fold. However, at still higher concentration of chromium oxide the specific activity of the nickel remained approximately constant (curve *1* of Fig.3).

The authors explain these results by assuming that the "promotion" of the nickel catalyst involves an interaction with the chromium oxide, yielding a surface compound which has a very high activity towards the exchange reaction. As the concentration of chromium oxide in the catalyst is increased, the concentration of active surface centres increases at first and then reaches a constant level. As a result, the specific activity also rises to a constant level, independent of the concentration of Cr_2O_3. The decrease in specific activity with decrease in chromium oxide content could also be explained in terms of increasing crystallite size. The same authors[41] observed a similar relationship between the specific activity of nickel and the concentration of non-reducible oxide in nickel–alumina catalysts: as the concentration of Al was raised from 0 to 10 at.% the specific activity rose from 0.057 to 2.22 mole D_2 m^{-2} s^{-1}, and remained constant at still higher Al concentrations (curve *2* of Fig. 3).

Müller and coworkers[42] studied the effect of nickel content in nickel–chromium catalysts on the total and the specific activity towards the hydrogenation of CO_2 to CH_4. The activity was measured in a circulating flow apparatus in the presence of a large excess of hydrogen. As Table 7 shows, a change in nickel concentration alters the total activity by more than an order of magnitude without significantly affecting the specific activity.

Table 7. Effect of Ni : Cr_2O_3 ratio on the activity of nickel–chromia catalysts in the hydrogenation of CO_2 at 175° (Ref. 42).

Ni:Cr_2O_3	∞ (100% Ni)	21.6	9.03	4.37	1.96	0.925	0.25
Total activity, mole $CO_2^{0.5}$ litre$^{0.5}$ g^{-1} h^{-1}	0.047	0.463	0.490	0.530	0.381	0.043	0.046
Specific activity, mole $CO_2^{0.5}$ litre$^{0.5}$ m^{-2} Ni h^{-1}	0.67	0.721	0.716	0.731	0.839	0.906	—

Iron. Shcheglov and coworkers[43] studied the effect of catalyst promotion on the specific activity of the catalyst towards the dissociation of ammonia. The measurements were made in a circulating flow apparatus at atmospheric pressure.

Table 8 shows that catalyst promotion results in a 15-fold increase in the rate constant (referred to 1 g of catalyst), whereas the specific activity increases at most by 30%. The authors conclude that the role of the promoting agent is to increase and stabilise the iron surface.

Similar conclusions were reached in studies of the effect of alumina content on the activity of iron catalysts in the synthesis of ammonia[44]. There was no direct relationship between the catalytic activity and the total surface area. As the proportion of aluminium oxide in the catalyst increases, the fraction of the surface occupied by free iron decreases. However, since the total surface area is increased, the area of metallic iron goes through a maximum. The yield of ammonia goes through a similar maximum. The rate constant, calculated by the Temkin–Pyzhov equation, varies in direct proportion to the iron surface (Fig. 4), and therefore the specific activity is constant.

Table 8. Effect of catalysts composition on the activity of iron towards the decomposition of ammonia[43].

Catalyst	Rate constants x 10^2*			
	375°		400°	
	k_g	k_{sp}	k_g	k_{sp}
Armco-iron	11	9.9	65	59
Promoted Fe catalyst	171	12.9	943	69

*k_g is the rate constant per 1 g of catalyst, k_{sp} is the rate constant referred to 1 m^2 of metallic iron surface (cm^3 NH_3 m^{-2} Fe h^{-1}).

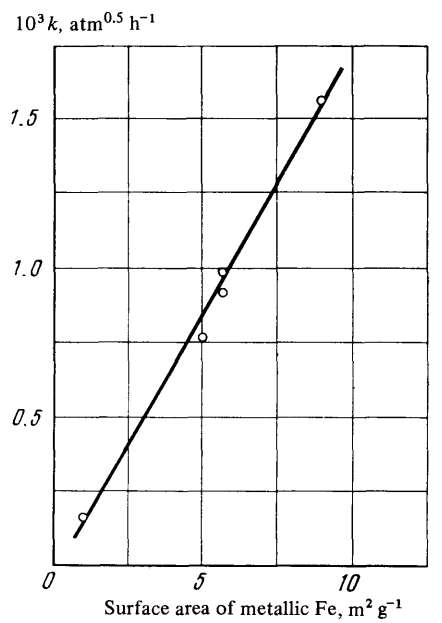

Figure 4. Metallic iron surface against rate constant calculated by the Temkin–Pyzhov equation[44].

The specific activity of iron towards the synthesis of ammonia was investigated by Lachinov and coworkers[45], who varied the composition of their catalysts over wide limits. It is clear from their experimental results, summarised in Table 9, that with the exception of sample 12a (which had a very small iron surface) the specific activity of the catalysts varies by no more than a factor of 2.7, which is probably within the limits of experimental error in this type of measurement.

In contrast to these results, the same group of workers[46] had previously found that the specific activity of iron increases from 30 to 1200 when the fractional occupancy of the surface by alkali is increased from 0.08 to 0.78. They had concluded that the active component in iron catalysts for ammonia synthesis is not elemental iron, but an iron compound formed on the catalyst surface during the reduction stage.

Table 9. Effect of Al_2O_3 content on the surface area and specific activity of Fe ammonia synthesis catalysts at 400° (Ref. 45).

Sample No.	Al_2O_3 content, wt.%	Surface area, $m^2 g^{-1}$		k_{sp}, $atm^{0.5} h^{-1} m^{-2}$ Fe
		total	metallic iron	
12a	0.0	1	1.0	0.75
8a	0.6	6	2.5	20.3
7a	1.1	8	3.4	15.5
6a	2.4	13	3.8	20.0
4a	5.4	24	7.7	11.7
3a	7.9	35	5.2	11.3
2a	13.4	91	4.1	16.3
1a	37.5	91	5.5	7.5

The effect of Al_2O_3 and K_2O additions on the specific activity in the synthesis of ammonia was investigated also with iron–cobalt catalysts containing 15% of cobalt. It was found that the additives have a significant effect on the surface area and on the total activity of the catalysts, but the rate constant (referred to 1 m^2 of metal surface) remains unchanged[47].

Table 10. Specific activity of silver catalysts for the oxidation of ethylene to ethylene oxide (Ref. 48).

Ag content of catalyst, $g l^{-1}$	17	33	43	73	10	23	53	83	50	1600 Ag pellets
Surface area of carrier, $m^2 g^{-1}$	5.0	5.0	5.0	5.0	2.8	2.8	2.8	2.8	0.5	—
Specific activity of silver, $10^5 k$, m^{-2}	2.8	5.1	4.7	2.8	5.9	5.6	4.2	3.1	3.1	2.8–4.2

Table 11. Specific activity of catalysts with different silver contents towards the oxidation of ethylene to ethylene oxide (Refs. 49, 50).

Silver content, wt.%	4.3	11.1	11.6	17.8	19.1	21.5	26.7
Specific activity, g ethylene oxide m^{-2} Ag $h^{-1} \times 10^2$	28	41	36	42	42	31	32

Silver. Soviet workers[48–50] have investigated the effect of method of preparation and of silver content on the activity of silver catalysts for the oxidation of ethylene to ethylene oxide. In the activation-controlled region the activity of the catalysts per 1 m^2 of silver surface was found to be approximately constant (Tables 10 and 11).

III. DEGREE OF DISPERSION OF METALLIC CATALYSTS AND THEIR SPECIFIC ACTIVITY

The dependence of the specific activity on the crystallite size of the active component has been actively investigated during the past 50 years. According to Taylor and others[4,7], who published their work in the 1920's, the catalytic activity resides mainly in the atoms which are weakly bound to the surface and therefore have an excess of free energy. Hence, the specific activity should increase on decreasing the size of the crystallites, thus increasing the proportion of atoms weakly bound to the surface. More recently, Bond has shown[51] from theoretical considerations that changes in crystallite size can influence the specific activity in different ways. 1) The specific activity may be independent of crystallite size. 2) Small crystals may be more active than large crystals: in this case the specific activity decreases if the crystal radius increases. Bond called this the "positive internal effect". 3) If the larger crystals are more active than the smaller crystals (negative internal effect) the specific activity increases with crystallite size. It is also possible for very small crystals to have a negative internal effect and larger crystals to have a positive internal effect: in this case the specific activity goes through a maximum. In the present section we shall discuss the results of experimental studies of the effect of degree of dispersion on the specific activity of catalyst particles. [Dispersion in this context is sometimes defined as the fraction of the total metal atoms which are the metal surface. (Ed. of Translation)].

Table 12. Specific activity of platinum towards the oxidation of sulphur dioxide and hydrogen (Refs. 53–55).

Catalyst	Surface of 1 g Pt, cm^2	Rate constants*			
		Oxidation of sulphur dioxide at 427°		Oxidation of hydrogen at 100°	
		k_g, $cm^3 s^{-1}$	k_{sp}, 10^2 cm s^{-1}	k_g, $cm^3 s^{-1}$	k_{sp}, cm s^{-1}
0.2% platinum on silica gel	$3 \cdot 10^5$	$1.1 \cdot 10^3$	0.37	$4.9 \cdot 10^8$	1400
0.5% platinum on silica gel	$7 \cdot 10^5$	$(0.7–2.8) \cdot 10^3$	0.1–0.40	—	—
Platinum sponge	$1.7 \cdot 10^3$	1.5–3.9	0.09–0.23	—	—
Wire 0.1 mm diameter	20.6	0.054	0.26	$1.1 \cdot 10^4$	535
Gauze	22.6	0.1	0.49	—	—
Foil	6.9	0.12	1.74	$6.2 \cdot 10^3$	900

*k_g is the rate constant per 1 g of catalyst, k_{sp} is the rate constant referred to 1 cm^2 of Pt surface.

Platinum, palladium, and rhodium. Boreskov and coworkers[52–56] made a comparative study of the activity of "massive" platinum samples (sponge, wire, gauze, foil) and of platinum deposited on silica gel towards the oxidation of sulphur dioxide and hydrogen, and towards the homomolecular $H_2–D_2$ exchange reaction. In the oxidation reactions (SO_2 and hydrogen) the activity was measured in the activation-controlled region by the circulating flow method, which ensures isothermal conditions in the catalyst bed. The surface area of metallic platinum was varied from 6.9 $cm^2 g^{-1}$ (foil) to 7×10^5

$cm^2\ g^{-1}$ (platinised silica gel containing 0.5% Pt), i.e. more than 100 000-fold. In spite of this enormous difference in the degree of dispersion of the catalysts, the specific activity towards the oxidation of SO_2 was found to vary only by a factor of 4 (excepting only the foil sample). The foil had an unexpectedly high specific activity, tentatively ascribed to the presence of impurities (Table 12).

The catalytic activity of the same samples towards the oxidation of hydrogen[55], referred to 1 g of platinum, was found to vary by 4 orders of magnitude, while the specific activity varied only by a factor of 2.5. The differences in specific activity of different samples were comparable to the differences in specific activity of a given sample in different experiments: this effect probably arises from the slow establishment of a steady state over the catalyst surface.

Similar values of the specific activities of massive platinum, platinum sponge, and platinum black were observed also in a study[56] of homomolecular exchange. In this case, the platinised silica gel samples had a substantially higher specific activity, which the authors ascribed to a significant catalytic activity of the silica gel itself (in the presence of platinum) towards the H_2 exchange reaction. More recent work[57] failed to confirm the higher specific activity of Pt deposited on silica gel, although the absolute values of specific activity observed were close to those reported by Boreskov and Avdeenko[56].

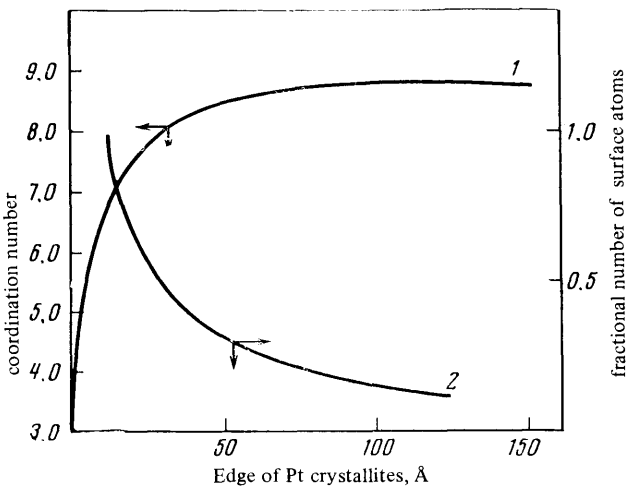

Figure 5. Coordination number (*1*) and fractional number of surface atoms (*2*) against platinum crystallite size (Ref. 58).

Poltorak and coworkers[57-62] published a series of papers on the effect of dispersion on the specific activity of platinum crystallites towards various reactions. The structural properties of the crystallites were evaluated from a theoretical treatment of the octahedral model. Plots of the coordination number (c.n.) and of the fractional number of surface atoms (γ) against the size of the platinum crystallites[58] are shown in Fig. 5. It is clear that the most important changes in structural properties occur when the edge length l is varied from 5 to 30–40 Å: further increase in crystallite size produces only minor changes in these parameters, and for crystals greater than 100 Å the changes are insignificant. These considerations lead to the conclusion that studies of the effect of dispersion on the activity of catalysts are not likely to be meaningful unless the catalyst is highly disperse. It is convenient to consider three cases: 1) crystallites containing less than 15 atoms, in which $\gamma \simeq 1$ and c.n. < 6, whose properties can be equated to those of micro-defects on crystal surfaces; 2) crystallites with $\gamma = 0.8-0.9$ ($l = 10-15$ Å), in which the properties of the atoms in the surface layer are similar to those of edge atoms in coarser crystal; 3) crystallites with $\gamma < 0.3$ and $l > 50$ Å, in which the properties of the surface atoms are no different from those of ideal crystal faces.

By applying these considerations, samples of platinised silica gel covering the appropriate range of crystallite size were prepared. The effect of platinum concentration on the catalytic activity towards the homomolecular H_2-D_2 exchange reaction was studied[57]; it was found that, in spite of the large difference in dispersion, samples in the first and second series had almost identical specific activities, and samples in the third series had a slightly lower specific activity (1.5–2-fold, almost within the limits of experimental error).

Table 13. Influence of dispersion on the specific activity of platinum (Refs. 60–62).

H/Pt	Average size of Pt crystallites, Å	Initial specific activity, mol. min^{-1} $atom^{-1}$ Pt		
		dehydrogenation of C_6H_{12}	dehydrogenation of C_3H_7OH (Ref.61)	hydrogenolysis of cyclopentane (Ref.60)
0.98	7	4.8	7.65	0.236
0.79*	—	—	—	0.28±0.026*
0.63	20	—	—	0.535
0.55	24	4.85	6.3	—
0.5	27	—		0.388
0.475	30	4.2	11.8	—
0.4	37	4.65	—	—
0.05	100	5.3	—	—

*From Ref. 62.

Mitrofanova and coworkers[60-62] studied the dehydrogenation of cyclohexane and isopropanol, and also the hydrogenolysis of cyclopentane. The catalytic activity was measured in a circulation apparatus. It is evident from the results (Table 13) that the specific activity of catalysts in the above reactions is not significantly influenced by the size of the crystallites, and hence that the ratio of surface to bulk platinum atoms does not play a major role. The authors conclude[58] that "in no single instance has the enhanced activity of crystal edges or structural defects, axiomatically assumed in theoretical discussions of heterogeneous catalysis, been experimentally confirmed for gas-phase reactions".

Constant specific activity of alumina–platinum catalysts towards the dehydrogenation of cyclohexane has been reported also by Zaidman and coworkers[63-65]. The dispersion of the catalysts was varied by varying the platinum content and the annealing temperature, and was

characterised by the H/Pt ratio. The activity was measured in a circulating flow system at low extents of reaction, for which the kinetic order is zero. It can be seen from Fig. 6 that the activity is proportional to H/Pt, and hence the specific activity of the platinum is constant within experimental error.

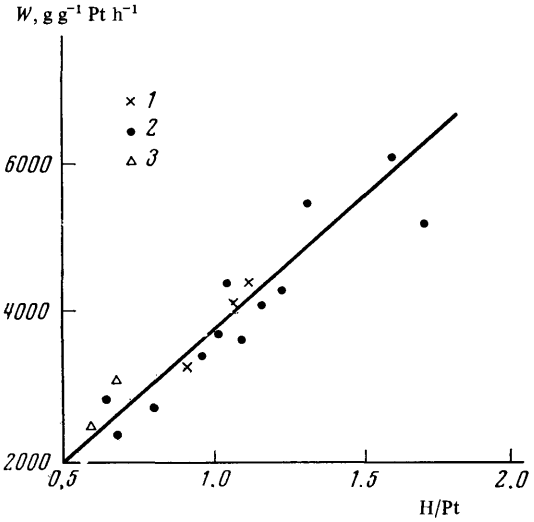

Figure 6. Activity of platinum in the dehydrogenation of cyclohexane against H/Pt (Refs. 63–65): *1*) 300°, *2*) 500°, *3*) 700°.

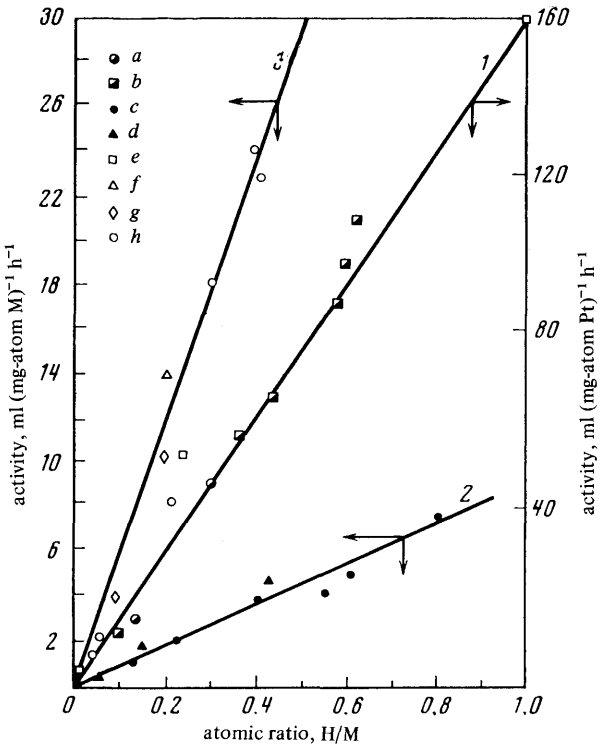

Figure 7. Benzene hydrogenation activity against fractional number of surface atoms (Refs. 66, 67): *1*) Pt, *2*) Pd, *3*) Ni; (*a*) Pt–SiO_2, (*b*) Pt–Al_2O_3, (*c*) Pd–SiO_2, (*d*) Pd–Al_2O_3, (*e*) Ni–Al_2O_3, (*f*) Ni–SiO_2.MgO, (*g*) Ni–SiO_2.Al_2O_3, (*h*) Ni–SiO_2.

Similar results were obtained in work [66,67] on the influence of the crystallite size of platinum and palladium on the specific activity of these metals towards the hydrogenation of benzene. The size of the crystallites was varied between 10 and 200 Å, and silica gel, alumina, SiO_2–MgO, and SiO_2–Al_2O_3 were used as carriers. The activity was found to be proportional to the degree of dispersion of the platinum (Fig. 7), showing that the specific activity is constant and independent of the degree of dispersion of the metal.

Dorling and Moss [68] also studied the relationship between the size of Pt crystallites deposited on silica gel, the surface area of the metal, and the activity of these catalysts towards the hydrogenation of benzene. The crystallite size was varied between 45 and 980 Å by varying the temperature of heat treatment. It can be seen from Table 14 that in spite of the large (15-fold) difference in crystallite size the specific activity of catalysts heated at 500° and below varies only by a factor of 2.

Larsen and coworkers [69] have studied the effect of dispersion on the activity of platinum towards the hydrogenation of aromatic compounds, using the extent of hydrogenation to characterise the activity. The reaction was found to proceed only to a maximum of 60% conversion, which was ascribed to achievement of equilibrium. It can be seen from Fig. 8 that for up to 30% reaction (i.e. 50% of the maximum) the relationship between percentage conversion and platinum surface area is approximately linear, but at higher extents of reaction the proportionality no longer holds.

Table 14. Influence of sintering temperature and dispersion on the specific activity of platinum towards the hydrogenation of benzene (Ref. 68).

Sintering temperature	120	250	300	400	500	600	800
Pt crystallite size, Å	45	220	210	360	640	980	890
Pt surface area, $m^2 g^{-1}$	2.0	1.32	1.52	3.0	1.53	0.2	0.04
Specific activity (molecules cm^{-2} Pt s^{-1}) × 10^{-13}	2.8	2.7	3.2	1.4	1.3	inactive	

Boudart and coworkers [70] studied the effect of crystallite size on the catalytic activity of platinum towards the hydrogenation of cyclopropane in order to account for the existence of an optimum particle size. Their measurements were made in a circulation system. The dispersion was varied by varying the platinum concentration and the temperature of heat treatment, and was characterised by the surface area as determined by H_2 adsorption, and also by the ratio of the number of surface atoms to the total number of atoms (%-age dispersion). For comparison, Pt foil 12.7 μm thick was also examined. It was found (Table 15) that the specific activity remained relatively constant (within a factor of 3) in spite of very large differences in dispersion (20 000-fold) and in the nature of the carrier.

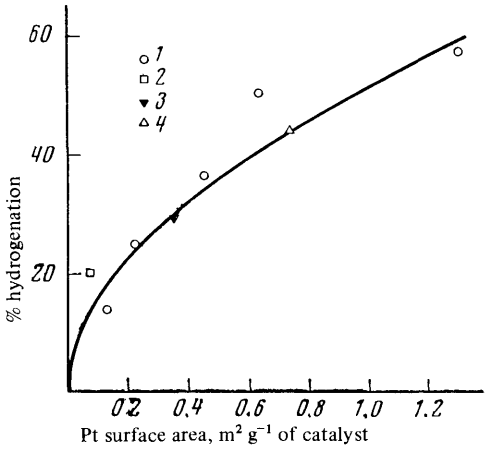

Figure 8. Influence of platinum surface area on the extent of hydrogenation of aromatic compounds in a petroleum fraction (Ref. 69): *1*) normal catalyst preparation, *2*) heated at 760°, *3*) heated in rotating furnace, *4*) impregnated 5 times.

Table 15. Effect of dispersion on the activity of platinum towards the hydrogenation of cyclopropane (Ref. 70).

Catalyst	Fraction of surface Pt atoms, %	Specific surface area of Pt, μmole H_2 g^{-1}	Activity at 0°	
			total mole C_3H_6 min^{-1} g^{-1}	specific mole C_3H_6* min^{-1} cm^{-2} Pt
0.3% Pt on η-Al_2O_3	44	10.2	82.4	8.2
0.3% Pt on γ-Al_2O_3	59	13.5	100	7.4
0.6% Pt on γ-Al_2O_3	73	33.5	186	5.4
1.96% Pt on η-Al_2O_3	64	97.0	637	6.5
ditto after sintering	7 6	11.5	44	3.8
4.3% Pt on silica gel	17	57.3	160	2.8
Foil (100% Pt)	0.0039	0.55	1.4	2.5

*Calculated from data in Table 1 of Ref. 70.

To explain these "strange" results the authors proposed the concept of "easy" and "difficult" catalytic reactions. In the former, most of the surface sites are active, and therefore the non-uniformity of the surface is immaterial. In the "difficult" reactions, on the other hand, surface non-uniformity can be expected to play an important role, and hence the reaction rate should be influenced by the dispersion of the metal, the method of preparation, and other factors. In a more recent paper by Boudart [71] a typical "difficult" reaction is discussed in detail (the isomerisation and hydrogenolysis of neopentane). The activity in this case was measured in a micro-reactor operating under pulsed conditions.

As Table 16 shows, changes in dispersion and in the method of preparation of the catalyst give rise to substantial differences in specific activity and selectivity for this system: the activity in the isomerisation reaction varied by a factor of 15 and the activity in the hydrogenolysis reaction varied by a factor of 300; the selectivity varied by a factor of 100. The large differences in activity were explained by the need for three-point adsorption of the neopentane molecule: "triplet" sites, able to adsorb the reacting molecule in the appropriate configuration, must be present on the surface. The concentration of triplets can be expected to depend on the dispersion and on the method of preparation of the catalyst.

Table 16. Specific activity and selectivity of platinum towards the isomerisation and hydrogenolysis of neopentane (Ref. 71).

Catalyst		Disperseness, %	Specific activity, (molecules Pt $atom^{-1}$ s^{-1}) × 10^3		Selectivity N_I/N_H
Pt content, wt.%	Carrier		isomerisation N_I	hydrogenolysis, N_H	
0.6	γ-Al_2O_3 [a]	73	2.6	4.7	0.55
1.96	η-Al_2O_3 [a]	64	5.3	13.0	0.41
0.60	γ-Al_2O_3 [b]	73	2.8	1.9	1.5
1.96	η-Al_2O_3 [b]	64	3.4	2.3	1.5
4.3	SiO_2	17	3.8	13	0.29
1.0	Spheron [c]	12	1.1	0.04	27
1.96	η-Al_2O_3 [d]	7.6	11	4.5	2.4
100	— [e]	0.028	0.73	0.08	9.1

Note. [a] reduced in H_2 at 425° for 10 h; [b] ditto, at 500°; [c] reduced at 500°, vacuum-baked at 900° for 16 h, stored in air, and reduced as for "b"; [d] heated in a stram of H_2 at 650° and reduced as for "b"; [e] heated in hydrogen and oxygen alternately, and finally reduced as for "b".

Boudart's hypothesis was put to the test by other workers. In one of the most interesting investigations of this topic, due to Dorling and coworkers [72], the activity of platinum towards the hydrogenation of ethylene was studied as a function of crystallite size and method of preparation. Catalysts were prepared by impregnating silica gel with a solution of H_2PtCl_6, and by adsorption of ammine. The platinum content, and the reduction conditions, were also varied. The catalytic activity was measured in a flow apparatus. Catalyst poisoning by the decomposition products of ethylene was observed in all cases (Table 17). The specific activity was found to vary by more than 2 orders of magnitude as a result of changes in Pt content and conditions of preparation. With the catalysts prepared by impregnation with H_2PtCl_6, samples containing less than 1% of Pt had the lowest activity. The highest activity was found in samples containing 1% Pt or more, and reduced at 80°. As the reduction temperature was raised, the activity fell to a limiting value of about 2×10^{12} molecules cm^{-2} Pt s^{-1}. Samples prepared from the ammine had an approximately constant specific activity of $2-3 \times 10^{12}$ molecules cm^{-2} Pt s^{-1}. From these results the authors concluded that the specific activity of platinum is constant ($2-3 \times 10^{12}$ molecules cm^{-2} Pt s^{-1}), and independent of the platinum crystallite size. The low specific activity of samples prepared by impregnation and containing less than 1% of platinum is due to poisoning effects, which can be very marked in catalysts with a low surface area. The enhanced activity of samples reduced at 80° is due to the promoting effect of traces of Cl, which are removed at higher reduction temperatures. Thus, the observed differences in specific activity are fortuitous.

Kraft and Spindler[73] studied the effect of dispersion on the activity of platinum (supported on Al_2O_3) towards the dehydrogenation of cyclohexane and the dehydrocyclisation of n-heptane. The activity was measured in a flow apparatus, and was characterised by the extent of reaction. The specific activity at low extents of reaction (23–31%) was found to be constant; at higher extents of reaction the specific activity fell by a factor of 3.5–4. This effect was ascribed to the approach to equilibrium. In the dehydrocyclisation of n-heptane no simple relationship between dispersion and specific activity was found.

Table 17. Effect of dispersion and preparative conditions on the specific activity of platinum towards the hydrogenation of ethylene (Ref. 72).

Catalyst	Average crystallite size, Å	Pt surface, $m^2 g^{-1}$	Reduction temp., °C	Specific activity at −80° (mol. cm^{-2} Pt s^{-1}) × 10^{-12}	Comments
Impregnated < 1% Pt	30—40	0.1—0.5	210	0.1—0.6	Low specific activity due to poisoning
Heated at 600°	200	0.2	80	3	
Impregnated 3.4% Pt	40	2	80	20	Specific activity decreasing due to loss of Cl_2 during reduction
			210	7	
			500	2	
Impregnated 9.8% Pt	50—75	3—5	80	15	
			210	8	
			500	2	
Impregnated 1-11.5% Pt	30—60	0.8—4.5	80	5—23	—
			210	2—8	
Ammine adsorption 2.45% Pt	13—30	3—4	300	2—3	Approximately constant specific activity

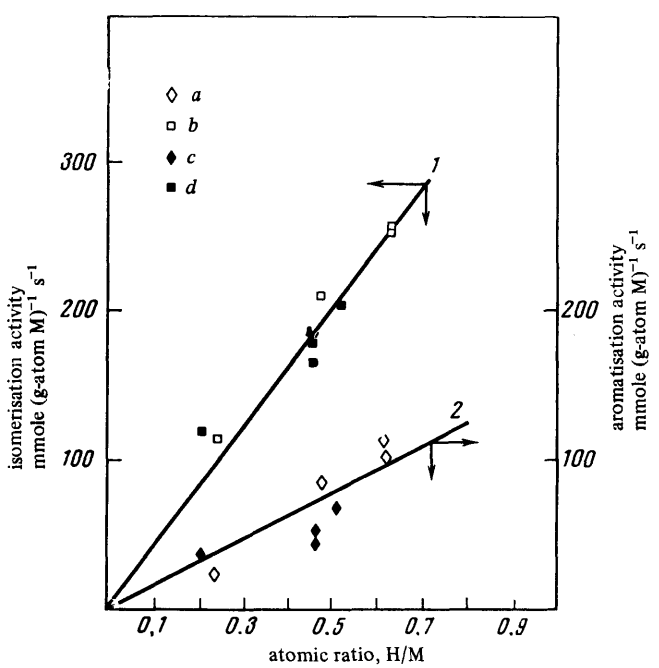

Figure 9. Effect of dispersion on the activity of platinum towards the isomerisation (*1*) and aromatisation (*2*) of hexane (Ref. 74): *a*) and *b*) 0.5% Pt; *c*) and *d*) 1.0% Pt.

Dautzenberg and Platteuw[74] studied the influence of dispersion on the activity of platinum towards the isomerisation and cyclisation of hexane. The measurements were made in the flow regime. Aluminium oxide, which is inert in isomerisation reactions, was chosen as the carrier. The platinum was deposited from $Pt(NH_3)_4(OH)_2$ solution in order to avoid the inclusion of acidic groups. It is evident from Fig. 9 that in both reactions the activity is directly proportional to the surface area of platinum. These results were confirmed by a subsequent observation[75] that the selectivity in the isomerisation of n-hexane is unaffected by changes in platinum particle size from <10 to ~80 Å.

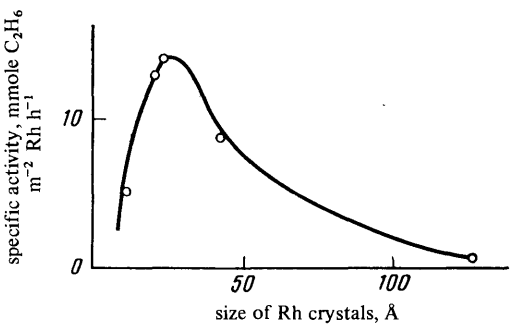

Figure 10. Length of crystallite edge against the specific activity of rhodium in the hydrogenolysis of ethane (Ref. 76).

The specific activity of rhodium towards the hydrogenolysis of ethane has been studied[76] as a function of particle size. The reaction rate was measured in a pulsed reactor. The specific activity was characterised by the number of millimoles of ethane reacting per hour on a square metre of rhodium surface at 253°. As Fig. 10 shows, samples in which the rhodium crystallites have a diameter of ~20 Å have the highest activity. When the crystallite size is decreased to 10 Å the specific activity falls by a factor of 3. The specific activity of coarsely gound samples of massive rhodium, and of samples deposited and heat treated at 800°, is 20–40 times lower than the maximum.

The effect of particle size on the activity of platinum in thin-film form towards the hydrogenolysis of n-hexane, 2- and 3-methylpentane, and methylcyclopentane has been studied[77] under static conditions. The reaction rate fell rapidly during the course of the reaction, reaching a steady value at an extent of conversion of 0.1–0.2%. This effect can be ascribed to "self-poisoning" of the catalyst. When the platinum crystallite size is increased from 15 to 58 Å both the initial and the steady-state specific activity decrease by an order of magnitude.

McKee[78] studied the effect of dispersion on the activity of platinum black towards the cracking of propane in a static apparatus with an initial propane pressure of 17.5 mmHg. The dispersion of the metal was varied by varying the sintering temperature between 150 and 220°, and it was characterised by the surface area measured by nitrogen adsorption. The particle size of the catalysts

was not stated. The activity fell during the reaction owing to the formation of a carbon deposit. The catalytic activity of the platinum (Fig. 11) decreases as the extent of sintering increases: in order to produce a measurable rate of reaction the surface area of the sample must be greater than some minimum value (depending on the reaction temperature). The dispersion also influences the activation energy of the reaction, which increases from 12 to 24 kcal mole^{-1} as the samples are more heavily sintered. These observations are explained by assuming that sintering causes a decrease not only in surface area but also in the concentration of surface defects which behave as active centres in the cracking reaction.

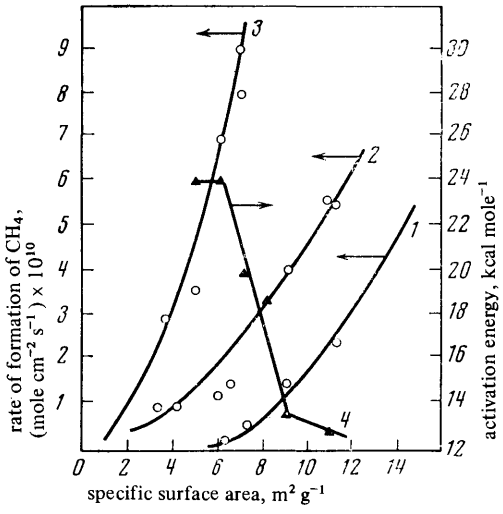

Figure 11. Effect of surface area on the activation energy and activity of platinum black towards propane cracking at different temperatures: *1*) 153°, *2*) 180°, *3*) 200°, *4*) activation energy (Ref. 78).

The specific activity of platinum samples of different degrees of dispersion towards the exchange reaction $HDO + H_2 \rightleftharpoons H_2O + HD$ has been studied [79] under flow conditions. The catalysts were prepared by three methods, and within each series the particle size was varied from 5 to 250 Å. The platinum surface area was measured by H_2 adsorption. The specific activity was characterised by the rate constant per unit surface area. By varying the sintering temperature the specific activity within each series could be varied by a factor of 3, reaching a maximum after sintering at 500°. Varying the crystallite size from 5 to 250 Å produced a change in the specific activity at 127° from 1.9×10^{-8} to 5×10^{-8} mole D_2 cm^{-2} s^{-1}.

Nickel. Rienäcker and coworkers [80] studied the activity of nickel powder and of heat-treated sheet nickel towards the decomposition of formic acid. In spite of the very large (more than an order of magnitude) difference in dispersion, the specific activity of the catalysts differed only by a factor of 1.5.

A group of Czech workers [81-83] has investigated the effect of dispersion on the activity of a nickel–magnesia catalyst towards the hydrogenation of benzene. The catalysts were prepared by thermal decomposition of the double oxalate of nickel and magnesium. Particle size was determined by X-ray diffraction and thermomagnetic methods.

Table 18. Effect of crystallite size on the specific activity of nickel in the hydrogenation of benzene at 40° (Ref. 81).

Sample No.	Prepared from	Metallic nickel content, wt %	Nickel surface m^2 g^{-1}	Crystallite size, Å	Specific activity, (mole min^{-1} m^{-2} Ni) × 10^7
7	Mixed Ni and Mg oxalates	32.3	97.0	22	4.9
11	ditto	86.6	52.0	148	4.9
3	Nickel oxalate	100	11.6	580	7.8
6	ditto	100	3.6	1870	5.25

Table 18 shows that the specific activity of nickel is constant within experimental error in spite of large differences in dispersion. The authors point out that their value of the specific activity is close to that reported [25] by Lyubarskii ($3-5\times10^{-7}$ mole min^{-1} m^{-2}).

Table 19. Effect of crystallite size on the specific activity of nickel in the dehydrogenation of benzene (Ref. 84).

Nickel content, %	4.26	10.2	28.9	52.5
Ni surface area, m^2 g^{-1}	12.86	26.2	56.6	43.1
Average crystallite size, Å	12.0	15.1	19.2	50.6
Specific activity, μmole min^{-1} m^{-2} Ni	6.2	4.2	3.6	3.8

Rijnten and coworkers [84] also failed to observe a significant effect of crystallite size on the specific activity of nickel towards the gas-phase hydrogenation of benzene (Table 19). It is evident from the Table that even in the region of large changes in the relative numbers of centres with different coordination (12–50 Å particle size) the changes in specific activity are only marginal.

In contrast to these findings, Sinfelt and coworkers [85] (who studied the effect of crystallite size of nickel deposited on $Al_2O_3-SiO_2$ on the rate of hydrogenolysis of ethane) observed a sharp decrease in the specific activity of nickel with increase of crystallite size (Fig. 12). The same workers [86] reported a 50-fold increase in the specific activity for the hydrogenolysis of ethane associated with an increase in crystal size from 12 to 24 Å, but in this case the situation was complicated by a simultaneous increase in nickel content from 1 to 10%. There is also a large difference in specific activity between nickel catalysts supported on Al_2O_3 and on $Al_2O_3-SiO_2$, in spite of the similarity in particle size (Table 20).

Van Hardeveld and Hartog [87] found that the specific activity of nickel catalysts towards the deuteriation of benzene remains approximately constant as the nickel particle size is varied from 20 to 185 Å, but the relative rates of deuteriation and exchange are significantly affected.

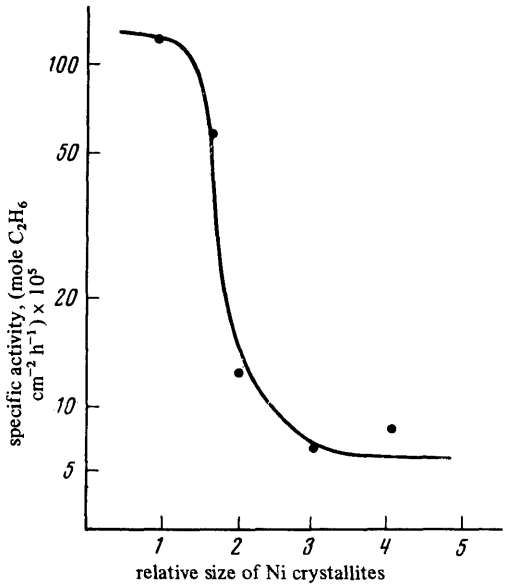

Figure 12. Specific activity of nickel in the hydrogenolysis of ethane at 267° against relative crystallite size. The size of the crystallites in the sample reduced at 370° is taken as unity (Ref. 85).

Table 20. Effect of crystallite size on the specific activity of nickel towards the hydrogenolysis of ethane (Ref. 86).

Ni content, wt.%	Carrier	Crystallite size, A	Specific activity, mole h^{-1} m^{-2} Ni
1	Silica gel	12	11
10	Silica gel	24	500
10	Al_2O_3	23	260
1	SiO_2 — Al_2O_3	26	0.08
10	SiO_2 — Al_2O_3	29	9.5

IV. DEPENDENCE OF THE SPECIFIC ACTIVITY OF CATALYSTS ON THE METHOD OF PREPARATION

Platinum and palladium. Schnabel and coworkers [88] studied the effect of the heat-treatment temperature of an activated charcoal on the specific activity of platinum (deposited on the charcoal) towards the dehydrogenation of cyclohexane, the C_5-dehydrocyclisation of iso-octane, and the hydrogenation of benzene. As the temperature was raised from 100 to 1070°, the specific activity of the platinum decreased by a factor of 2 for the first reaction and varied by not more than a factor of 4 for the second. The sample deposited on charcoal heat treated at 300° was inactive towards the hydrogenation of benzene. Samples prepared by depositing platinum on BAU charcoal heated at 1100° and treated by the Curtius method have a specific activity of 3.8×10^{-2} and 2.76×10^{-2} mole m^{-2} Pt respectively (i.e. practically identical). Another paper [89] from the same laboratory describes the changes in specific activity of platinum deposited on BAU charcoal heat treated at 300–2300° towards the C_5-dehydrocyclisation of iso-octane. It can be seen from Table 21 that the specific activity varies by less than a factor of 2.

Table 21. Specific activity of platinum on BAU activated charcoal towards the dehydrocyclisation of iso-octane (Ref. 89).

Carrier heat-treatment temperature, °C	300	1400	2000	2300	2800	1000 vacuum
Specific activity of Pt at 310° (mmole m^{-2} Pt h^{-1}) × 10^2	4.7	4.0	6.3	7.6	9.3	5.7

The specific activity of Pt and Pd catalysts prepared by different methods has been found [90,91] to be approximately constant also in respect of the hydrogenation of benzene.

Nickel. Tetenyi and coworkers [92] have studied the influence of method of preparation on the dispersion and specific activity of nickel black towards the dehydrogenation of cyclohexane and the decomposition of isopropanol and t-butanol. They were unable to establish any definite correlation between the activity and the dispersion of the nickel crystallites, the specific activity increasing more than 30-fold for relatively small changes in crystallite size. The conclusion from this work was that the specific activity depends on the method of preparation of the catalysts.

Crawford and coworkers [93], who studied the effect of sintering temperature on the specific activity of nickel black towards the hydrogenation of ethylene, disagree with this conclusion. They found that the specific activity varies only from 8.9 to 1.1 min^{-1} over a range of sintering temperatures between 25 and 400°, and they conclude that the loss of activity could be due to poisoning of the small catalyst surface by impurities evolved from the apparatus.

Catalysts prepared by reduction of NiO obtained by thermal decomposition of the hydroxide, basic carbonate, and acetate, and also by reduction of various mixtures of NiO, SiO_2, Al_2O_3, and Cr_2O_3 have been examined in the writer's laboratory [28]. Their catalytic activity towards the hydrogenation of benzene was found to be directly proportional to the surface area of metallic nickel and independent of the starting materials and of the method of preparation (Fig. 1).

Sinfelt and coworkers [94] studied the activity of nickel catalysts on silica gel towards the hydrogenolysis of ethane in a flow system. By varying the preparative conditions they were unable to vary the surface area by a factor of 3, but the specific activity varied only by a factor of 1.5.

Shephard [95] has described a detailed study of the effect of washing, and of heat treatment at 340–1160°, on the specific activity of an industrial nickel–alumina catalyst for the hydrogenolysis of propane. The catalytic activity was measured in a flow system. With the exception of one

sample, the catalytic activity before the leaching treatment was found to be proportional to the surface area of nickel. After being leached the catalysts contained a small amount of sodium, and their activity was somewhat higher. However, it is pointed out that these results could be due to insufficient precision in the measurement of surface area by hydrogen adsorption.

The specific activity of the nickel in nickel–chromia and nickel–magnesia catalysts for the hydrogenation of CO and CO_2 has been found to be independent of the temperature of heat treatment [96,97].

Vasserberg and coworkers [98] studied the effect of the preparation on the activity of nickel catalysts for the hydrogenation of CO_2. The catalysts were prepared by gas-phase deposition of carbonyl nickel on Al_2O_3 (series I) and by impregnation with a solution of $Ni(NO_3)_2$ (series II); three samples of industrial catalysts were also examined. Surface areas were measured by O_2 chemisorption. The activity was measured in a vacuum system with circulation, and characterised by the first-order rate constant of the reaction. It was found that samples of series I (containing less than 0.75% Ni) and of series II (containing 1.5% Ni or less) do not adsorb significant amounts of O_2 and have negligible catalytic activity. In samples with a higher nickel content the specific activity varies between 5.3 and 25.6×10^{-3} min^{-1} m^{-2} Ni.

Iron. Samchenko and coworkers [99,100] studied the effect of preparative conditions on the activity of doubly promoted iron catalysts in the synthesis of ammonia. The catalysts were characterised both in terms of total surface area and in terms of fractional occupancy of the surface by metallic iron, alkali, and aluminium oxide. The rate constants calculated for a unit area of alkali and Al_2O_3 were very variable, but the specific activity of the free iron surface was practically constant for all the samples, irrespectively of composition.

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The experimental work discussed in this review justifies the following statements: 1) in spite of the widely held view that the specific activity of catalysts should be a function of dispersion, method of preparation, etc., in the vast majority of cases the specific activity is found to be approximately constant; 2) contradictory results are reported by different workers: some workers find a constant specific activity whilst others, working on the same system, find large changes in specific activity under the influence of various factors. The constancy or otherwise of the specific activity is unrelated to the nature of the catalyst or to the type of reaction under study. In this Section we shall attempt to analyse the possible causes of these discrepancies, and to clarify as far as possible the validity of "Boreskov's rule" [55], which predicts an approximately constant specific activity.

The discrepancy between the results of different workers may be due to the following causes: 1) inadequacy of the experimental procedures used to determine the surface area of metal on the carrier, and also incorrect characterisation of the catalytic activity; 2) neglect of heat and matter transport processes; 3) influence of uncontrolled impurities in the catalyst and in the reaction mixture; 4) blocking of the surface by reaction products, and 5) measurements of the activity before the catalyst surface has reached a steady state in the reaction mixture.

In order to measure the specific activity correctly, the following conditions must be satisfied: a) the catalytic surface area (in this case, the area of metal on the carrier) must be measured correctly, and b) the catalytic activity must be correctly characterised. The surface area of metals on carriers is usually measured [101,102] under conditions when gas adsorption occurs only on the metal. The shortcoming of this method is the possible dependence of the adsorption capacity per unit area of the metal upon the dispersion. For example, the H/Pt or O/Pt ratio can vary from 1 to 2 when the particle size of Pt on Al_2O_3 is varied [103,104]. Similar effects have been observed on nickel. Hence, even if the true specific activity is strictly constant it is possible for the apparent specific activity to vary by a factor of 2 unless due allowance is made for changes in the gas/metal ratio.

There is still no generally accepted method of measuring the activity of catalysts. The most satisfactory method [18,19] appears to be to characterise the activity in terms of the rate constant. If the kinetic equation is not known, the activity of the catalyst can be characterised by the reaction rate at a given extent of reaction. Consistent results are obtained if the extent of reaction is small, the kinetic order of the reaction is nearly zero, and the system is not allowed to approach equilibrium. On the other hand, serious discrepancies can result if the extent of reaction is large enough to bring the system near equilibrium. The changes in specific activity reported by Larsen and coworkers [69] are probably due to this effect.

The effect of diffusion on catalytic reactions has been investigated by Boreskov [105–107], Slin'ko [108–110], and their coworkers. Diffusional limitations can have a very marked effect on the observed reaction rate. Thus, on varying the size of Al_2O_3 granules from 0.10–0.15 to 2–3 mm the specific activity of a given catalyst towards the decomposition of ethanol decreases by more than an order of magnitude as a result of diffusional control [111]. The extent of diffusional control depends on the porosity of the catalyst structure: the smaller the typical pore radius, and the larger the grain size, the lower will be the temperature at which rate limitation by the diffusion of reactants will set in [112]. If the experimental catalysts have different pore structures, and the measurements are not made under activation-limited conditions, the observed activities can be in error through differences in the amount of diffusional limitation. Furthermore, the imposition of diffusional limitation influences the selectivity of the catalyst in the direction of smaller yields of intermediates and greater yields of final products [113]. Hence, one of the most important prerequisites to ensure reliable results is the adoption of activation-limited conditions. Unfortunately, only a minority of authors specifies whether their results were obtained under activational or diffusional control. Very probably, some of the faster reactions studied on relatively large-grained catalysts were taking place in the diffusion-limited region. This effect could explain the reported dependence [92] of catalytic activity on crystallite size, since that investigation of a very active catalyst (nickel black) was carried out without the necessary precautions.

Impurities, often uncontrolled, can contaminate the catalyst both at the preparation stage and during the investigation. The reaction can be inhibited or accelerated by impurities. Thus, small amounts of alkali metals are known to lower the activity of oxides towards reactions involving an acidic mechanism [114,115], and traces of Al_2O_3 (less than 0.1%) can increase very substantially the activity of silica gel [116,117]. Similar effects have been reported [118,119] for metallic catalysts. Dorling and coworkers [72] have shown that the large changes in the

specific activity of platinum towards the hydrogenation of ethylene brought about by changes in preparative conditions are due to traces of HCl, which is sorbed by the catalyst and has a promoting effect on the reaction. Higher heat-treatment temperatures decrease the surface area of platinum and at the same time remove the HCl, thus lowering the specific activity.

Changes in catalytic activity associated with the take-up of impurities from the reaction medium are due to the formation of surface compounds between the impurity and the catalyst. The mechanism of the poisoning effect, and its reversibility, are determined by the stability of this compound under the experimental conditions. If the compound is not very stable it can be dissociated by lowering the partial pressure of the impurity or raising the temperature, and the activity of the catalyst can be restored to its initial value [120]. If, on the other hand, a very stable surface compound is formed by adsorption, the poisoning effect is irreversible [120-122].

Quite small concentrations of impurities are usually sufficient to produce significant poisoning effects. For example, Lyubarskii found [26] that a sulphur concentration of 10 parts per million (p.p.m.) in benzene is sufficient to cause appreciable poisoning of a nickel–chromia catalyst. In another investigation [123], 5 p.p.m. of water were found to deactivate small quantities of catalyst completely towards the polymerisation of ethylene: to obtain a measurable reaction rate the amount of catalyst in the reactor had to be kept above some "threshold" level. A similar effect has been reported by Poltorak and coworkers [124] for the decomposition of H_2O_2.

The poisoning effect of impurities will be stronger, of course, the higher the impurity concentration and the smaller the surface area of the active component of the catalyst. This is the most likely explanation of the large differences in specific activity obtained from studies in different laboratories of the effect of dispersion and of the temperature of heat treatment. Thus, Dorling and Moss [68] observed an approximately constant specific activity with increasing heat-treatment temperature until the surface area of Pt had fallen to 0.2 $m^2 g^{-1}$, when the catalyst suddenly became inactive. Similarly, Crawford and coworkers [93] found that the specific activity of their nickel films fell by a factor of 3 when the annealing temperature was raised from 300 to 400°. It is quite possible, also, that the deactivation of nickel catalysts containing small amounts of nickel reported by Dergachev and coworkers [98] was due to poisoning by traces of mercury (present in the vacuum system as a manometric fluid).

The opposite effect, activation of the catalyst by impurities in the reacting system, is far less commonly observed [72].

It follows from these considerations that a correct judgement of the constancy or otherwise of the specific activity can be made only in the knowledge of the impurity content of the reacting system and of the type of interaction to be expected between the impurity and the catalyst.

In addition to the impurities introduced with the reactants, any relatively involatile reaction products retained on the catalyst surface can affect the reaction rate. Catalyst poisoning by "fragments" of organic molecules has been observed in many reactions, including simple reactions (like the hydrogenation of ethylene [72,126]) as well as reactions involving the decomposition of large organic molecules [125].

Carbonisation of the catalyst can affect the selectivity as well as the rate of the reaction. Thus, Panchenkov and coworkers [127] found that the selectivity of an industrial alumina–silica catalyst for the cracking of n-decane changes very significantly with increasing reaction time (and hence extent of carbonisation of the catalyst): the yield of intermediate products (olefins) goes through a maximum, and the yield of the final products increases continuously.

We may conclude from these observations that time-variations in the activity of the catalyst may be responsible for some of the erroneous results obtained in studies of the influence of various factors on the specific activity. McKee's results [78] for the cracking of propane on platinum black were very probably vitiated by the non-stationary activity of the catalyst.

Changes in catalytic activity due to changes in catalyst composition brought about by interactions with the reacting medium are less clearly recognised, but nonetheless very common. According to Boreskov [128], these interactions can lead to: 1) deep-seated changes in chemical composition, accompanied by phase transitions of the active component; 2) changes in chemical composition without phase transitions; 3) compositional changes in the surface layer of the catalyst. All these changes are accompanied by more or less pronounced changes in specific activity. A good example of this effect is Boreskov and Matveev's observation [129] of a 500-fold increase in the specific activity of zinc oxide due to partial reduction of the catalyst during the decomposition of methanol: a phase of metallic zinc is not formed, but the stoichiometric ratio of oxygen to zinc in the oxide phase is lowered by the reducing action of the medium. A similar effect takes place during the reaction between H_2 and O_2 on platinum [130]. Boreskov also showed that the interaction between the catalyst and the reacting system can produce changes in the kinetics of the reaction as well as in the specific activity of the catalyst [131].

The steady-state composition (and hence activity) of the catalyst depends on the composition of the reacting system and on temperature: sufficient time must be allowed for the catalyst to reach a steady state.

Different workers, investigating similar (or even identical) catalysts and reactions by flow and by pulsed methods, usually find that the specific activity is constant if they are using the flow method and variable if they are using pulsed methods. It seems likely that in the pulsed regime [36-38,85,86] the surface layer cannot reach steady state, and the observed specific activity is seriously in error. We may suggest that the large differences in specific activity observed in pulsed measurements [36-38,85,86] are not due to the "difficulty" of the reaction, or to the "need" for a special surface topography [71], since other workers [33,35,70,74,75] found no evidence of this type of specificity. The most likely reason for the discrepancy is the use of a pulsed method to measure the activity, since it is difficult to believe that steady state can have been achieved in the short time (3–5 min) allowed for each experiment.

Thus, this review of the published work leads us to conclude that in most cases the specific activity is found to be constant if the correct experimental procedure has been used. Large changes in dispersion, and in the method of preparation of the catalyst, yield only a 3-fold change in specific activity. This relative constancy may be due to interaction between the catalyst surface and the reaction medium, which converts the initial surface structure into a final state independent of the previous history of the catalyst. Lastly, we cannot exclude the possibility of genuine differences in specific activity arising from the

retention of a non-steady-state structure in low-temperature reactions, but we have not found any experimental evidence of this effect in the published literature. Significant differences in specific activity are not encountered under the normal conditions of the majority of industrial catalytic processes.

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The Rate of Extraction Under Kinetic Conditions (Reaction in the Bulk Phase)

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Under kinetic conditions the rate of extraction depends on the rate of one or two slow reactions in the aqueous phase with the ion A^- or the molecule HA and also on the rate of reaction in the aqueous phase not involving the extractant. This has been examined for the extraction of trace amounts of bivalent and tervalent elements from aqueous solutions of their salts by solutions of an acid HA in organic solvents. The rate of extraction varies in a complex manner both with the rate constants for the corresponding reactions and with the stability constants of the complex ions formed; for this reason, studies on the mechanism of the reactions determining the rate of extraction in which no account was taken of complex formation in general give erroneous results. The possibility of using the proposed methods to determine the mechanism of the extraction of macroamounts of a univalent element has been demonstrated.
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I. INTRODUCTION

The study of the rate of extraction has significant practical interest, since the efficiency or size of extraction apparatus depends on the rate. The rate of extraction is also of theoretical interest, since it makes it possible to establish the mechanism of extraction, which cannot be done by studying extraction equilibria alone.

The extraction of inorganic compounds is usually accompanied by chemical processes: the formation of salts in extraction by acids and amines and of solvates in extraction by neutral extractants[1]. Apart from the reactions with extractants, other reactions may occur, for example complex formation and hydrolysis in the aqueous phase, which determine the rate of extraction. We refer to such processes not involving the extractant as "side" reactions[2]. There is no doubt that the slow shift of equilibrium in hydrolysis accounts for the time variation of the partition coefficients in the extraction of zirconium from nitric acid solutions by solutions of dicresylphosphoric acid in organic solvents[3].

Since the reactions can occur both in the bulk phases and at the interface, heterophase and heterogeneous reactions are distinguished[4].

The wide-scale and increasing application of extraction in technology increases interest in the question of the rate of extraction, which has been noted, for example, in a review published in 1964.[5] The number of studies on this topic has now greatly increased. However, in most of the published work the authors confine themselves to characterising the dependence of the degree of extraction or the partition coefficient on time without establishing the mechanism of the process determining the rate of extraction.

Extraction is always associated with the transfer of a substance from one phase to another (mass transfer) and therefore its rate can be determined by the rate of the reaction occurring, the rate of mass transfer, or the rates of both processes.

If the rate of extraction depends only on the rate of the chemical reaction, the process is said to occur under kinetic conditions, when the rate of extraction depends only on the rate of mass transfer, it is said to occur under diffusion-dependent conditions, and, when the rate of extraction depends on the rate of both the reaction and of mass transfer, the process is said to take place under mixed conditions.

Under kinetic conditions, the rate of mass transfer is so high that at any instant an equilibrium distribution between the phases of the compound passing from one phase to the other is virtually attained[6,7]; however, in extraction this is valid only for the given compound and not for all the compounds of the element being extracted which exist in the system investigated.

For example, when in the extraction of iron from aqueous solutions of inorganic acids by acetylacetone solutions FeA_3 (A is the acetylacetonate anion) is formed slowly in the aqueous phase and only this compound passes to the organic phase, then, under kinetic conditions, equilibrium in its distribution between the phases is established very rapidly ("instantaneously"), but a long time is needed to establish the equilibrium in the determination of analytical concentrations of iron.

Under diffusion-dependent conditions, the rates of the chemical reactions in the given system are so high that equilibrium between the compounds present is virtually attained in every phase but there is no equilibrium between the phases.

The rate of mass transfer depends on the rate of stirring of the phases, which determines the rate of transfer of material from the bulk of the phase to its surface and from the surface to the bulk and also on the area of the interface. Under kinetic conditions, the rate of mass transfer is so high that a change in the area of the interface and in the rate of stirring hardly disturbs the equilibrium distribution of the compound extracted and the change in its concentration is due solely to the rate of the chemical reaction; for this reason, the rate of extraction in

this region is independent of both the area of the interface and of the rate of stirring of the phases.

Under diffusion-dependent and mixed conditions, the rate of extraction depends on the rate of mass transfer and hence on the rate of stirring and the area of the interface. Only after having demonstrated that this type of dependence exists can one assert that the process takes place under one of the above conditions.

However, if the extraction is accompanied by a reaction at the interface, then under kinetic conditions the rate of extraction is independent of the rate of stirring for a constant area of the interface but varies with the area for a constant rate of stirring. This is in fact why in the determination of the conditions under which the process takes place it is necessary to determine the dependence of the rate both on the rate of stirring for a constant area of the interface and on the area of the interface for a constant rate of stirring.

Under mixed conditions as well as under diffusion-dependent conditions, the rate of extraction varies with the rate of stirring and with the area of the interface, which makes it difficult to solve the problem of the process conditions, but, as will be shown below, there are methods whereby one can deduce whether one process (diffusion-dependent conditions) or two processes with comparable rates take place.

With increased rate of mixing of the phases, there is usually an increase of the degree of comminution and hence of the area of the interface and therefore the absence of a dependence of the rate of extraction on the rate of stirring is frequently regarded as evidence that the process occurs under kinetic conditions. However, it has been noted in the literature that a constant rate of dissolution of a solid can be maintained by increasing the rate of rotation of the stirrer[8].

Since only the absence of a dependence of the rate of extraction both on the rate of stirring and on the area of the interface is convincing evidence for a transition of the process to kinetic conditions with the reaction in the bulk of one or both phases, in order to establish the extraction mechanism it is necessary to determine at least the relative surface areas of the phases. A number of methods have been proposed for this, among which the most convenient for extraction (in the case of dispersed phases) are the light scattering and photographic methods. The methods have been described and examples of their applications in studies on the rate of mass transfer have been given, for example, in Refs. 9–18.

When light passes through an emulsion, the specific surface S/V (S is the area of the emulsion and V its volume) is determined from the equation

$$\frac{I_0}{I} = 1 + \beta \frac{S}{V} \quad , \qquad (1)$$

where I_0 is the intensity of the light which has passed through the continuous phase (without emulsion), I the intensity of the light which has passed through the emulsion, and β a coefficient which depends on the refractive indices of the phases. This equation makes it possible to find the ratio of the surface areas of the emulsion in two experiments with different rates of stirring without knowing β and hence one can solve the problem of whether or not the change in the surface area affects the rate of the process. We may note that, in order to determine the degree of light scattering, one can employ a nephelometer using its cell as an extraction vessel[19].

The dimensions of drops and hence their surface areas can be determined by the sedimentation method[20], but the method suffers from the disadvantage that the process has to be interrupted and the surface areas must be determined in independent experiments.

Under diffusion-dependent conditions in a system with constant partition and mass transfer coefficients, the change in the concentration in the receiving phase over a time t, when the concentration is initially zero, is given by the equation

$$\ln \frac{C_{2p} - C_2}{C_2} = -\frac{K_2(q+1)}{V} S t \quad , \qquad (2)$$

where V is the phase volume ($V_1 = V_2$), S the area of the interface, $q = C_{2p}/C_{1p}$ the partition coefficient, and K_2 the mass transfer coefficient referred to the receiving phase.

Then, in the first experiment (area S_1) we have $\ln 2 = K_2(q+1)S_1 t/V$ after a time interval such that, for example, $C_2 = 0.5C_{2p}$, where C_{2p} is the equilibrium concentration in the given system. In another experiment (area S_2) the change in concentration during the same time interval can be found from the equation $\ln (C_{2p} - C_2)/C_{2p} = -\ln (2S_1/S_2)$. If $S_1/S_2 = 2$, then

$$\ln \frac{C_{2p} - C_2}{C_{2p}} = -\ln 4 \text{ and } C_2 = 0.75 C_{2p} \quad .$$

Thus, for constant mass-transfer and partition coefficients, the change in area by a factor of two leads to a change in concentration in the receiving phase (during the same period) by a factor of 1.5, which can be readily detected. If the increase in area has occurred as a result of an increase of the rate of stirring, then, under diffusion-dependent conditions, there is an increase of the mass-transfer coefficient and the change in concentration is even greater.

In the study of the rate of mass transfer one frequently employs apparatus with a constant area of the interface, for example that proposed by Lewis[21]. In such apparatus the phases are separated by a horizontal partition with an annular aperture in which the level of the interface is established and each phase is agitated by its own stirrer. However, in this system the thickness of the ring has some importance, since the conditions governing the stirring of the liquids in the gap may differ from those in the bulk of the phases, which may affect the process conditions.

In the study of the rate of mass transfer one frequently employs cylindrical vessels with vertical partitions. Their purpose is to prevent the breakdown of the surface during the stirring of the phases, i.e. to prevent the formation of waves[22–24].

However, apparatus with a constant area of the interface has a small specific surface and hence the rate of mass transfer is also low, as a result of which many processes which occur under kinetic conditions when the phases are dispersed can occur under mixed or diffusion-dependent conditions in apparatus with a constant area of the interface[19].

The employment of apparatus of the Lewis type with a variable width of the annular aperture can be useful in testing the hypothesis that the process occurs under kinetic conditions with a surface reaction, since in such apparatus one can vary the area of the interface keeping constant the rate of stirring or one can vary the rate of stirring keeping constant the area of the interface.

In studies on diffusion accompanied by a chemical reaction and on mass transfer with chemical reaction[25,26] it has been shown that, for a fairly high rate of reaction (for this reason it takes place in the diffusion film), the rate of the process under the conditions of a constant area

of the interface is independent of the rate of stirring. Such conditions are referred to as fast reaction conditions[27]. They resemble the kinetic conditions with a surface reaction. An example of mass transfer with a rapid or surface reaction is the interaction of certain organic [sic!] formates and acetates with aqueous solutions of alkalis accompanied by the transfer of the acid to the aqueous phase and its neutralisation. These reactions are used to determine the dependence of the surface area of the emulsion on the rate of stirring and on the design of the stirrers[28-31]. They can be used to test the constancy of the area of the interface when the rate of stirring is varied in apparatus of the Lewis type and particularly in cylindrical vessels with partitions.

If it has been shown that at a certain rate of stirring, the process proceeds under kinetic conditions, then, by changing the rate of stirring, it is impossible to increase the rate of extraction, since the latter is determined by the rate of the chemical reaction. In this case the rate of extraction can be increased only by increasing the rate of reaction (by increasing the concentration or temperature). Under diffusion-dependent or mixed conditions, the rate of extraction can be raised by increasing the area of the interface and the rate of stirring as long as the process does not pass to kinetic conditions.

The extraction mechanism and the rate of the reactions taking place can be determined most simply under kinetic conditions. As will be shown below, even in this case the problem is more difficult than the determination of the mechanism and of the rates of reactions in a homogeneous system, but the difficulty becomes even more marked under mixed conditions.

An important complication in the study of extraction kinetics is associated with the measurement of concentration when one of the phases is dispersed. The main method, in which the stirring of the phases is stopped and the latter are allowed to separate before removing the samples, distorts the results, since the hydrodynamic conditions and the area of the interface change during this period. This type of method can be used only for fairly slow processes. The effect of the interruptions on the results of the measurement of the rate can be tested by carrying out two experiments under the same conditions. In one experiment samples are removed twice or more frequently and in the other only one sample is removed after stirring for a period equal in duration to the overall time of stirring in the first experiment. Comparison of the results will then reveal the effect of the interruption of stirring.

A method has been proposed[14] for the measurement of concentration in a continuous aqueous phase in the presence of an emulsion on the basis of conductivity. The application of this method is restricted to systems with one electrolyte in the aqueous phase and does not allow the employment of trace amounts of radioactive elements, the use of which frequently simplifies the interpretation of the experimental data, because the concentrations of the other components, reacting with the given element, can be regarded as constant. It is much easier to measure the concentration in apparatus with a constant level of the interface. In this case one can measure the conductivity in the aqueous and sometimes in the organic phases[32,33], the radioactivity of the phase can be determined (for example on the basis of γ-radiation) when radioactive isotopes are employed[34-37], and removal of samples for analysis is simplified (samples can be removed without stopping the stirrer).

A significant defect of many studies on extraction kinetics is that the authors did not establish the conditions under which the process occurred, introducing thereby an uncertainty into their results.

In a number of studies[38-46] the authors assumed that the extraction proceeds under kinetic conditions (with the reaction in the aqueous phase) and described the rate of extraction by an equation of the type

$$-\frac{d[M]_w}{dt} = \varkappa [M]^m \ [A]^n , \qquad (3)$$

where [M] is the analytical concentration of the element being extracted, [A] the concentration of the extractant anions in the aqueous phase when the extractant is an acid HA, and κ the rate constant for the reaction determining the rate of extraction. Under these conditions, one frequently employs trace amounts of the compound (element) being extracted and for this reason [A] in a given experiment at constant pH is itself constant. Then Eqn. (3) can be put in the form

$$-\frac{d[M]_w}{dt} = \varkappa' [M]_w^m , \qquad (4a)$$

where $\kappa' = \kappa[A]^n$ and $[A] = K_{HA}[HA]_0/q_{HA}[H^+]$, $[HA]_0$ being the concentration of the acid HA in the organic phase, q_{HA} is the partition coefficient, and K_{HA} the dissociation constant. If $m = 1$, integration of Eqn. (4a) yields

$$\ln \frac{[M]_w}{[M]_w^0} = -\varkappa' t , \qquad (4b)$$

where $[M]_w^0$ is the initial concentration of M in the aqueous phase. If $m > 1$, then integration gives

$$\frac{1}{[M]_w^{m-1}} - \frac{1}{([M]_w^0)^{m-1}} = (m-1)\ \varkappa' t . \qquad (4c)$$

These equations make it possible to find m and κ' for the given value of [A] by varying t. Assuming that m is constant and having determined κ' for different concentrations of the extractant [A], it is possible to find κ and n. For example, it was established in this way that in the extraction of zinc from aqueous solutions of its salt by dithizone solutions in organic solvents, $m = 1$ and $n = 1$ and therefore the authors[38] suggest that the rate of extraction is determined by the rate of the reaction $Zn^{2+} + A^- \rightleftharpoons ZnA^+$, while the reaction $ZnA^+ + A^- \rightleftharpoons ZnA_2$ and mass transfer are rapid. The extraction mechanisms have been determined similarly also in other investigations[39-46]. However Eqns. (4a), (4b), and (4c) do not reflect the essential property of extraction—its reversibility. It follows from these equations that, when t tends to infinity, $[M]_w$ tends to zero and the plot of $\ln\{[M]_w/[M]_0\}$ as a function of t will be linear up to infinity, although it is evident that, under the specified conditions, $\ln\{[M]_w/[M]_w^0\}$ will approach a limit equal to $\ln\{[M]_{w,e}/[M]_w^0\}$, where $[M]_{w,e}$ is the equilibrium concentration.

In addition, the equations quoted above include the analytical concentration of the element M in the aqueous phase, although the latter contains its various species, namely complex ions and molecules. Thus in the example quoted the ions and the species ZnA^+ and ZnA_2 exist in the aqueous phase, which follows from the hypothesis, adopted in the study quoted, that the processes take place in steps. In the extraction of acids and salts from solutions, complexes with the corresponding ions are formed in the aqueous phase and for this reason the concentration of the cations of M or of any compounds involved in the reaction determining the rate of extraction can differ significantly from the analytical concentration of the element M. For example, in a study[47] of the rate of extraction of beryllium

by thenoyltrifluoroacetone (TTA) from a mixture of hydrochloric and perchloric acids (with a constant overall concentration) the equation for the rate of extraction was put in the form $-d[Be^{2+}]/dt = K^*[Be]^a[HA]_o^b[H^+]^c[ClO_4^-]^d$, where $[HA]_o$ is the concentration of TTA in the organic phase, $K^* = \kappa K_A/D$, K_A the dissociation constant of TTA, D its partition coefficient, and κ the reaction rate constant. The concentration of ClO_4^- ions has been included in the equation, since it has been established that the rate of extraction increases with increase in the concentration of perchloric acid (and with the corresponding decrease in hydrochloric acid concentration). To account for this dependence, the authors suggest that beryllium perchlorate passes to the organic phase where it is very rapidly converted into the thenoyltrifluoroacetonate and perchloric acid is also rapidly re-extracted. However, beryllium chloride complexes are formed in the aqueous solution (the authors quote the stability constants) and therefore the analytical concentration is not equal, for example, to the concentration of Be^{2+} ions and the rate equation must include the concentration of those beryllium cations or complex ions directly involved in the reaction determining the rate of extraction and not the analytical concentration of beryllium. In particular, when TTA reacts with Be^{2+} ions, the concentration of the latter must increase with increase of the concentration of perchloric acid, since the concentrations of chloride ions and beryllium chloride complexes then decrease.

It has been noted in the literature that complex formation can decrease the rate of extraction[40]†. In particular it has been shown[48] that, in the extraction of zinc by dithizone, the introduction of chloride ions into the aqueous phase reduces the rate of extraction and increases the rate of re-extraction. However, the introduction of certain substances to the aqueous phase sometimes increases the rate of extraction. For example, the extraction of iron by thenoyltrifluoroacetone is slow, but the introduction of ammonium thiocyanate into the aqueous phase increases its rate[49]. In the extraction of chromium by TTA or hydroxyquinoline, sodium acetate[50], ammonium fluoride, and other compounds[51-53] have a similar effect. These examples show that the rate of extraction is not determined by the analytical concentration of the element being extracted and the expression for the rate of extraction in terms of the latter constitutes only an empirical description of the process and does not yield information about the mechanism of extraction.

Finally, in the investigations quoted no account is taken of the fact that each phase is an open system and therefore a change in the concentrations of certain compounds is caused not only by a chemical reaction but also by the transfer of compounds from one phase to another. Problems associated with the rate of reactions in open systems have been considered in the literature[4,54], but usually for processes in flow-type apparatus of different kinds and not for extraction.

In this connection, the mechanism of extraction under kinetic conditions with complex formation in the aqueous phase has been examined in greater detail, in particular for complex formation involving the extractant or its ions. An acid HA was employed as the extractant and it was assumed for simplicity that complex anions involving A^- are not formed in the aqueous phase (this does not alter the general approach to the problem, but reduces the number of parameters introduced into the corresponding equations) and in the organic phase there are no solvates formed by the extractant with the salt being extracted. We shall restrict the treatment to reactions in the bulk of the aqueous phase and in the first place to the extraction of trace amounts of the corresponding substance; also we shall disregard the use of isotope exchange for this purpose, which has been briefly described already[55].

Some results of such analysis have already been published[56,57]; this review gives a systematic description of the problem and a number of possible mechanisms, which were not analysed previously, are discussed.

II. ONE SLOW REACTION WITH THE EXTRACTANT (AN ACID HA) IN THE AQUEOUS PHASE

We shall consider the determination of the rate of extraction under kinetic conditions in the case of one slow reaction of the metal being extracted, forming the ions M^{3+} in the aqueous phase, with the extractant (an acid HA) under conditions such that the rate of reaction is determined by the concentrations of the reactants (the activity coefficients are virtually unity). The molecules MA_3 formed in the aqueous phase pass to the organic phase. In the general case the flux of the molecules MA_3 from the aqueous to the organic phase is

$$j = K_w([MA_3]_w - [MA_3]_w^*) \quad , \qquad (5)$$

where $[MA_3]_w$ is the concentration of these molecules in the aqueous phase and $[MA_3]_w^*$ the concentration which must occur in this phase at a given instant to ensure its equilibrium with the organic phase. Then $[MA_3]_w^* = [MA_3]_o/q_{MA_3}$, where q_{MA_3} is the partition coefficient of the compound MA_3, $[MA_3]_o$ the concentration of MA_3 in the organic phase, and K_w the mass transfer coefficient referred to the aqueous phase‡. We believe that the mass-transfer coefficient of a specific compound as well as its partition coefficient are independent of phase composition (concentrations of the components) over a fairly wide concentration range; for this reason, the driving force of the mass-transfer process can be expressed in terms of the concentrations as $[MA_3]_w - [MA_3]_w^*$. This is confirmed by the determinations of a number of mass transfer coefficients for compounds which remain unchanged in extraction[58,59]. However, under kinetic conditions there is virtually an equilibrium between the phases with respect to the compound MA_3, so that the driving force of the process is extremely small, but the mass transfer coefficient is very high (in the limit the driving force is zero and the mass transfer coefficient is infinite). The flux is a finite quantity determined by the rate of reaction.

The necessity to determine the rate from the variation of the analytical concentration of the element extracted in one or both phases constitutes a difficulty in the employment of trace amounts of the element. In the extraction of macroamounts it is possible to determine the concentrations of individual compounds by physical methods, for example by spectrophotometry, NMR, etc., but we have been unable to find examples of such studies in relation to the rate of extraction. Moreover, when the concentrations of individual compounds cannot be determined in the

† The same investigation quotes a number of references to other publications where the effect of complex formation on the rate of extraction is also noted.

‡ Eqn. (5) is also used in the form $j = K_o\{[MA_3]_o^* - [MA_3]_o\}$, where $K_o = K_w/q_{MA_3}$ is the mass transfer coefficient referred to the organic phase.

extraction of macroamounts, the number of variables increases, which, as shown below, makes it difficult to interpret the experimental results.

We examined previously[56,57] the effect of the rate of complex formation on the rate of extraction of trace amounts of an element M^{3+} by an acid HA under kinetic conditions when the reactions occur in the aqueous phase and the rate of extraction is determined by the rate of one of three reactions:

$$M^{3+} + A^- \underset{\varkappa_2}{\overset{\varkappa_1}{\rightleftarrows}} MA^{2+} \quad , \tag{I}$$

$$MA^{2+} + A^- \underset{\varkappa_4}{\overset{\varkappa_3}{\rightleftarrows}} MA_2^+ \quad , \tag{II}$$

$$MA_2^+ + A^- \underset{\varkappa_6}{\overset{\varkappa_5}{\rightleftarrows}} MA_3 \quad . \tag{III}$$

The other two reactions and mass transfer are very rapid ("instantaneous"), so that they reach equilibrium at any instant. It is then assumed that the effect of the rate of mass transfer of the acid HA and of the rate of its dissociation is eliminated by the fact that the phases are equilibrated with respect to the macrocomponents, including the extractant, and the changes in their concentrations may be neglected when trace amounts of the element extracted are employed§.

The processes occurring in the system are described by the equations

$$-\frac{d[M^{3+}]}{dt} = \varkappa_1[M^{3+}][A^-] - \varkappa_2[MA^{2+}] \quad , \tag{6a}$$

$$\frac{d[MA^{2+}]}{dt} = \varkappa_1[M^{3+}][A^-] - \varkappa_2[MA^{2+}] - \varkappa_3[MA^{2+}][A^-] + \varkappa_4[MA_2^+] \quad , \tag{6b}$$

$$\frac{d[MA_2^+]}{dt} = \varkappa_3[MA^{2+}][A^-] - \varkappa_4[MA_2^+] - \varkappa_5[MA_2^+][A^-] + \varkappa_6[MA_3]_w \quad , \tag{6c}$$

$$\frac{d[MA_3]_w}{dt} = \varkappa_5[MA_2^+][A^-] - \varkappa_6[MA_3]_w - \frac{V_o}{V_w}\cdot\frac{d[MA_3]_w}{dt} \quad , \tag{6d}$$

where the last term on the right-hand side corresponds to the rapid transfer of part of MA_3 to the organic phase. We have

$$\frac{d[MA_3]_o}{dt} = q_{MA_3}\cdot\frac{d[MA_3]_w}{dt} \quad , \tag{7}$$

where V_W and V_O are the volumes of the aqueous and organic phases.

Since only one reaction is slow and the others are rapid, equilibrium is established in the latter. For example, when reaction (I) is slow, there is at any instant equilibrium in the formation of MA_2^+ from MA^{2+} and A^- and of MA_3 from MA_2^+ and A^-. This makes it possible on the basis of Eqns. (6) and (7) to express the time dependence of the analytical concentration of M in one of the phases (for example the aqueous phase) in terms of the rate constant for the reaction which determines the rate of the process, the equilibrium constants for the complex formation reaction and the dissociation of the acid, and also the partition coefficients of the acid and MA_3.

Several different methods for the investigation of extraction kinetics are possible. For example, an element M can be introduced in microamounts into the aqueous phase of specified composition in equilibrium with the organic phase. In this case the aqueous phase does not initially contain the compound extracted (MA_3).

§ For this reason the concentration of the anions A^- is $[A^-] = K_{HA}[HA]_o/q_{HA}[H^+]$, where K_{HA} is the dissociation constant of the acid, q_{HA} its partition coefficient, and $[H^+]$ the concentration of hydrogen ions (constant in each experiment).

If, for example, reaction (II) is slow and reactions (I) and (III) as well as the partition of MA_3 between the phases are rapid, then at any instant

$$[MA^{2+}] = K_1[M^{3+}][A^-] \quad , \tag{8a}$$

$$[MA_3]_w = K_3''[MA_2^+][A^-] \quad , \tag{8b}$$

$$[MA_3]_o = q_{MA_3}[MA_3]_w = q_{MA_3}[MA_2^+][A^-]\quad K_3'' \quad , \tag{8c}$$

where K_1 and K_3'' are the stability constants of the MA^{2+} ions and MA_3 molecules. Having determined $d[MA_3]_w/dt$ and $d[MA_3]_o/dt$ from these equations, we find

$$\left(1 + K_3''[A^-] + \frac{V_o}{V_w}q_{MA_3}K_3''[A^-]\right)\frac{d[MA_2^+]}{dt} = \varkappa_3[MA^{2+}][A^-] - \varkappa_4[MA_2^+] \quad , \tag{9}$$

since in the extraction of trace amounts of the element $[A^-]$ is constant.

The analytical concentration in the aqueous phase at any instant is

$$C_w = [M^{3+}] + [MA^{2+}] + [MA_2^+] + [MA_3]_w = \frac{[MA^{2+}]}{K_1[A^-]} + [MA_2^+] + [MA^{2+}] + K_3''[MA_2^+][A^-] \quad . \tag{10}$$

This equation makes it possible to express the concentration $[MA^{2+}]$ in terms of C_W and $[MA_2^+]$ and since

$$[MA_2^+] = \frac{[MA_3]_w}{K_3''[A^-]} = \frac{[MA_3]_o}{q_{MA_3}K_3''[A^-]} = \frac{V_w(C_w^0 - C_w)}{V_o q_{MA_3}\cdot K_3''[A^-]} \quad ,$$

where C_W^0 is the initial concentration of M^{3+} in the aqueous phase, it follows that, having determined $d[MA_2^+]$ from this equation and having substituted $[MA_2^+]$ and $d[MA_2^+]/dt$ in Eqn. (9), we find after appropriate rearrangements

$$-\frac{dC_w}{dt} = a_2C_w - b_2C_b^0 \quad , \tag{11}$$

where

$$a_2 = \frac{\varkappa_3[A^-]\left\{\frac{V_o}{V_w}K_3''[A^-]\,q_{MA_3} + K_3''[A^-] + 1 + \frac{\varkappa_4}{\varkappa_3[A^-]}\left(1 + \frac{1}{K_1\cdot[A^-]}\right)\right\}}{\left(1 + \frac{1}{K_1[A^-]}\right)\left(1 + K_3''[A^-] + \frac{V_o}{V_w}q_{MA_3}\,K_3''[A^-]\right)} \quad . \tag{12a}$$

since $\varkappa_4/\varkappa_3[A^-] = [MA^{2+}]_e/[MA_2^+]_e$, where the subscripts "e" denotes equilibrium concentrations, it follows that, having substituted this value in Eqn. (12a), having multiplied the numerator and denominator by $[MA_2^+]$, and having used Eqns. (8a), (8b), and (8c), we obtain

$$a_2 = \frac{\varkappa_3[A^-](V_o[MA_3]_{o,e} + V_w[MA_3]_{w,e} + V_w[MA_2^+]_e + V_w[MA^{2+}]_e + V_w[M^{3+}]_e}{\left(1 + \frac{1}{K_1[A]}\right)(V_w[MA_2^+]_e + V_w[MA_3]_{w,e} + V_o[MA_3]_{o,e})} = \frac{\varkappa_3K_1[A^-]^2\,C_w^0}{(K_1[A^-] + 1)\,(C_w^0 - [MA^{2+}]_e - [M^{3+}]_e)} \quad . \tag{12b}$$

The quantity b can be found similarly, but it is determined more simply from the condition that at equilibrium $dC_W/dt = 0$, so that

$$b_2 = \frac{a_2\ C_{w,e}}{C_w^0} \quad . \tag{13}$$

A similar derivation of the equations was made earlier[56,57] for a system with equal phase volumes. The same equation for the coefficient a was obtained when reaction (II) was slow. The rate of extraction is also described by Eqn. (11) when reaction (I) or (III) is slow, but the corresponding coefficients are

$$a_1 = \frac{\varkappa_1\ [A^-]\ C_w^0}{C_w^0 - [M^{3+}]_e} \tag{14}$$

for reaction (I) and

$$a_3 = \frac{\varkappa_3 K_2' K_2 [A^-]^3 C_w^0}{(K_2' + K_2[A^-] + K_2 K_2' [A^-]^2)(C_w^0 - [M^{3+}]_e - [MA^{2+}]_e - [MA_2^+]_e)} \quad (15)$$

for reaction (III).

In these equations

$$K_2 = \frac{[MA_2^+]}{[M^{3+}][A^-]}, \qquad K_2' = \frac{[MA_2^+]}{[MA^{2+}][A^-]} .$$

The volumes of the phases enter into equations in which the rate constant ratio has not been replaced by the ratio of the equilibrium concentrations [Eqn. (12a)]. In Eqns. (12b), (14), and (15) the change in phase volumes alters the equilibrium concentrations.

Integration of Eqn. (11) yields

$$\ln \frac{C_w - C_{w,e}}{C_w^0 - C_{w,e}} = -at , \quad (16)$$

where a is defined by one of the Eqns. (12b), (14), and (15) and $C_{w,e}$ is the analytical equilibrium concentration of M in the aqueous phase.

It follows from Eqn. (16) that, when $C_{w,e} \ll C_w$ and particularly when $C_{w,e} \ll C_w^0$, it is converted into Eqn. (4b) but the coefficient a is not equal to κ_1'. In particular, a more complex dependence of the rate of extraction on the anions A^- will be observed than would follow from the expression for κ'. For example, when the rate of extraction is determined by the rate of reaction (II), then a_2 will be proportional to $[A^-]^2$ only when $K_1[A^-] \ll 1$ and $\{[MA^{2+}]_e + [M^{3+}]_e\} \ll C_w^0$. If $K_1[A^-] \gg 1$ but the second of the above conditions holds, then a_2 will be proportional to $[A^-]$ and therefore one can reach the erroneous conclusion that the rate is determined by reaction (I).

It follows from Eqn. (11) that $-dC_w/dt = C_w - C_{w,e}$ and therefore in the general case the rate of extraction cannot be of first order with respect to C_w, must be of first order with respect to $C_w - C_{w,e}$, and the first order with respect to C_w, established in the studies quoted here and in others[60], will be observed only when $C_w \gg C_{w,e}$. The observed first order with respect to C_w can be explained by the fact that the authors of many investigations restricted their treatment to the linear part of the time variation of $\ln(C_w/C_w^0)$, which is insufficient to deduce the extraction mechanism.

If the rate of extraction is determined by the rate of the reaction

$$M^{3+} + 2A^- \underset{\varkappa_8}{\overset{\varkappa_7}{\rightleftarrows}} MA_2^+ ,$$

it is also described by Eqn. (16), but in this case

$$a' = \frac{\varkappa_7 [A^-]^3 C_w^0}{C_w^0 - [M^{3+}]_e} \quad (17)$$

and therefore, when $[M^{3+}] \ll C_w^0$, the same variation with the concentration of the anions A^- (derived from the acid HA) will be observed as for reaction (II) when $K_1[A^-] \ll 1$ [Eqn. (12b)].

Thus the observation that the reaction is of second order with respect to the extractant, in accordance with Eqns. (12b) and (17), as was done, for example, by McClellan and Freiser[41] and Bodnya and Alimarin[61], does not allow one to decide whether the slow reaction is the addition of a second ligand (a bimolecular reaction) or whether the metal ion combines immediately with two anions (a trimolecular reaction).

In those cases where the system contains a complex-forming agent X and the equilibria in the reactions $MX_i + X = MX_{i+1}$ are established very rapidly (they do not affect the rate of extraction) and there are no mixed complex ions or molecules MX_iA_j, the following expressions hold for reactions (I)–(III) when the phase volumes are equal:

$$a_1 = \frac{\varkappa_1 [A^-] C_w^0}{(1 + f_0)\{C_w^0 - [M^{3+}]_e (1 + f_0)\}} , \quad (18a)$$

$$a_2 = \frac{\varkappa_3 K_1 [A^-]^2 C_w^0}{(K_1[A^-] + f_0 + 1)\{C_w^0 - [M^{3+}]_e (1 + f_0) - [MA^{2+}]_e\}} , \quad (18b)$$

$$a_3 = \frac{\varkappa_3 K_2' K_2 [A^-]^3}{(K_2[A^-] + K_1[A^-] + f_0 + 1)\{C_w^0 - M^{3+}]_e (1 + f_0) - [MA^{2+}]_e - [MA_2^+]_w\}} , \quad (18c)$$

where $f_0 = \sum_1^i \beta_i [X]^i$ and $\beta_i = [MX_i]/[M][X]^i$ are the stability constants of the complexes MX_i.

In the extraction by an acid HA of a bivalent metal, with formation of MA^+ and MA_2 in the aqueous phase, the rate of extraction corresponding to the partition of the molecules MA_2 is also characterised by Eqn. (16). If the slow reaction is M + A = MA and the phase volumes are equal, then

$$a_1 = \frac{\varkappa_1 [A^-] C_w^0}{C_w^0 - [M^{3+}]_e} , \quad (19a)$$

On the other hand, if the slow reaction is MA + A = MA_2, then

$$a_2 = \frac{\varkappa_3 K_1 [A^-]^2 C_w^0}{(K_1[A^-] + 1)(C_w^0 - [MA^{2+}]_e - [M^{3+}]_e)} , \quad (19b)$$

where K_1 is the equilibrium constant for the reaction $M^{2+} + A^- = MA^+$. For a large partition coefficient, when $C_w^0 \gg C_{w,e}$ and $C_w^0 \ll [MA^+]_e + [M^{2+}]_e$ and especially $C_w^0 \gg [M^{2+}]_e$, the rate of extraction is in both cases described by the same equation $\ln(C_w/C_w^0) = -\kappa[A^-]$, where κ can be either κ_1 or κ_3, provided that the condition $K_1[A^-] \gg 1$ holds. Thus, in order to deduce the mechanism of the reaction determining the rate of extraction, it is necessary to know the composition of the compounds existing in each phase and also their stability constants. The knowledge of these constants is necessary also for the choice of conditions which allow one to distinguish the possible reactions. Thus, in the extraction of a bivalent metal under consideration, the determination of the nature of the reaction taking place requires a concentration of the anion A^- such that the condition $K_1[A^-] \ll 1$ hold but the concentration of the extractant greatly exceeds that of the element being extracted (to ensure the condition that only trace amounts of the latter are extracted). Such conditions in the extraction by an acid HA can be created by carrying out the extraction from a fairly acid solution, assuming that the concentration of the anions A^- is much higher than the analytical concentration of the element M or that the acid dissociates very rapidly.

Thus the conclusion[62] that extraction can serve as a method for the investigation of very rapid reactions is valid (a low concentration of the interacting components ensures a rate suitable for measurement), but the determination of the reaction mechanism from measurements of the rate of extraction is extremely difficult.

It follows from Eqn. (16) that, at a given concentration of HA in the case of a single slow reaction, the quantity $\ln[(C_w - C_{w,e})/(C_w^0 - C_{w,e})]$ is a linear function of time, as under diffusion-dependent conditions with constant partition and mass transfer coefficients. The difference between these processes is that a change in the rate of stirring and in the area of the interface does not alter the rate of extraction under kinetic conditions but does change it under diffusion-dependent or mixed conditions.

In the extraction of molybdenum in different valent states from a hydrochloric acid solution by solutions of oxine, acetylacetone, and other extractants in chloroform, the authors[63] assumed that it is possible to ignore the reversibility of the process and to characterise the rate of extraction by the degree reaction which they believe to be $F = q_t/q_p = 1 - e^{-\kappa_1' t}$, where $q_t = C_O/C_W$ is the ratio of the concentrations at any instant, q_p is the partition coefficient (the ratio of the equilibrium concentrations), and $\kappa_1' = \kappa_1[A^-]$, assuming that the rate of extraction is determined by the rate of formation of the ions MA^+. We believe that the degree of reaction must be characterised by the fraction of substance which has reacted relative to the overall amount which can react, for example by the quantity $F = C_O/C_{O,e} = (C_W^0 - C_W)/(C_W^0 - C_{W,e})$ (only then is the degree of reaction zero at the initial instant and unity at equilibrium). Indeed, it follows from Eqn. (16) that $F = 1 - e^{-at}$, but

$$F = \frac{C_o}{C_{o,e}} = \frac{q_t}{q_e} \cdot \frac{C_w}{C_{w,e}} \neq \frac{q_t}{q_e} \quad .$$

This can explain the authors' observation in a number of experiments of a discrepancy between the experimental results and the proposed equation.

In the study of the rate of extraction of trace amounts of the extractable compound the process can be achieved in another way: the phases must be equilibrated with the microcomponents, separated, and the aqueous phase must be brought into contact with the organic phase obtained in the same way but without the element to be extracted (extraction); the organic phase containing the extractable element is brought into contact with the aqueous phase without the compound (re-extraction). The same process can be carried out by equilibrating initially the phases without the extractable compound and separating them, after which, having introduced into the aqueous phase trace amounts of the element to be extracted without altering the composition of the phases with respect to the macrocomponents (a very small volume of the solution with the extractable element is employed), the phase is allowed to stand until equilibrium is reached, after which the phases are again brought into contact.

In contrast to the methods described previously, in this case all the compounds already exist in the aqueous phase at the instant of contact between the phases and are in equilibrium with the extractant. Therefore under kinetic conditions the quantity q_t will be non-zero at $t = 0$ and in the plot of its time variation will tend to a finite quantity when t tends to zero. A similar phenomenon was observed, for example, in a study[50] involving a "side" reaction in the course of the extraction of antimony from hydrochloric acid solutions by alcohols.

However, in certain investigations where the phases were initially equilibrated without the extractable element and the latter was then introduced into the aqueous phase[39,40], the authors state that the solution was adjusted to the required pH directly before extraction but they did not estimate the effect of the change in the hydrogen ion concentration on the partition coefficient of the extractant. When such an effect obtains, the concentration of the extractant can vary in the course of extraction, but this was disregarded in the experiments.

The introduction of the extractant, for example an acid HA, into the aqueous phase with subsequent extraction by the pure solvents constitutes a modification of the method described. Thus, it has been found[64] that in the extraction of indium by solutions of 1-(2-pyridylazo)-2-naphthol in chloroform, equilibrium is established in 45—50 min. When this extractant is added in the form of an alcoholic solution to the aqueous phase and the latter is then shaken with chloroform, a high initial degree of extraction is rapidly reached; however, it gradually diminishes and equilibrium is established in 30—35 min. In this case there is initially a partition of both the compound formed and of the extractant and the decrease of the concentration of the latter in the aqueous phase disturbs the equilibrium, which leads to the dissociation of the extractable compound in this phase and hence to its re-extraction from the organic phase. Such a process can be used to determine the rates of the reactions occurring, provided that it has been shown that kinetic conditions obtain.

In the case of extraction of a tervalent element by an acid HA in which the aqueous phase is equilibrated with the organic phase without the extractable element, the phases are separated, the extractable element is introduced into the aqueous phase, and the latter is allowed to stand until the attainment of equilibrium in it, the initial analytical concentration of the extractable element in the aqueous phase is

$$C_{w(init)} = [M^{3+}]_{int} + [MA^{2+}]_{int} + [MA_2^+]_{int} + [MA_3]_{int} \quad , \qquad (20)$$

where the subscript "init" shows that the concentrations refer to the initial aqueous solution in equilibrium with the organic phase used in the experiment with respect to the extractant (the acid HA).

As a result of the "instantaneous" distribution of the molecules MA_3 between the phases, in the initial instant of the extraction their concentration in the organic phase is $[MA_3]_O^0 = q_{MA_3}[MA_3]_W^0$, and for equal phase volumes we have

$$[MA_3]_{int} = [MA_3]_o^0 + [MA_3]_w^0 = [MA_3]_w^0(q_{MA_3} + 1) = \frac{[MA_3]_o^0(q_{MA_3} + 1)}{q_{MA_3}} \cdot \qquad (21)$$

Under these conditions, the rate of extraction is also characterised by Eqn. (11) but $C_{W(init)}$ enters into the coefficient a instead of C_W^0. The derivation of the equation for the rate of extraction in the system under consideration is similar to that quoted above.

Thus the linear time variation of $\ln[(C_W - C_{W,e})/(C_W^0 - C_{W,e})]$ under kinetic conditions and the experimental conditions adopted shows that the rate of extraction may be determined by one slow reaction (below it will be shown that, for two reactions at comparable rates, the corresponding relation is not linear). The coefficient a can be found from the slope of the resulting straight line, but, in order to deduce the mechanism of the reaction determining the rate of extraction and to determine its rate constant, it is necessary to know the stability constants of the compounds existing in the given system, which may make the solution of the problem significantly more difficult. For example, in the extraction of iron from perchloric acid solutions with acetylacetone, it is essential to know the stability constants of the complex ions and molecules FeA^{2+}, FeA_2^+, and FeA_3. However, the data published in different studies for these constants differ appreciably. Thus, according to Badoz-Lambling[65], at zero ionic strength the dissociation constants of these ions are $K_1 = 3 \times 10^{-12}$, $K_2 = 8 \times 10^{-23}$, and $K_3 = 2 \times 10^{-27}$; according to Izatz et al.[66], $K_1 = 1.6 \times 10^{-10}$, $K_2 = 1.6 \times 10^{-19}$, and $K_3 = 6.4 \times 10^{-27}$. Bearing in mind that the dissociation constant of acetylacetone is 1.12×10^{-9} litre mole^{-1}, the difference between the complex formation constants will lead to a considerable difference between the equilibrium concentrations entering into the equations

for a, which hinders the choice of the appropriate mechanism.

However, when the slow stage determining the rate of extraction is the formation of the extractable compound (MA_3 in the extraction of a tervalent element or MA_2 in the extraction of a bivalent element), the coefficient a can be calculated from the experimental equilibrium data without knowing the constants. Then

$$C_w^0 - [M^{3+}]_e - [MA^{2+}]_e - [MA_2^+] = C_w^0 - (C_{w,e} - [MA_3]_{w,e}) = C_{o,e} + \frac{C_{o,e}}{q_{MA_3}} = \frac{C_{o,e}(q_{MA_3}+1)}{q_{MA_3}}$$

$$K_3' K_2 [A^-]^3 + K_2 [A^-] + K_2^+ \left(K_2 [A^-]^2 + \frac{K_2 [A^-]}{K_3'} + 1 \right) =$$

$$= K_2' \left(\frac{[MA_2^+]_e}{[M^{3+}]_e} + \frac{[MA^{2+}]_e}{[M^{3+}]_e} + 1 \right) = \frac{K_2'}{[M^{3+}]_e} ([MA_2^+]_e + [MA^{2+}]_e + [M^{3+}]_e) =$$

$$= \frac{K_3'}{[M^{3+}]_e} (C_{w,e} - [MA_3]_{w,e}) = \frac{K_2'}{[M^{3+}]_e} \left(C_{w,e} - \frac{C_{o,e}}{q_{MA_3}} \right) = \frac{K_2' \cdot C_{w,e}}{[M^{3+}]_e} \left(1 - \frac{q_p}{q_{MA_3}} \right),$$

where $q_p = C_{o,e}/C_{w,e}$ is the partition coefficient and $C_{o,e}$ and $C_{w,e}$ are the analytical equilibrium concentrations.

On substituting these values in Eqn. (15) and on replacing C_w^0 by $C_{w,e}(q_p + 1)$, we obtain after rearrangement

$$a_3 = \frac{\varkappa_3 K_2 (q_p + 1)}{K_3 (q_{MA_3} + 1) \left(1 - \frac{q_p}{q_{MA_3}} \right)}, \qquad (22)$$

where

$$K_3 = \frac{[MA_3]_{w,e}}{[M^{3+}]_e [A^-]^3} = \frac{C_{o,e}}{q_{MA_3} [M^{3+}]_e [A^-]^3}. \qquad (23)$$

Assuming that the rate constants and the stability constants of the complex ions are constant, it is possible to find the ratio of the coefficients a_3 in two experiments at different concentrations of the acid HA. It follows from Eqn. (22) that this ratio is

$$\frac{a_3'}{a_3''} = \frac{(q_p' + 1)(1 - q_p''/q_{MA_3})}{(q_p'' + 1)(1 - q_p'/q_{MA_3})}. \qquad (23a)$$

Thus, when the partition coefficient of MA_3 molecules is known and the partition coefficient q_p has been found experimentally, it is possible to test whether the ratio of the coefficients a_3 is consistent with Eqn. (23a) and whether reaction (III) determines the rate of extraction. When the experiments are performed at a low concentration of the acid HA or at a fairly high acidity, $q_p \ll q_{MA_3}$ so that Eqn. (23a) assumes the form

$$\frac{a_3'}{a_3''} = \frac{q_p' + 1}{q_p'' + 1}. \qquad (23b)$$

For the extraction of a bivalent metal, we obtain similarly

$$a_2 = \frac{\varkappa_2 K_1}{K_2} \frac{(q_p + 1)}{(q_{MA_2} + 1)(1 - q_p/q_{MA_2})}, \qquad (24)$$

where K_1 is the stability constant of the ion MA^+ and K_2 is the overall stability constant of MA_2 molecules (dissociation into simple ions).

If reaction (I) or (II) is slow in the extraction of a tervalent metal or the former is slow in the extraction of a bivalent metal, it is necessary to know the stability constants of the compounds formed in order to deduce the mechanism.

The concentrations of the anions A^-, which are determined under the specified conditions (specified microconcentrations of the extractable element) from the equation $[A^-] = K_{HA}[HA]_o/[H^+]q_{HA}$, where $[HA]_o$ is the concentration of the acid in the organic phase, enter into the above equations for the coefficient a. The equation for $[A^-]$ can be used to determine the variation of the rate of extraction with hydrogen ion concentration for a constant value of $[HA]_o$. If the ionic strength hardly changes with hydrogen ion concentration and the degree of dissociation of the acid in the aqueous phase is very low, then its dissociation constant and the partition coefficient will not vary. Evidently, when there are no reactions in the system involving H^+ of OH^- ions (for example hydrolysis reactions), then, on applying Eqn. (4a), the rate constant κ_1 will include the hydrogen ion concentration raised to the power n, where n is the number of molecules of the acid HA or the ions A^- involved in the corresponding reaction. However, when Eqns. (12b), (14), and (15) are applied, the coefficients a will vary in a more complex manner with hydrogen ion concentration, since the latter determines not only the concentration of the anions A^- but also the equilibrium concentrations $[M^{3+}]_e$, $[MA^{2+}]_e$, etc.

A significant difference between the reaction orders with respect to the extractant and hydrogen ions has been noted, for example, in the extraction of nickel and cobalt by dithizone derivatives. It has been found[41] that, when Eqn. (4a) is employed, the order is 1.35 and 1.53 with respect to the extractant and 0.73 and 0.75 with respect to hydrogen. On the other hand, the corresponding values for zinc are 1.91 and 1.71.

The variation of the rate of extraction with hydrogen ion concentration is regarded[67] as evidence that the reaction determining the rate of extraction proceeds in the aqueous phase. This is true if the partition coefficient of the acid is independent of hydrogen ion concentration.

In the above scheme of reactions (I)—(III) occurring in extraction it was assumed that there is interaction with the anions of the acid HA, but one can also postulate the interaction with its molecules. For example, whereas it has been assumed in some studies[49,64,68,70] that in the interaction of Fe^{3+} ions with thenoyltrifluoroacetone there is a slow reaction of these ions with enolate ions, in the analogous reaction with acetylacetone the interaction with the molecules in the keto-form[71], and in another investigation[72] with both forms, was postulated.

Thus, in order to deduce the extraction mechanism, it is necessary to consider the possibility of, for example, the following reactions:

$$M^{3+} + HA \underset{\varkappa_2'}{\overset{\varkappa_1'}{\rightleftarrows}} MA^{2+} + H^+ \text{ (V)}, \quad MA^{2+} + HA \underset{\varkappa_4'}{\overset{\varkappa_3'}{\rightleftarrows}} MA_2^+, \qquad \text{(VI)}$$

$$MA_2^+ + HA \underset{\varkappa_6'}{\overset{\varkappa_5'}{\rightleftarrows}} MA_3 + H^+ \text{ (VII)}, \quad MA_{3_w} \rightleftarrows MA_{3_o}. \qquad \text{(VIII)}$$

Having expressed the equilibrium constants for the reactions in the form

$$K_1^* = \frac{[MA^{2+}][H^+]}{[M^{3+}][HA]_w}; \quad K_2^* = \frac{[MA_2^+][H^+]}{[MA^{2+}][HA]_w}; \quad K_3^* = \frac{[MA_2^+][H^+]^3}{[M^{3+}][HA]_w^3} \qquad \text{(25c)}$$

it is possible to show that the rate of extraction is also characterised by Eqn. (11), but the corresponding coefficients are given by

$$a_1^* = \frac{\varkappa_1'[HA]_w C_w^0}{C_w^0 - [M^{3+}]_e} , \quad (26a)$$

$$a_2^* = \frac{\varkappa_2' K_1^* [HA]_w^2 C_w^0}{(K_1^*[HA]_w + [H^+])(C_w^0 - [M^{3+}]_e - [MA^{2+}]_e)} , \quad (26b)$$

$$a_3^* = \frac{\varkappa_3' K_2'^* K_2^* [HA]_w^3 C_w^0}{(K_2'^*[H^+]^2 + K_2''[H^+][HA]_w + K_2'^* K_2^*[HA]_w^2)(C_w^0 - [M^{3+}]_e - [MA^{2+}]_e - [MA_2^+]_e)} . \quad (26c)$$

If $C_w^0 \gg [M^{3+}]_e$, which is possible when the partition coefficients and the equilibrium constants for the corresponding reactions are high, it follows from Eqns. (14) and (26a) that

$$a_1 = \frac{\varkappa_1 K_{HA}[HA]_o}{q_{HA}[H^+]} ; \quad (27a)$$

$$a_1^* = \frac{\varkappa_1'[HA]_o}{q_{HA}} . \quad (27b)$$

Consequently, at a constant concentration of the acid HA in the organic phase, the quantity a_1 will be inversely proportional to the hydrogen ion concentration. This type of relation has been observed in certain experiments when Eqn. (4a) was used; a_1^* is independent of this concentration if q_{HA} is independent of the composition of the solution. Thus, there is a possibility of distinguishing reactions (I) and (V). However, in reactions involving HA molecules, for example with acetylacetone, there arises the problem of determining the reactive species (the enol or keto-form). There is a significant difference (depending on the hydrogen ion concentration) between the coefficients a_2 and a_2^*, but it is more difficult to analyse.

If reaction (VII) is slow, then, as in the preceding case, it is possible to show that, subject to the conditions $q_{MA_3} \gg q_p$, we have, for two experiments at the same value of $[HA]_O$,

$$\frac{a_3^{*'}}{a_3^{*''}} = \frac{[H^+]'}{[H^+]''} \cdot \frac{(q_p' + 1)}{(q_p'' + 1)} , \quad (28)$$

which makes it possible to choose one of the reactions [(III) or (VII)].

The examples quoted naturally by no means exhaust completely all the possible reactions in extraction under kinetic conditions. Thus even reaction (V) can proceed in two stages

$$M(H_2O)_x^{3+} + HA \rightleftarrows M(H_2O)_{x-i} \cdot HA^{3+} + i H_2O;$$

$$M(H_2O)_{x-i}HA^{3+} \rightleftarrows M(H_2O)_j A^{2+} + H^+ H_2O + (x - i - j - 1) H_2O$$

It has been noted in a number of studies that the rate of reactions in the aqueous phase can be determined by the rate of loss of water molecules[73,74]. In particular, in a study of the rate of formation of nickel complexes of malonic and succinic acids (in the case of a homogeneous reaction) it was established[74] that the rate of the forward reaction is determined by the rate of loss of water molecules and therefore the rate constants for this reaction are independent of the nature of the ligand, while the rate constants for the reverse reaction differ appreciably.

It has also been suggested for the reactions of zinc with dithizone quoted previously[62] that the rate depends only on the rate of elimination of water from the hydration shell. However, here the rate constant for the elimination of water is a factor of ten higher than the constant found from extraction experiments. The conclusion that the rate of reaction is determined by the rate of loss of water must be based on a comparison of the rates of the given reaction and of the exchange of water, for example on the basis of Eigen's data[73]. Such a comparison and the absence of a dependence of the rate of reaction on the nature of the ligand are probably the only means of proving that the rate is determined by the rate of loss of water.

Thus, studies on the mechanism of extraction under kinetic conditions are difficult even in the case of one slow reaction. The investigation of the corresponding reactions in a homogeneous system using physical methods permitting the determination of the concentrations of the individual compounds is important for such studies. However, if it has been shown that the process occurs under kinetic conditions and is determined by the rate of one reaction, the use of Eqn. (16) and of the empirical dependence of the coefficients a on the extraction conditions can facilitate the choice of the optimal conditions for the extraction process.

III. TWO SLOW REACTIONS WITH THE EXTRACTANT IN THE AQUEOUS PHASE

If two consecutive reactions occur at comparable rates under kinetic conditions in the aqueous phase of the given system, for example in the extraction of a bivalent metal by an acid HA,

$$M_w^{2+} + A^- \underset{\varkappa_2}{\overset{\varkappa_1}{\rightleftarrows}} MA_w^+; \; MA^+ + A^- \underset{\varkappa_4}{\overset{\varkappa_3}{\rightleftarrows}} MA_2 ,$$

then, as shown before[75], the concentration in the aqueous phase for equal phase volumes is given by the equation

$$C_w = C_1 e^{z_1 t} + C_2 e^{z_2 t} + \frac{a_3}{a_2} , \quad (29)$$

where z_1 and z_2 are the roots of the characteristic equation $z^2 + a_1 z + a_2 = 0$;

$$a_1 = \varkappa_1[A^-]_w + \varkappa_2 + \varkappa_3 + [A^-]_w + \frac{\varkappa_4}{q_{MA_2} + 1} , \quad (30a)$$

$$a_2 = (q_{MA_2} \varkappa_1\varkappa_3[A^-]_w^2 + \varkappa_1\varkappa_3[A^-]_w^2 + \varkappa_1\varkappa_4[A^-]_w + \varkappa_2\varkappa_4)/(q_{MA_2} + 1) , \quad (30b)$$

$$a_3 = -(\varkappa_1\varkappa_3[A^-]_w^2 + \varkappa_1\varkappa_4[A^-]_w + \varkappa_2\varkappa_4) C_w^0/(q_{MA_2} + 1) , \quad (30c)$$

$$\frac{a_3}{a_2} = C_{w,e} , \quad (30d)$$

C_1 and C_2 are integration constants which, as required by Eqn. (29) satisfy the condition

$$C_w^0 = C_1 + C_2 + C_{w,e} . \quad (30e)$$

It follows from Eqns. (29) and (30d) that

$$\frac{C_w - C_{w,e}}{C_w^0 - C_{w,e}} = \frac{C_1 e^{z_1 t}}{C_w^0 - C_{w,e}} \left[1 - \frac{C_2}{C_1} e^{(z_2 - z_1)t}\right] , \quad (31)$$

and for this reason $\ln[(C_w - C_{w,e})/(C_w^0 - C_{w,e})]$ is not a linear function of time. We shall assume that $z_2 < z_1$, whereupon we have, for fairly high values of t when $(C_2/C_1)e^{(z_2 - z_1)t} \ll 1$,

$$\ln \frac{C_w - C_{w,e}}{C_w^0 - C_{w,e}} \approx z_1 t + A , \quad (32)$$

where $A = C_1(C_w^0 - C_{w,e})$. It is seen from Eqn. (32) that for high values of t the logarithmic term on the left-hand side is a linear function of time. For low values of t, the equation represents a curve whose slope diminishes with increase of t until a constant value is reached.

Thus the initial section of the relation between $\ln[(C_w - C_{w,e})/(C_w^0 - C_{w,e})]$ and time (t is small) shows whether one or more than one reaction determine the rate

of extraction in the given system under kinetic conditions.

From the linear part of the plot of $\ln[(C_W - C_{W,e})/(C_W^0 - C_{W,e})]$ as a function of t, it is possible to determine z and C_1. Knowing C_1, one can find C_2 from Eqn. (30e) and then z_2 from the curved part of the plot. The same quantities can be calculated with the aid of the coordinates of two points on the curved part of the plot by solving the resulting system of two equations.

Since $a_1 = -(z_1 + z_2)$, $a_2 = z_1 z_2$, and $a_3 = a_2 C_{W,e}$, it follows that, knowing the partition coefficient of MA_2 (q_{MA_2}) and the stability constants of the ions MA^+ and molecules MA_2,

$$K_1 = \frac{[MA^+]}{[M^{2+}][A^-]} = \frac{\varkappa_1}{\varkappa_2} \tag{33a}$$

and

$$K_2' = \frac{[MA_2]}{[MA^+][A^-]} = \frac{\varkappa_3}{\varkappa_4} , \tag{33b}$$

it is possible to find from the above equations all the rate constants (κ_1, κ_2, κ_3 and κ_4) by carrying out a series of experiments with different concentrations of the acid $[A^-]$. Since there are five equations relating the rate and equilibrium constants [Eqns. (30a), (30b), (30c), (33a), and (33b)], it is possible to determine one of the equilibrium constants (when it is unknown) from kinetic data.

Since $\ln[(C_W - C_{W,e})/(C_W^0 - C_{W,e})]$ is also a nonlinear function of time under mixed conditions, the conclusion that the deviation from linearity is due to two reactions with comparable rates requires evidence that in the given case kinetic conditions obtain.

This type of relation probably also obtains for a large number of consecutive reactions but analysis of the relevant cases is fairly difficult. A deviation from linearity will probably be observed for parallel reactions, for example for slow reactions with the extractant and a complex-forming agent present in the aqueous phase.

The rate of extraction under mixed conditions for a reaction in the bulk of one of the phases, for example the receiving phase[76], can be described similarly.

It has been found[60] for the extraction of chromium(III) from 1 N perchloric acid by acetylacetone solutions that $\ln(C_W/C_W^0)$ is a linear function of time if the latter is longer than 90 min at pH 4 and longer than 5 min at pH 7. This can be caused either by the occurrence of two reactions with the extractant (if the equilibrium concentration of chromium is much lower than its concentration at any instant whereupon the equation describes the corresponding process) or by a side reaction and a reaction with the extractant, since the specified pH was established by adding alkali directly before extraction whereby equilibrium might have been only slowly established, for example in a hydrolysis reaction. Evidently in this case the determination of the reaction order by the van't Hoff method with the aid of Eqn. (4a) employed by the authors is doubtful.

IV. EXTRACTION WITH A SIDE REACTION

The determination of the rate of extraction in the presence of a slow side reaction has been examined[77]. The following scheme was analysed: a slow reaction

$$A_w + D_w = AB_w + E_w \tag{IX}$$

takes place in the aqueous phase and only the compound A passes very rapidly to the organic phase, where it either does not change or a very rapid reaction takes place.

Microconcentrations of A are employed, while the concentrations of D and E are high and hardly change. For example, A = $HSbCl_6$, D = H_2O, AB = $HSb(OH)Cl_4$, E = HCl, the compound A being extracted by alcohols[78]. In this case the variation of the concentrations of A in the aqueous and organic phases, subject to the condition that the phase volumes are equal, is described by the equations

$$\frac{d[A^-]_w}{dt} = -\varkappa_1'[A]_w + \varkappa_2'[AB]_w - K'[A]_w + K'[A]_o , \tag{34a}$$

$$\frac{d[A]_o}{dt} = K'[A]_w - K''[A]_o , \tag{34b}$$

where $\kappa_1' = \kappa_1[D]_W$, $\kappa_2' = \kappa_2[E]_W$, κ_1 and κ_2 are the rate constants for the forward and reverse reactions, $K' = K_W S/V_W$, and S is the area of the interface.

Therefore $d[A]_W/dt + d[A]_O/dt = -\kappa_1'[A]_W + \kappa_2'[AB]_W$ and under kinetic conditions we have at any instant $[A]_O = q_A[A]_W$, where q_A is the partition coefficient of the compound A assumed to be constant.

It follows from the above equations that

$$\left(1 + \frac{1}{q_A}\right)\frac{d[A]_o}{dt} = -\varkappa_1'\frac{[A]_o}{q_A} + \varkappa_2'\left(C_w - \frac{[A]_o}{q_A}\right) , \tag{35a}$$

where $C_W = [A]_W + [AB]_W$ is the analytical concentration of A in the aqueous phase at any instant.

Since $C_W = C_{W(init)} - [A]_O$, where $[A]_O$ is the concentration of A in the organic phase, Eqn. (34a) can be put in the form

$$-\frac{dC_w}{dt} = aC_w - b , \tag{35b}$$

where

$$a = \frac{\varkappa_1' + (q_A + 1)\varkappa_2'}{q_A + 1} , \tag{36a}$$

$$b = \frac{(\varkappa_1' + \varkappa_2')C_{w(init)}}{q_A + 1} = aC_{w,e} . \tag{36b}$$

After integrating Eqn. (35b) and assuming that $C_W = C_W^0$ when $t = 0$, we obtain

$$\ln\frac{C_w - C_{w,e}}{C_w^0 - C_{w,e}} = -at . \tag{37}$$

However, under kinetic conditions when there is an equilibrium in the initial aqueous phase, $C_W^0 \neq C_{W(init)}$, where $C_{W(init)}$ is the initial concentration in the aqueous phase (concentration before contact between the phases)¶, since under these conditions part of A is very rapidly ("instantaneously") transferred to the organic phase when the phases come into contact. For this reason, in the initial instant of extraction the following condition holds: $C_{W(init)} = C_W^0 + [A]_O^0$, where $[A]_O^0$ is the concentration of A in the organic phase in the initial instant of the extraction process (at $t = 0$). Hence, when t tends to zero, $[A]_O$ does not tend to zero but to a value $[A]_O^0$.

C_W^0 and $[A]_O^0$ can be found from the conditions for equilibrium in the initial aqueous solution and for equilibrium in the partition of A at the starting point. Indeed at equilibrium in the initial aqueous solution $C_{W(init)} = [A]_{W(init)} + [AB]_{W(init)} = (1 + \tilde{K}')[A]_{W(init)}$, where $\tilde{K}' = \tilde{K}[D]_W/[E]_W$ and $\tilde{K}$ is the equilibrium constant for reaction

¶ In the paper by one of the present authors[77] $C_{W(init)}$ is designated by C_W^0 and the concentration at $t = 0$ (after the instantaneous distribution of the extractable species) by $C_{W(t=0)}$.

(IX) under consideration. When A is distributed between the phases, we have at the starting point

$$[A]_{w(init)} = [A]^0_w + [A]^0_o = \frac{[A]^0_o}{q_A} + [A]^0_o = \left(\frac{1}{q_A} + 1\right)[A]^0_o .$$

Therefore

$$[A]^0_o = \frac{[A]_{w(init)}}{\left(\frac{1}{q_A}+1\right)} = \frac{C_{w(init)}}{(1+\tilde{K}_1)\left(\frac{1}{q_A}+1\right)}; \quad C^0_w = C_{w(init)} - [A]^0_o = \frac{\left(\frac{1}{q_A} + \frac{\tilde{K}'}{q_A} + \tilde{K}'\right) C_{w(init)}}{\left(\frac{1}{q_A}+1\right)(1+\tilde{K}')} .$$

The analytical partition coefficient $q_p = [A]_{o,e}/C_{w,e}$, where $C_{w,e}$ is the analytical concentration of A in the equilibrium aqueous phase but $C_{w,e} = [AB]_{w,e} + [A]_{w,e} = (\tilde{K}' + 1)[A]_{w,e}$, so that

$$q_p = \frac{[A]_{o,e}}{(\tilde{K}'+1)[A]_{w,e}} = \frac{q_A}{\tilde{K}'+1}, \text{ a } C^0_w = \left(\tilde{K}' + \frac{1}{q_p}\right) q_p \quad C_{w,e} = \left(\tilde{K}' + \frac{1}{q_p}\right)[A]_{o,e} .$$

One must bear in mind that C^0_w can be found from experimental data (even if $\tilde{K}'$ and q_p are unknown) by extrapolating C_w or C_o as a function of t to $t = 0$. Knowing C^0_w and the equilibrium concentrations, it is possible to find K' and q_p.

In the given case the rate of extraction is characterised by the variation of the concentration in the aqueous phase, but it is not difficult to obtain the corresponding equation for the rate in terms of the variation of the concentration in the organic phase. Since for the reaction under consideration $C_w = C_{w(init)} - [A]_o$, $C^0_w = C_{w(init)} - [A]^0_o$, and $C_{w,e} = C_{w(init)} - [A]_{o,e}$, substitution of these values in Eqn. (31) yields $\ln \dfrac{[A]_{o,e} - [A]_o}{[A]_{o,e} - [A]^0_o} = -at$. Putting the last equation in the form $[A]_{o,e} - [A]_o = \{[A]_{o,e} - [A]^0_o\} e^{-at}$, we obtain $[A]_o = [A]_{o,e} - \{[A]_{o,e} - [A]^0_o\} e^{-at}$. It follows from this equation that

$$q_t = \frac{[A]_o}{C_w} = \frac{[A]_{o,e} - ([A]_{o,e} - [A]^0_o) e^{-at}}{C_{w(init)} - [A]_o} = \frac{[A]_{o,e} - ([A]_{o,e} - [A]^0_o) e^{-at}}{C_{w(init)} - [A]_{o,e} + ([A]_{o,e} - [A]^0_o) e^{-at}} = \frac{[A]_{o,e} - ([A]_{o,e} - [A]^0_o) e^{-at}}{C_{w,e} + ([A]_{o,e} - [A]^0_o) e^{-at}} .$$

When $t = 0$, we have $q_t = q_o = [A]^0_o / \{C_{w(init)} - [A]^0_o\}$ whence $[A]^0_o = C_{w(init)}/(1 + 1/q_o)$. Bearing in mind that $\tilde{K}' = \kappa'_1/\kappa'_2$, the equation for the coefficient a can be put in the form $a = \kappa'_1[1/(q_A + 1) + 1/\tilde{K}']$. If q_A and $\tilde{K}'$ are fairly large and κ'_1 is small because the corresponding reaction is slow, the case $a \ll 1$ is possible and therefore $e^{-at} \simeq 1 - at$. Only in this case will the equation for q_t not contain an exponential term.

Hydrolysis or dehydrolysis in the extraction of antimony chloride complexes from hydrochloric acid solutions by oxygen-containing solvents (for example alcohols), which has been investigated by Iofa[78], can serve as an example of side reactions of this kind. Iofa found that q_t expressed as a function of extraction time does indeed have a finite value at $t = 0$.

V. DETERMINATION OF THE PHASE IN WHICH THE REACTION TAKES PLACE

If it has been established that the extraction proceeds under kinetic conditions with the reaction in one of the bulk phases, the determination of the phase in which the reaction occurs is of significant interest. In the extraction of electrolytes from aqueous solutions by organic extractants dissolved in non-polar solvents under the conditions where the extractant (in the given case an acid HA) is fairly soluble in the aqueous phase and the initial salt is completely dissociated in the aqueous phase and therefore has extremely low solubility in the organic phase, one can suggest with a great deal of confidence that the reaction takes place in the aqueous phase. The hypothesis put forward by Sekine et al.[47] that in the extraction of beryllium from aqueous solutions containing hydrochloric and perchloric acids beryllium perchlorate passes to the organic phase is therefore unlikely. However, when the extractant exists in several forms in the organic phase, for example the enolic and keto-forms of acetylacetone or thenoyltrifluoroacetone, which reach equilibrium slowly, and the extractable element reacts rapidly with one of these forms, the rate of extraction of macroamounts of the element M can be determined by the rate of the keto–enol transformation.

Thus the low rate of extraction of the lanthanides by thenoyltrifluoroacetone observed by Healy[79] is accounted for by the low rate of the keto–enol transformation, since according to the author these elements react only with the enol form.

In a qualitative study[80] of the rate of extraction of zirconium by benzoylacetone and thenoyltrifluoroacetone in various solvents, it was concluded, from the dependence of the relative amount of the enol form on the polarity of the diluent and the solubility of the ketone in water, that the enol forms of the ketones react. In the extraction of trace amounts in the presence of a high concentration of the extractant the transformation of one form into another does not limit the rate of the process, provided that equilibrium in the distribution of the extractant has been attained (the phases have been "equilibrated" without the extractable element).

When the dissociation of the extractable salt in the aqueous phase is incomplete (complex formation with the anion of the initial salt), the molecular form (undissociated molecules), whose partition coefficient is possibly insignificant, may pass to the organic phase also when the solubility of the extractant in water is low and the rate of extraction is then determined by the rate of reaction in the organic phase. For example, the partition coefficient of $AuCl_4$ between xylene and 2 M HCl is 0.005, but increases significantly following the addition of tributyl phosphate (TBP) to the organic phase[81]. If the given reaction is not a surface process, then, bearing in mind the low solubility of TBP in water, one can suggest with some confidence that the formation of a solvate, which increases the partition coefficient, takes place in the organic phase, although this should of course be tested experimentally.

Above it was already noted that in the extraction by an acid HA the dependence of the rate of extraction on hydrogen ion concentration has been regarded as evidence that the reaction determining the rate of extraction occurs in the aqueous phase. However, this is true only under

certain conditions, in particular when the partition coefficient is independent of the acid on hydrogen ion concentration, which occurs, for example, in the partition of acetylacetone.

Comparison of the rates of extraction by solutions of a single extractant in different diluents, enabled a number of investigators[82,83] to find that the rate of extraction is higher the higher the concentration of the extractant in the aqueous phase for an equal concentration in the organic phase {the lower the partition coefficient $q = [HA]_o/[HA]_w$}. Hence it was concluded that the reaction determining the rate of extraction takes place in the aqueous phase. This conclusion would be correct if the rates of reactions were determined by the concentrations and not the activities. However, the different concentrations of the extractant in the aqueous phase for the same concentration in different organic phases imply that the activities of the extractant in the organic phases are different (they are higher the higher the solubility in the aqueous phase). The increase of activity may be caused, in particular, by a decrease in the degree of interaction with the diluent, an increase in the degree of dissociation of the polymer when the latter is formed in the organic phase, and other factors, let alone the change in the activity coefficient as a result of a change in the relative molecular dimensions and intermolecular interactions. Evidently an increase of the activity of the extractant in the organic phase would increase the rate of reaction in this phase if it occurred. When the concentration of the extractant in the same diluent is varied, its activity coefficients can change much less than on varying the diluent and therefore in a certain concentration range they may be regarded as constant and the kinetics may be interpreted on the basis of the concentrations. This yields "effective" rate constants and equilibrium constants, which include these constant activity coefficients. For this reason, the change in the rate constants when the concentration is altered appreciably may be related to a change in the activity coefficients and not in the reaction mechanism.

In a study[6] of heterophase processes under kinetic conditions accompanied by the reaction A + B = AB with known partition coefficients of all the substances, an equation was obtained for the amount of substance which has reacted (for example the amount of AB formed), whereby one can determine the phase in which the reaction takes place. The possibility of applying this type of equation to our systems is complicated by the existence of a number of compounds in the aqueous phase and the necessity to distinguish the analytical partition coefficient and the partition coefficient of the extractable compound. It is therefore necessary to analyse this equation and compare it with the equations for the rate of extraction determined by the rate of the reaction in the organic phase.

When different diluents and the same extractant are employed, the determination of the reaction rate constants is of significant interest, since this might constitute more reliable evidence for the occurrence of the reaction in one phase than a qualitative comparison of the rates.

VI. THE RATE OF EXTRACTION UNDER KINETIC CONDITIONS FOR MACROCONCENTRATIONS OF THE COMPONENTS

The extraction of microamounts of the extractable substance (element) for which the concentration of the extractant remains almost constant was examined previously. With a suitable preparation of the solutions for the experiment (equilibration of the phases with respect to the macrocomponents), this ruled out the influence of the rate of transformation of one form of the extractant into another when the extractant can exist in different forms. Equations for the rate of extraction under the conditions of comparable concentrations of the extractant and the extractable compound are derived in the present section for the extraction of a univalent element by an acid HA having only one form. In this case, assuming that the rate of extraction is determined solely by the rate of the reaction $M^+ + A^- = MA$ occurring in the aqueous phase, we have at any instant

$$[HA]_w = q_{HA}[HA]_w \quad , \tag{38a}$$

$$[MA]_o = q_{MA}\,[MA]_w \quad , \tag{38b}$$

$$[HA]_w = K_{HA}[H^+][A^-] \quad , \tag{39a}$$

$$[A^-] = \frac{[HA]_w}{K_{HA}[H^+]} = \frac{[HA]_o}{q_{HA}\ K_{HA}\ [H^+]} \quad . \tag{39b}$$

For equal phase volumes, we obtain, as in a system with microconcentrations of the extractable element,

$$\frac{d\,[MA]_w}{dt} + \frac{d\,[MA]_o}{dt} = \varkappa_1[M^+]_w[A^-]_w - \varkappa_2[MA]_w \quad . \tag{40}$$

Since the analytical concentration of M in the aqueous phase is $C_w = [M^+]_w + [MA]_w$, and in the organic phase $C_o = [MA]_o$, it follows that

$$[M^+]_w = C_w - [MA]_w = C_w^0 - C_o - \frac{C_o}{q_{MA}} = C_w^0 - \left(1 + \frac{1}{q_{MA}}\right) C_o \quad , \tag{41}$$

where C_w^0 is the concentration of M^+ in the initial aqueous solution.

We have from Eqns. (38b), (40), and (41)

$$\left(1 + \frac{1}{q_{MA}}\right)\frac{dC_o}{dt} = \varkappa_1[A^-]\left\{C_w^0 - \left(1 + \frac{1}{q_{MA}}\right) C_o\right\} - \frac{\varkappa_2\ C_o}{q_{MA}} \quad . \tag{42}$$

[A] is determined using the material balance equations

$$[HA]_o = [HA]_o^0 - [HA]_w - [A^-]_w - [MA]_o - [MA]_w \quad , \tag{43a}$$

$$[H^+]_w = [H^+]_w^0 + [A^-]_w + MA]_w + [MA]_o \quad , \tag{43b}$$

where $[HA]_o^0$ and $[H^+]^0$ are the initial concentrations of the acid HA in the organic phase and of hydrogen ions in the aqueous phase. Then

$$[A^-] = \frac{[HA]_w}{q_{HA}\ K_{HA}\left\{[H^+]_w^0 + [HA]_o^0 - [HA]\left(1 + \frac{1}{q_{HA}}\right)\right\}} \quad , \tag{44a}$$

$$[HA]_o = [HA]_o^0 - [HA]_w - \frac{[HA]_o}{q_{HA}\ K_{HA}\left\{[H^+]_w^0 + [HA]_o^0 - [HA]_o\left(1 + \frac{1}{q_{HA}}\right)\right\}} - [MA]_w - [MA]_o \quad . \tag{44b}$$

On replacing $[HA]_w$ by $[HA]_o/q_{HA}$, it is possible to find $[HA]_o$ from Eqn. (44b). When $[HA]_o^0$, $[H^+]_w^0$, C_o, and $[HA]_o$ are known, it is easy to determine $[H^+]$ and $[A^-]$. Evidently, under these conditions Eqn. (42) is converted into a complex expression. However, if the degree of dissociation of the acid is low and $[A^-]$ can be neglected in Eqns. (43a) and (43b), it follows from the latter that

$$[HA] = \frac{[HA]_o^0 + \left(1 + \frac{1}{q_{MA}}\right) C_o}{1 + \frac{1}{q_{HA}}} \quad , \tag{45a}$$

$$[H^+]_w = [H^+]_w^0 - \left(1 + \frac{1}{q_{MA}}\right) C_o \quad . \tag{45b}$$

Putting, for brevity, $1 + 1/q_{MA} = a$ and $1 + 1/q_{HA} = b$, we have

$$[HA]_o = \frac{[HA]_o^0 - aC_o}{b} \quad , \tag{46a}$$

$$[H^+]_w = [H^+]_w^0 + aC_o \quad , \tag{46b}$$

$$[A^-] = \frac{[HA]_w^0 - aC_o}{q_{HA} K_{HA} b ([HA]_o^0 + aC_o)} \quad . \tag{46c}$$

Having substituted the value of $[A^-]$ from Eqn. (46c) in Eqn. (42), we obtain after appropriate rearrangements

$$f\frac{dC_o}{dt} = \frac{(a' - C_o)(C' - C_o)}{b' - C_o} + gC_o \quad . \tag{47}$$

In this equation $f = bq_{HA}K_{HA}/\kappa_1$, $a' = [HA]_o^0/a$, $b' = [H^+]_w^0/a$, $C' = C_w^0/a$, and $g = \frac{\kappa_2 q_{HA} K_{HA} h}{a\kappa_1 q_{MA}} = \frac{K_{HA}(q_{HA}+1)}{K_{MA}(q_{MA}+1)}$.

After adjusting Eqn. (47) to a common denominator and rearrangement, we obtain

$$\frac{(b' - C_o)\,dC_o}{C_o^2 - pC_o + r} = \frac{1+g}{r}\,dt \, , \tag{48}$$

where

$$p = \frac{a' + b'g + C'}{1 - g} \quad .$$

Integration of this equation subject to the condition $C_O = 0$ when $t = 0$ leads to the expression

$$(b' - x_1)\lg\frac{x_1 - C_o}{x_1} - (b' - x_2)\lg\frac{x_2 - C_o}{x_2} = \frac{(1-g)(x_1 - x_2)}{2.303f}\,t, \tag{49}$$

where x_1 and x_2 are the roots of the equation $C_O^2 - pC_O + r = 0$.

The condition $C_O^2 - pC_O + r = 0$ corresponds to equilibrium and therefore one of the roots, for example x_2, is equal to $C_{O,e}$—the equilibrium concentration in the organic phase, which can be determined experimentally. In this case $x_1 = r/x_2 = r/C_{O,e}$. If q_{HA}, q_{MA}, K_{HA}, K_{MA}, a', b', C', and g are known, then there is only one unknown in Eqn. (44), namely f, which includes the rate constant κ_1. Thus, having determined experimentally C_O at a time t, it is possible to find f, and, knowing the equilibrium constant K_{MA} for the given reaction, κ_2 can be determined.

The above equations show that the determination of the rate constant for a comparatively simple reaction in extraction requires the knowledge of the stability constant of the compound formed and of its partition coefficient and the corresponding calculations involve a considerable error, since the equations include coefficients which are complex functions of the initial concentrations, the equilibrium constants, and partition coefficients.

Evidently, in extraction whose rate is determined by the rate of a chemical reaction accompanied by the formation of several compounds of the extractable element, the corresponding equations will be still more complex.

When the concentrations of the components are altered appreciably, there is a possibility of a considerable change in their activity coefficients, which complicates still further the study of the extraction mechanism. For this reason, the use of radioactive traces is extremely desirable in the study of the extraction mechanism.

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Mass Spectrometry of Transition Metal π-Complexes

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The problems of the fragmentation of transition metal π-complexes under the influence of electron impact are examined. The mass spectra of this class of compounds reflect fairly well the differences in the nature and stability of the metal-ligand bond as well as structural and other differences. Together with the rupture of the metal-ligand bond, electron impact results in the partial fragmentation of the ligands linked to the metal atom by π-bonds, the nature and degree of fragmentation depending on the nature and molecular weight of the ligand.
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I. INTRODUCTION

Volatile transition metal compounds can be conventionally divided into the following groups in terms of the type of the metal–ligand bond.

A. Chelate complexes, for example acetylacetonates.

B. Complexes with ligands of the π-acceptor type (carbon monoxide, nitric oxide, phosphines, arsines, nitriles, etc.).

C. Complexes with ligands linked by π-bonds. The ligands in such complexes are organic substances with double, triple, and conjugated bonds.

Studies on the mass-spectrometry of organometallic alkyl and phenyl compounds and metal complexes with ligands such as carbon monoxide have been described fairly completely in recently published reviews [1,2] and other reviews [3-5] deal with the mass spectra of certain transition metal π-complexes.

The present review deals with studies on the mass-spectrometry of transition metal π-complexes. The problems of the fragmentation of π-complexes and the correlation between the fundamental characteristics of the mass-spectra and the metal–ligand bond energies are considered initially. The review is also concerned with problems relating to the identification of ions containing the atoms of polyisotopic elements and with the occurrence of ion–molecule reactions in the mass spectrometer. The problems associated with the measurement of appearance potentials and the calculations on their basis of the average metal–ligand bond dissociation energy are not discussed, since they have been dealt with in detail in other reviews [2,6]. The mass-spectra of the π-complexes have been classified in accordance with the nature of the ligands, since the latter are in fact responsible for the main characteristics of the mass-spectra of the π-complexes.

II. METAL π-COMPLEXES WITH AROMATIC LIGANDS

The mass-spectra of the π-complexes of transition metals having the general formula L_1ML_2 (L = C_7H_7, C_5H_5, or C_6H_6) reflect the differences between the electron-donating capacities of the ligands but at the same time have many features in common.

Dicyclopentadienyl Compounds

Compounds of this class have been frequently investigated mass-spectrometrically [7-11]. The molecular ion peaks in the mass spectra of such complexes are as a rule the most intense and successive dissociation of the cyclopentadienyl groups from the molecular ion leads to the formation of metal ions and the fragment $C_5H_5M^+$, the peaks of which are also fairly intense. The cyclopentadienyl groups are also to a considerable degree fragmented. The group C_3H_3 and ethylene and acetylene molecules are mainly split off. When hydrogen atoms and methyl or other radicals are split off from the molecular ion, a series of ions are formed whose peak intensities are low. On fragmentation of molecular ions, the charge as a rule remains on the metal-containing fragment. The majority of fragmentation processes are accompanied by metastable transitions, with intense and distinct peaks [9].

The ionisation potentials of dicyclopentadienyl complexes are lower or equal to those of the atoms of the complex-forming elements [8,9,12,13]. This permitted the conclusion [8,9] that, in the ionisation of compounds such as ferrocene, an electron is removed from a non-bonding orbital localised at the metal atom. This conclusion is satisfactorily consistent with data calculated for ferrocene by the molecular orbital method [14].

The intensity of the metal ion peaks in the mass-spectra of the isoelectronic dicyclopentadienyl complexes of iron, ruthenium, and osmium (Table 1) decreases on passing from ferrocene to osmocene. This indicates an increase in the strength of the metal–cyclopentadienyl bond with increase of the atomic number of the complex-forming element. The metal–ligand bond energies for ferrocene and ruthenocene quoted in Table 1, calculated from the appearance potentials of iron and ruthenium ions, confirm this. An analogous correlation between the mass spectra and the appearance potentials was observed for chromium, molybdenum, and tungsten hexacarbonyls [15-18].

The relative intensity of the metal ion peaks in the spectra of a series of dicyclopentadienyl compounds of vanadium, iron, nickel, and chromium increases, amounting respectively to 12.5, 16.1, 18.9, and 28.2% of the overall intensity of the peaks [8]. The increase is due to the decrease of the average metal–ligand bond dissociation energy, which is 88, [19] 74, [20] 62, [20] and 54 [21] kcal $mole^{-1}$ respectively.

The substitution of hydrogen atoms in the ligands can have a significant influence on the nature of the fragmentation. The study of the mass-spectra of substituted ferrocenes [22-28] showed that simple substituents (methyl and ethyl groups and halogen atoms) hardly affect the nature and degree of fragmentation. More complex substituents give rise to a number of characteristic features associated with the fragmentation of the substituent itself. In compounds containing alkyl and vinyl substituents in the same ring, cyclopentadienyl (Cp) groups without substituents are split off preferentially [25].

Table 1. Relative peak intensities of the principal ions in the mass-spectra and the metal–ligand bond dissociation energies in the dicyclopentadienyl complexes of iron, ruthenium, and osmium (%).

Ion	Fe	Ru	Os
$(C_5H_5)_2M^+$	100	100	100
$C_5H_5M^+$	36	21.7	2.7
M^+	27	2.8	0.5
D_{M-L}, kcal mole^{-1}	78	112	—

The mass-spectra of cyclopentadienyl compounds also reflect satisfactorily the degree of polarity of the metal–cyclopentadienyl bond. In order to demonstrate the influence of the nature of the metal–cyclopentadienyl bond on the characteristics of the fragmentation and the nature of the mass-spectrum, it is useful to compare the mass-spectra of dicyclopentadienyl π-complexes with those of ionic and σ-linked dicyclopentadienyl compounds. Thus the fragmentation of ionic dicyclopentadienyl magnesium and manganese compounds † [8,9] proceeds in the same way as in compounds of the ferrocene type. However, an increase in the amount of ionic character of the metal–cyclopentadienyl bond reduces the relative intensity of the molecular ion peaks and increases the intensity of the fragment ion peaks (Table 2).

Table 2. Relative peak intensities of the principal ions in the mass-spectra of the dicyclopentadienyl complexes of iron, magnesium, and manganese (%).

Ion	Fe	Mg	Mn
$(C_5H_5)_2M^+$	100	100	100
$C_5H_5M^+$	36	171	157
M^+	27	139	136

† In contrast to ferrocene and other dicyclopentadienyl transition metal compounds, Cp_2Mn is an ionic compound. Detailed information about studies dealing with the demonstration of the ionic character of the metal–cyclopentadienyl bonds in this compound can be found in other reviews [29,30].

Under the influence of electron impact, thallium cyclopentadienide splits off the cyclopentadienyl group, giving rise to a metal ion whose peak intensity is a maximum in the spectrum [31,32].

The mass-spectra of metal dicyclopentadienyl complexes with σ linkages (see, for example, the mass-spectrum of Cp_2Pb) [33] are close to the mass-spectra of ionic dicyclopentadienyl compounds.

Tricyclopentadienyl Compounds

Tricyclopentadienyl complexes of the lanthanides, which are partly ionic and partly of the π-complex type, constitute an extremely interesting class. The relative intensity of the molecular ion peaks in the mass-spectra of these compounds is fairly high [34-37]. The elimination of the first cyclopentadienyl group leads to the formation of the ions Cp_2M^+, the relative intensity of whose peaks is as a rule maximal in the spectrum. Further fragmentation leads to the pattern which is well known for ferrocene.

In contrast to the dicyclopentadienyl compounds of transition metals, the ionisation potentials of the tricyclopentadienyl complexes exceed by 1–2 eV the ionisation potentials of the lanthanide atoms, which can probably be accounted for by the removal on ionisation of an electron which is not localised at the atom of the complex-forming element but at the ligand, as in chelated chromium acetylacetonates [38].

Tetracyclopentadienyl Compounds

The mass-spectra of the tetracyclopentadienyl π-complexes of uranium and thorium [34,39] have intense peaks due to the molecular ion and the ions formed as a result of the elimination of cyclopentadienyl groups from the latter. The peaks due to the Cp_3M^+ ions are the most intense in the spectra. As for the di- and tricyclopentadienyl complexes, in the mass-spectra of the tetracyclopentadienyl complexes of uranium and thorium contain fairly intense peaks due to ions associated with the partial fragmentation of the ligands.

Table 3. Relative peak intensities of the principal ions in the mass-spectra of bisbenzenechromium and bisbenzenevanadium (%). [40]

Ion	Cr	V
$(C_6H_6)_2M^+$	28.5	85.6
$C_6H_6M^+$	37.6	83.5
M^+	100	100
$(C_6H_6)_2M^+$	6.2	18.0

Bisarene Compounds

The intensities of the molecular ion peaks in the mass-spectra of bisbenzenevanadium [40] and bisbenzenechromium [7,13,40,41] are much higher (Table 3), which is evidence for a fairly high stability of the metal–benzene bond. However, in contrast to the dicyclopentadienyl

compounds, in the mass spectra of the bisarene complexes the peaks due to the metal ions and not the molecular ions are the most intense. This difference is evidence that the stability of the metal–ligand bond in compounds of the type LML decreases following the replacement of cyclopentadienyl groups by benzene molecules. On the other hand, comparison of the relative intensities of the molecular ion peaks in the mass-spectra of bisbenzenechromium and bisbenzenevanadium leads to the conclusion that the benzene–vanadium bond is stronger than the benzene–chromium bond. These conclusions are satisfactorily consistent with thermochemical measurements[42].

The fragmentation of bisarene compounds is extremely simple and leads to the successive elimination of benzene molecules from the molecular ion with retention of the charge on the metal-containing fragments, which is confirmed by the presence in the mass-spectra of intense and distinct peaks due to metastable transitions.

The intensities of the peaks due to the $MC_5H_5^+$, $MC_4H_4^+$, $MC_3H_3^+$, MC_2H^+, and other ions in the mass-spectra of the bisarene compounds are extremely low. This shows that the fragmentation of the π-linked ligands in the bisarene compounds hardly occurs, in contrast to the cyclopentadienyl complexes, which is related to the greater stability of the benzene ring compared with other aromatic systems and the low metal–ligand bond energy.

The study of the mass-spectra of methyl, isopropyl, and phenyl derivatives of bisbenzenechromium [43–45] showed that the nature of the mass-spectra and the fragmentation of the molecular ions in these compounds and in bisbenzenechromium are similar. In the mass-spectra of the bisarene compounds of chromium with asymmetric ligands—benzenecumenechromium and diethylbenzeneethylbenzenechromium [44,45]—the relative intensities of the peaks due to the CrL_1^+ and CrL_2^+ ions differ appreciably, which is evidence for the preferential elimination of ligands containing a smaller number of alkyl substituents. A mass-spectrometric study of benzenehexamethylbenzenemanganese[46] also showed that benzene is split off from the molecular ion more readily than hexamethylbenzene.

The peaks due to molecular ions and not the metal ion, as for bisarenechromium compounds, are the most intense in the mass-spectra of bisbenzenemolybdenum and its ethyl derivatives[47]. The sharp increase of the relative intensity of the molecular ion peaks on passing from bisbenzenechromium to bisbenzenemolybdenum is evidence, as for cyclopentadienyl and carbonyl complexes, for an increase in the strength of the metal–ligand bond with increase of the atomic number of the complex-forming element.

The ionisation potentials of the bisarene compounds are somewhat lower, as for the dicyclopentadienyl complexes, than the ionisation potentials of the complex-forming elements. The introduction of methyl substituents into bisbenzenechromium reduces the ionisation potential, but the decrease is not quite so distinct as for the free ligands[43].

A characteristic feature of the bisarene compounds is the permanent presence in their mass-spectra of fairly intense peaks due to the hydrocarbon ions of the ligands. The complete agreement of the relative intensities of the peaks due to these ions with the relative intensities of the corresponding ions in the mass-spectra of the free ligands, the formation of metallic films on the components of the ion source, the increase of the intensity of the peaks of these ions with increase of the temperature of the ion source, and the equality of the appearance potentials of the corresponding hydrocarbon ions in the mass-spectra of the bisarene compounds and the free ligands led to the conclusion[40,44] that the formation of the hydrocarbon ions is associated with the presence of free ligands in the ion source of the mass-spectrometer. The latter are formed as a result of the partial thermal decomposition of the bisarene compounds in the ion source.

Transition Metal Complexes with Asymmetric Aromatic Ligands

The mass-spectra of compounds of the type $C_5H_5MC_7H_7$, where M = V, Cr, Mo, or W, and compounds of the type $C_5H_5MC_6H_6$, where M = Mn or Cr,[7,40,48–50] reflect satisfactorily the differences between the electron-donating capacities of the C_5H_5, C_7H_7, and C_6H_6 groups. The elimination of the cyclopentadienyl group from the molecular ions of these complexes takes place after the C_7H_7 and C_6H_6 groups have been split off.

A characteristic feature of the fragmentation of the complexes containing the C_7H_7 group is the elimination from the latter of an acetylene molecule with formation of the ion Cp_2M^+ via the mechanism

$$C_5H_5MC_7H_7^+ \rightarrow (C_5H_5)_2M^+ + C_2H_2 ,$$

and the ion in its turn splits off in succession cyclopentadienyl groups with formation of the $C_5H_5M^+$ fragment and metal ions, so that the fragmentation of the C_5H_5 and C_6H_6 groups joined by π-bonds to the complex-forming atom is analogous to that of the dicyclopentadienyl and bisarene compounds.

Thus, comparison of the mass-spectra of compounds of the type $(C_5H_5)_2M$, $C_5H_5MC_7H_7$, $C_5H_5MC_6H_6$, and $(C_6H_6)_2M$, for example the mass-spectra of the isoelectronic iron, chromium, and manganese compounds (Table 4), readily demonstrates the decrease of the relative intensity of the molecular ion peak on passing from ferrocene to bisbenzenechromium. This decrease is evidence for the weakening of the metal–ligand bond due to the decrease of the electron-donating activity of the ligands in the series $C_5H_5 > C_7H_7 > C_6H_6$.

Table 4. Relative peak intensities of the principal ions in the mass-spectra of the isoelectronic complexes of chromium, manganese, iron with aromatic ligands (%)*.

Ion	$(C_5H_5)_2Fe$	$C_7H_7CrC_5H_5$	$C_5H_5MnC_6H_6$	$(C_6H_6)_2Cr$
$L_1ML_2^+$	61.5	50.4	22.6	17.2
$MC_5H_5^+$	22.4	9.5	45.1	
$C_6H_6M^+$	—	—	—	22.6
M^+	16.1	40.1	32.3	60.2

*The overall intensity of the peaks due to the ions $L_1ML_2^+$, L_1M^+, L_2M^+, and M^+ was adopted as 100%.

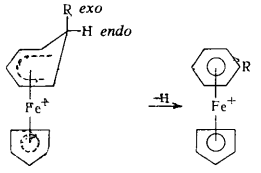
Complexes Containing Olefins Linked by π-bonds

The molecular ions of complexes containing, apart from the cyclopentadienyl group, π-linked olefins[50–53] split off the cyclopentadienyl group after the complete or

partial elimination of the olefin. Thus in the molecular ion of the $CpRh(C_2H_4)_2$ complex[50,52] the rupture of the metal–cyclopentadienyl bond is preceded by the stepwise elimination of the ethylene ligand species:

$$CpRh(C_2H_4)_2^+ \rightarrow CpRhC_2H_4^+ \rightarrow CpRh^+ \rightarrow Rh^+.$$

In complexes containing cyclo-olefins linked by π-bonds to the metal atom there is appreciable dehydrogenation of the olefin apart from the dissociation of the metal–ligand bond and partial fragmentation of the ligand species consisting in the elimination of the neutral C_2H_4, C_2H_2, and C_3H_3 groups. In a number of cases there is a stereoselective formation of aromatic fragments[54,69]:



The replacement of one cyclopentadienyl group in ferrocene by the indenyl ligand greatly complicates the nature of the fragmentation[51]. The molecular ion in the complex $CpFeC_9H_7$ loses the cyclopentadienyl group, simultaneously with the elimination of the indenyl ligand and the formation of the $CpFe^+$ ion, giving rise to the $C_9H_7Fe^+$ ion. In contrast to $CpFe^+$, the latter does not split off the indenyl ligand with formation of a metal ion but eliminates the iron atom, forming the ion $C_9H_7^+$, with a high intensity spectral peak.

The fragmentation mechanism becomes even more complicated when the indenyl group is replaced by its hydrogenation product C_9H_9 and C_9H_{11}. Dehydrogenation with formation of the $FeC_9H_8^+$ ion, which in turn loses the metal atom simultaneously with the elimination of the C_9H_8 group giving rise to the ion $C_9H_8^+$ and the products of its further fragmentation, is characteristic of these complexes. Fragmentation processes leading to the contraction of the ring with formation of the aromatic fragments $CpFeC_7H_7^+$, Cp_2Fe^+, and $CpFeC_6H_6^+$ are also characteristic of compounds containing the indenyl ligand and its hydrogenation products.

Table 5. The ionisation potentials of chromium, vanadium, manganese, and cobalt and of their complexes with benzene, the cyclopentadienyl group, and carbon monoxide.

Ion	V	Cr	Mn	Co	References
$(C_6H_6)_2M$	7.56	6.91	7.25	6.2	8
$C_6H_6MC_7H_7$	7.24	5.96	—	—	40
$(C_6H_6)_2M$	6.26	5.91	—	—	40
$C_6H_6MC_5H_5$	—	6.13	6.92		40
M	6.74	6.764	7.432	7.86	72
$C_6H_6M(CO)_3$	—	7.30	—	—	64
$C_5H_5M(CO)_4$	8.2				59
$C_5H_5M(CO)_3$	—	—	8.3	—	59
$C_5H_5M(CO_2)$	—	—	—	8.3	59
$M(CO)_6$	7.53	8.48			16
$M_2(CO)_{10}$	—	—	8.5	—	73
$M_2(CO)_4$	—	—	—	8.1	73

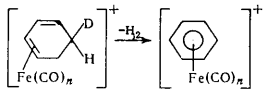
The olefin–metal complexes not containing the cyclopentadienyl group have been comparatively less well investigated by mass-spectrometry. The study of the mass-spectra of biscyclo-octa-1,5-dieneplatinum and biscyclo-octa-1,5-dienenickel[55], cycloheptadienylcycloheptatrienyltitanium[56], cyclo-octenylcyclo-octa-1,5-dienecobalt[57], and biscyclo-octatetraenethorium[58] showed that the fragmentation of complexes of this kind is analogous to that of the bisarene compounds, but the fragmentation of the π-linked hydrocarbon ligands takes place to a greater extent. The replacement of both cyclopentadienyl groups in ferrocene by indenyl groups leads to the elimination of the iron atoms from the molecular fragment ions $C_9H_7Fe^+$, which results in the presence in the mass spectrum of ions due to the indenyl ligand apart from the peaks due to metal-containing ions[51].

III. METAL π-COMPLEXES WITH AROMATIC AND π-ACCEPTOR LIGANDS

Mononuclear Complexes

The mass-spectra of the cyclopentadienyl complexes of cobalt[59], manganese[10,59–61], vanadium[59,61], rhenium[61], and iron[62] having the general formula $CpM(CO)_n$, cyclobutadienyltricarbonyliron[63], and benzenetricarbonylchromium[13,64,65] reflect satisfactorily the differences between the strengths of the metal–ligand bonds and the donor-acceptor properties of carbon monoxide, benzene, and the cyclopentadienyl group. The hydrocarbon ligands in these compounds are split off only after the complete loss of all the carbonyl groups from the molecular ion. Under these conditions, the CpM^+ ions also loses C_2H_2, C_2H_4, and other neutral groups, while there is hardly any fragmentation of the benzene ring with dissociation of carbon–carbon bonds.

The peaks due to the CpM^+ ion are the most intense in the mass-spectra of cyclopentadienyl derivatives of metal carbonyls, while the peaks of the metal ion are the most intense in the spectrum of benzenetricarbonylchromium. The carbonyl complexes with cyclic olefins behave similarly[60,62,66–69]. However, in this case the elimination of the carbonyl group and the olefin may prove to be equally probable, as has been observed for complexes of the type $C_5H_5M(CO)_2$(cyclo-olefin).[60] Moreover, dehydrogenation processes with subsequent aromatisation of the six-membered ring are characteristic of metal carbonyl complexes containing olefins, particularly those with adjacent CH_2 groups[54,69]:



The stereoselective formation of aromatic fragments proceeds in parallel with the decarbonylation of the molecular and fragment ions.

The fragmentation of substituted benzenetricarbonylchromium complexes $(CO)_3CrC_6H_5X$[64,70] depends significantly on the nature of the substituent X. The mass-spectra of the complexes with X = CH_3 and C_6H_5 hardly differ from the mass spectrum of benzenetricarbonylchromium. For electronegative substituents (Cl, F), the peaks of the rearranged ions CrX^+, the formation of which proceeds via the mechanism

$$CrC_6H_5X^+ \rightarrow CrX^+ + C_6H_5,$$

and is accompanied by a peak due to a metastable transition, exhibit an appreciable intensity in the mass spectra. The ions $CrC_6H_5X^+$ and $CrC_6H_4X^+$ lose an HX molecule with formation of the ions $CrC_6H_4^+$ and $CrC_6H_3^+$.

In the presence of more complex substituents (OCH_3, $COCH_3$, $OCOCH_3$, etc.) the peaks of the ions formed as a result of the fragmentation of the group X appear in the mass-spectra. The fragmentation of substituted cycloheptatriene and π-benzyl complexes of chromium tricarbonyl takes place similarly [71].

The ionisation potentials of benzenecarbonyl and cyclopentadienylcarbonyl complexes of transition metals (Table 5) are somewhat higher than those of the bisarene and dicyclopentadienyl compounds, but are lower than the ionisation potentials of the corresponding carbonyls.

The ionisation potential of benzenetricarbonylchromium decreases following the introduction of electron-donating substituents and increases following the introduction of electron-accepting substituents into the benzene ring [74]. However, a linear relation between the ionisation potentials of the arenetricarbonylchromium complexes and those of the free arenes, as in the case of the carbonylphosphine complexes of chromium, molybdenum, and tungsten[75], is not observed.

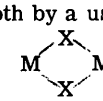
In cyclopentadienyl- and benzene-carbonylnitrosyl complexes of the type $CpM(NO)_x(CO)_y$ and $C_6H_6N(NO)_x(CO)_y$ [68, 76-78] nitric oxide and carbon monoxide are eliminated with equal probabilities. Fragmentation with dissociation of the Cp–M and C_6H_6–M bonds begins only after the complete elimination of the carbonyl and nitrosyl groups. A very unusual rearrangement has been observed by Müller [77] in the mass-spectrum of $CpV(NO)_2$. .CO. The ion $CpVNO^+$, formed after the elimination of the NO and CO groups, decomposes with formation of pyridine.

Whereas the loss of CO and NO groups from the carbonylnitrosyl complexes is equally probable, the mass-spectra of complexes with phosphines, arsines, and sulphur-containing and other ligands reflect the differences between the donor–acceptor capacities of carbon monoxide, nitric oxide, sulphur, and phosphines. Thus a study of the mass-spectrum of $CpMn(CO)_2N_2$ showed [79] that, for example, molecular nitrogen is a more powerful electron donor than carbon monoxide. The elimination of ligand species from the molecular ions derived from the carbonylphosphine complexes of the type $CpM(CO)_m(PX_3)_n$ and $C_6H_6M(CO)_m(PX)_n$ (X = H, Cl, Me, Et, etc.) [80-84] proceeds in the following sequence: the carbonyl groups are split off first, the phosphine molecules next, and only then does the elimination of the Cp and C_6H_6 groups begin. The elimination of the phosphine group is accompanied by its partial fragmentation, which leads to the presence in the mass-spectra of lines due to the ions $CpMPX_2^+$, $CpMPX^+$, and $CpMP^+$. The lines due to the CpM^+ ion in the spectra of the cyclopentadienyl complexes and due to the metal ion in the spectra of the benzene complexes show the greatest intensity. In the olefin complexes of manganese of the type $C_4H_4Mn(CO)_2EPh_3$ (E = P, As, or Sb) [85] the olefins are split off after the elimination of the CO and EPh_3 groups and there is a steady decrease of the strength of the bond between the metal and phosphine, arsine, and stibine.

The substitution of a hydrogen atom in the ligands PH_3, AsH_3, H_2S, H_2Se, etc. influences significantly the ionisation potential of the complex, the dependence of the latter on the ionisation potential of the corresponding ligand being linear [86].

Dinuclear and Polynuclear Complexes

Certain cyclopentadienyl complexes exist as dimers in the gas phase. Molecular ions and ions formed by their fragmentation have been detected in the mass-spectra of such compounds {see, for example, the mass-spectrum of $[PtCp]_2$}. [87] Simultaneously with the elimination of the cyclopentadienyl group and the formation of the M_2^+ cluster, the metal–metal bond is broken with formation of metal ions and the fragment CpM^+. Partial fragmentation of the π-linked cyclopentadienyl group is also observed.

In complexes containing ligands of the π-acceptor type apart from cyclopentadienyl groups the metal atoms can be joined both by a usual metal–metal bond and by bridge-type bonds:  Carbon monoxide, nitric oxide, phosphines, and other two- and three-electron ligands can serve as bridging groups.

Under the influence of electron impact, complexes with bridge-type bonds $CpMX_nMCp$ (where X = carbon monoxide, phosphines, and other ligands) [88-91] split off Cp groups forming the ions MX_nM^+ with fairly intense peaks. The removal of bridging groups leads to the breakdown of the cluster with formation of the ions M^+, CpM^+, $C_3H_3M^+$, etc. There are no peaks for M_2^+ ions in the mass-spectra of complexes of this kind. It is striking that the bridging ligands are linked to the metal atoms much more strongly than the same ligands occupying terminal positions.

In complexes with a usual metal–metal bond or with one such bond and several bridge-type bonds [90, 92-97] the successive removal of ligand species from the molecular ion leads to the formation of the ion M_2^+. There is a simultaneous rupture of the metal–metal bond with subsequent further fragmentation of the resulting fragments.

Structural differences are shown particularly clearly by the mass-spectra of $[CpFe(CO)_2]_2$ and $[CpMo(CO)_3]_2$. [90] Thus in the mass-spectrum of $[CpMo(CO)_3]_2$, which has a metal–metal bond, the peaks of the ion $CpMoMoCp^+$ have the maximum intensity, while in the mass-spectrum of $[CpFe(CO)_2]_2$, where the linkage between the iron atoms in the molecule is formed by CO bridging groups, the intensity of the peaks due to ions containing two iron atoms is low and the peak for the $CpFe^+$ ion is the most intense. A similar difference has been observed [98] for the molybdenum and chromium complexes $[CpM(CO)_3]_2$, although in this case the reason for the difference is in all probability the thermal instability of the chromium complex.

A similar behaviour has been observed for complexes containing different transition metal atoms [97, 99, 100].

IV. COMPLEX-CONTAINING GROUPS LINKED BY σ-BONDS

Certain transitions metals form complexes containing, apart from π-linked ligands and ligands of the π-acceptor type, also groups linked to the atom of the complex-forming element by σ-bonds, namely hydrogen and halogen atoms, organic groups, etc.

Dicyclopentadienylmetal Hydrides and Halides

Studies on the dicyclopentadienyl complexes of rhenium, tungsten, tantalum, and molybdenum hydrides showed [8, 9, 101, 102] that there are no significant differences between the mass-spectra of the dicyclopentadienyl complexes and the dicyclopentadienylmetal hydrides. After the elimination of hydrogen atoms from the molecular

ions, the Cp_2M^+ ions undergo fragmentation, which gives rise to the pattern well known for compounds of the ferrocene type.

In the cyclopentadienyl complexes of titanium, zirconium, hafnium, and niobium halides [11,103-105] the halogen atoms are retained somewhat more strongly by the molecular ions than are hydrogen atoms in the dicyclopentadienylmetal hydrides, but the type of fragmentation of both classes of compounds is similar. This can also be said of the uranium and thorium complexes Cp_3MF and Cp_3MI. [34,38]

Complexes with σ-Linked Organic Groups

The mass-spectra of cyclopentadienyl complexes with σ-linked organic groups are in many cases complicated by the fragmentation of the latter. The nature and degree of fragmentation of complexes of the type $CpM(CO)_xR_y$, [61,106-111] $Cp_2M(CO)_xR_y$, [11,112-115] and $CpMX_xR$ [116,117] (where X = fluorine, chlorine, bromine, or iodine atoms and R = organic or inorganic groups) are largely determined by the dimensions and stability of the organic groups linked by σ-bonds to the metal atom and also by the amount of ionic character of the metal–group and metal–halogen bonds [117]. The ion $CpMC_7H_7^+$, containing a π-linked tropylium cation, which is absent from the mass-spectrum of the corresponding fluorinated complex, has been detected in the mass-spectra of complexes containing the $CH_2C_6H_5$ group [110].

Heteronuclear Complexes

The so called heteronuclear metal complexes, namely compounds with σ-bonds between atoms of a transition metal and elements of the main Groups, exhibit somewhat unusual behaviour.

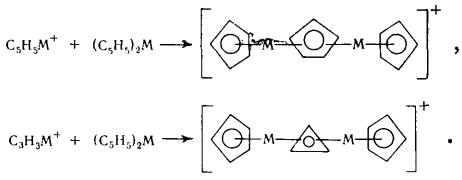
Under electron impact, extensive rupture of the metal–element bond takes place in such compounds simultaneously with the elimination of the ligand species. The charge is then retained preferentially by the fragment containing atoms of the elements of the main Groups. Thus in the mass-spectra of compounds of the type $CpM(CO)_mEX_n$ (where E = mercury, silicon, germanium, or tin; X = halogen atoms or organic groups) [62,90,118,119] and the compounds $CpRu(AsPh_3)_2SnCl_3$ [120] and $[HgM(CO)_nCp]_2$ [90,119] (M = Co or Fe) the peaks of ions containing a mercury, germanium, silicon, or tin atom are the most intense, while in the mass-spectra of the molybdenum and tungsten complexes $Et_2GeM(CO)_3Cp$ [121] the peaks of ions containing the M–Ge groups have the highest intensity.

Thus the mass-spectra of the metal complexes reflect the differences in the strength and nature of the metal–ligand and metal–metal bonds as well as structural and other differences. The principal characteristics of the mass-spectra of compounds of this class are a function of the electron-donating activity of the ligand and the atomic number of the complex-forming element. On the other hand, compounds of this type have features which will be discussed in the next section.

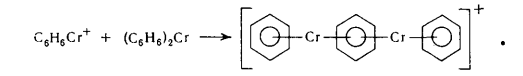
V. CHARACTERISTICS OF THE MASS-SPECTRA OF METAL π-COMPLEXES AND PROBLEMS OF THE ISOTOPIC ANALYSIS OF ELEMENTS IN THE FORM OF THEIR π-COMPLEXES

Ion–Molecule Reactions

One of the distinctive features of the complexes under consideration is their capacity to enter into ion–molecule reactions. At a pressure in the region of the ion source of $10^{-5}-10^{-6}$ mmHg, the mass-spectra of metal π-complexes can show peaks due to ions with a mass number exceeding the molecular weight of the complex. Thus, in a study of the mass-spectra of ferrocene and a mixture of ferrocene and nickelocene peaks due to the ions $Cp_3Fe_2^+$ and Cp_3FeNi^+ as well as peaks due to ions formed on their fragmentation with ejection of the cyclopentadienyl group were observed [122]. These ions, for which a double sandwich structure was suggested, are formed in the ion source of the mass-spectrometer as a result of the ion–molecule reactions



Similar reactions are characteristic also of other dicyclopentadienyl compounds, in particular of dicyclopentadienylchromium [123]. Bisbenzenechromium is also capable of forming ion–molecule association complexes [123]:



Both consecutive loss of ligand species and partial fragmentation of the cyclopentadienyl groups, mainly the elimination of ethylene and acetylene molecules with formation of the fragments $Cp_2C_3H_3M^+$, $CpC_3H_3M^+$, etc., are characteristic of the secondary ions Cp_3M^+, while the ion $(C_6H_6)_3Cr_2^+$ splits off only benzene molecules and there is virtually no partial fragmentation of the ligand species.

The mass-spectra of $CpM(CO)_n$ (M = V, Mn, or Co) [124] and $CpCr(NO)(CO)_2$ [123] contain peaks due to the ions $Cp_2M_2(CO)_n^+$ and $Cp_2M_2(CO)_n(NO)^+$ (formed as a result of reactions between ions and neutral molecules), which successively lose CO, NO, and cyclopentadienyl groups. As for the ions Cp_3M^+, a characteristic feature of these ions is the fragmentation of the cyclopentadienyl ligand species π-linked to the metal atom. The secondary ion $(C_6H_6)_2Cr(CO)_3^+$ behaves similarly in the mass-spectrum of benzenetricarbonylchromium [123], but there is no partial fragmentation of the C_6H_6 groups. Clusters containing three and more metal atoms are observed. Ion–molecule association complexes of this kind are characteristic also of trinuclear complexes [125].

Ion–molecule reactions of another type involve the addition of fluorides (PF_3, AsF_3, SbF_3, SF_4, and NF_4) to the metal-containing ions in the mass-spectrum of $CpMn(CO)_3$. [126]

Rearranged and Metastable Ions

Another characteristic feature of metal π-complexes is their capacity to form rearranged ions with fairly intense mass-spectral peaks.

Thus the rearranged ions MH^+ are as a rule absent from the mass-spectra of metal complexes with aromatic and π-acceptor ligands. However, in the mass-spectra of complexes containing σ-linked organic groups the intensity of peaks of ions of this kind is high, particularly in the case of fluorinated groups [91,109]. This can be explained by the higher strength of the metal–fluorine bond compared with the metal–hydrogen bond.

Another type of rearrangement processes characteristic of metal π-complexes are those involving the migration of cyclopentadienyl groups. In the mass-spectra of dinuclear compounds with one cyclopentadienyl group at each metal atom there are peaks due to the Cp_2M^+ ions [94,127]:

$$CpCr_2S_2Cp^+ \rightarrow Cr_2Cp^+ .$$

The cyclopentadienyl group can migrate also to a heteroatom σ-linked to the atom of the complex-forming element. Thus in the mass spectrum of $Cp(CO)_2FeSn.Cl_2Fe(CO)_2Cp$ the intensity of the peaks of the rearranged ion $CpSnCl^+$ is maximal [90]. Trialkylgermylmolybdenum and trialkylgermyltungsten complexes $Cp(CO)_3MGePh_3$, the mass-spectra of which show the presence of the $CpGe^+$ ion, behave analogously.

In many instances rearrangement processes lead to the formation of ions containing a metal–metal bond [128,129]:

$$Cp(CO)Fe(CO)_2Fe(CO)Cp^+ \rightarrow Cp_2Fe_2^+ ,$$
$$(CO)_5MnHgMn(CO)_5^+ \rightarrow Mn_2(CO)_n^+ .$$

A characteristic feature of the mass-spectra of π-complexes is also the unusually great abundance of peaks due to metastable transitions. Intense, distinct peaks accompany processes involving the abstraction from the molecular ions of cyclopentadienyl and carbonyl groups and benzene molecules:

$$CpM(CO)_n^+ \rightarrow CpM(CO)_{n-1}^+ + CO ,$$
$$C_6H_6M(CO)_n^+ \rightarrow C_6H_6M(CO)_{n-1}^+ + CO ,$$
$$Cp_2M^+ \rightarrow CpM^+ + Cp ,$$
$$(C_6H_6)_2M^+ \rightarrow C_6H_6M^+ + C_6H_6 .$$

Very intense peaks are observed also for metastable transitions accompanying the fragmentation of the cyclopentadienyl groups:

$$Cp_2M^+ \rightarrow CpMC_3H_3^+ + C_2H_2 ,$$
$$CpM^+ \rightarrow C_3H_3M^+ + C_2H_2 .$$

Still more intense metastable transition peaks accompany the decomposition of the fragment ions:

$$C_6H_6M^+ \rightarrow M^+ + C_6H_6 ,$$
$$C_5H_5M^+ \rightarrow M^+ + C_5H_5 .$$

The metastable transition peaks are diffuse and the corresponding apparent mass is determined from the relation [6]

$$m^* = \frac{m_2^2}{m_1} ,$$
$$m_1^+ = m_2^+ + (m_1 - m_2) .$$

Characteristics of the Mass-spectra of Polyisotopic Metal Complexes

Acton was the first to employ volatile metal carbonyls and their derivatives to investigate the natural abundance of metal isotopes [130]. (Acton's studies have been reviewed in detail by Bruce [1].) Transition metal π-complexes also constitute a convenient means for the investigation of isotope composition. Using cyclopentadienyl compounds, the natural abundance of ruthenium isotopes was investigated [131] and the relative amounts of vanadium and rhenium isotopes were checked. The presence in the mass-spectra of π-complexes of intense peaks due to the metal ion and the satisfactory agreement of these peaks with the isotope ratio make it possible to employ π-complexes for the isotopic analysis of metals.

No less important is the problem of the identification of ions in the mass-spectra of π-complexes. The identification of ions in the mass-spectra obtained on low-resolution apparatus is frequently extremely difficult. Such difficulties are somewhat diminished in the case of organometallic compounds. The differences between the relative concentrations of isotopes in the π-complexes of polyisotopic transition metals lead to the formation of different characteristic molecular and fragment ions, represented by a group of peaks the intensities of which agree satisfactorily with the isotope ratio. This greatly facilitates the identification of the metal-containing ions in low-resolution mass-spectra.

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Catalysts for the Oxidative Ammoniolysis of Propene

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The effect of the electronic structure of the lattice cations, of the environment of the adsorption centres, of the relative positions of the propene and oxygen adsorption centres, of the electronic work function of the solid, and of the acidity of its surface on the activity of catalysts for the oxidative ammoniolysis of propene is examined on the basis of the literature data. The bibliography includes 185 references.

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I. INTRODUCTION

The development of the manufacture of polymeric materials, synthetic fibres, synthetic rubber, dyes, physiologically active substances, and other products of organic synthesis has led to the appearance of new effective methods for the conversion of petrochemical and coke-chemical raw materials into valuable polyfunctional organic compounds. These include oxidative ammoniolysis—an effective method for the synthesis of nitrogen-containing compounds developed recently [1-3].

The high selectivity, universality, and low cost of oxidative ammoniolysis make it one of the most promising new large-scale chemical processes. The list of nitrogen-containing substances obtained with the aid of oxidative ammoniolysis already includes several tens of names and processes such as oxidative ammoniolysis of methane [1], propene [2-4], isobutene [5], and aromatic compounds (toluene, xylene) [3,6-8] are now employed on an industrial scale.

The oxidative ammoniolysis of olefins has acquired particularly great industrial importance. It is sufficient to point out that acrylonitrile is nowadays manufactured from propene in about 30 plants with an overall output of more than 1.5 million tonnes per year in countries including the USA (in seven plants with an output of 616 000 tonnes) [8] and Japan (in nine industrial combines with an output of 670 000 tonnes per year) [9].

The studies published in recent years [1,2,10,11,12] reflect fairly completely the bulk of patent information concerning the catalysts for the oxidative ammoniolysis of propene. In Table 1 this compilation is supplemented by data from patents and the periodical literature published during 1968–1972.

Judging from the literature data, among the large number of a wide variety of compounds employed as catalysts for the synthesis of acrylonitrile only the bismuth phosphomolybdate catalyst [4,12], the uranium–antimony catalyst, (the so called catalyst-21), [52] and the iron–antimony catalyst [89] have found industrial applications. All these catalysts are made from metasilicic acid gel. The ASAHI Company improved the bismuth phosphomolybdate catalyst by incorporating iron compounds in its composition, thereby increasing the yield of acrylonitrile obtained to 72–76%. [27]

Societa Edison S.p.A. (Italy) employs the catalyst prepared from the highest oxides of tellurium, cerium, and molybdenum on silica gel [73] and SNAM Progetti S.p.A. employs vanadium and bismuth molybdates [90]. A catalyst in the presence of which the yield of acrylonitrile increases to 80–82% was developed recently by the Sohayo Company [sic], [91] but its composition was not disclosed.

Despite many studies on the preparation and properties of catalysts for the oxidative ammoniolysis of propene, the search for new effective catalysts for this process as well as for the mild selective oxidation of hydrocarbons is still continuing, largely by empirical procedures. There have been only a few studies in which relations were discovered whereby it is possible to regulate the catalytic properties of substances in these processes.

According to Lazukin et al. [92], the oxide catalyst "inherits" the activities and selectivities of its components. In order to obtain an effective catalyst, it is necessary to combine a highly active but relatively unselective metal oxide with a relatively inactive but highly selective oxide.

Alkhazov [93] believes that catalysts for the oxidative dehydrogenation of olefins can be formed only by combining in pairs oxides in the "highly isomerising and moderately oxidising" group.

According to the data of Kolovertnov and Boreskov [94], the catalytic activity of binary oxide catalysts for the oxidation of methanol to formaldehyde is a function of the amount of ionic character of the M–O bond determined from the ionisation constants of metal hydroxide compounds. The activity and selectivity of individual molybdates and vanadates are determined mainly by molybdenum and vanadium, which form part of the salt anion. The cation, stabilising the hexavalent or quinquevalent state of molybdenum or vanadium, regulates the activity.

A similar view has been expressed by Sachtler and Dorgelo [95], who investigated the oxidation of benzaldehyde to benzoic acid in the presence of the SnO_2–V_2O_5 catalyst. The authors believe that tin dioxide promotes the stability of the quinquevalent state of vanadium.

It has been suggested [96,97] that the catalytic properties of effective catalysts for the oxidation and oxidative ammoniolysis of olefins are due to the presence in their composition of doublets comprising different or identical cations. Batiste et al. [98] believe that, for mild oxidation

Table 1. Catalysts for the oxidative ammoniolysis of propene.

Catalyst	Carrier	Conditions governing the preparation of catalyst	Reaction conditions	Process parameters	References
Bismuth phosphomolybdate Bi:Mo:P = 9:1 2:1	Metasilicic acid gel	Joint precipitation and pelleting with formation of the compound $(Bi_9PMo_{12}O_{52})_x(SiO_2)_y.SiO_2$ content 50%	420-550°, $C_3H_6:NH_3:O_2:H_2O$(vapour) = 1.0:1.0:1.8:3.5, fluidised bed	Conversion 80%. Selectivity 65%	12,13
Bismuth phosphomolybdate with added cobalt and nickel oxides		Mixing of solns. of bismuth and cobalt (nickel) nitrates, ammonium paramolybdate, and phosphoric acid. Heat treatment for 12 h at 550°	$C_3H_6:NH_3$:air = 10:11:110, contact time 1-20 s	Yield of acrylonitrile 62%	14-16
Bismuth phosphomolybdate	Silica gel	Impregnation of silica gel with soln. containing the active components	$C_3H_6:NH_3:O_2:H_2O$(vapour) = 1.0:1.1:1.2-1.8:1.0-4.0, stationary bed, 480°, contact time 1.5-5.0 s	Conversion 70% Selectivity 60%	17,18
	Modified silica gel	Deposition of components from the same nitrate soln. Content of active components 12-14 wt.%	Fluidised bed, contact time 6 s	Conversion 85% Selectivity 60%	19
Bismuth phosphomolybdate	Corundum, porosity 32%	Impregnation of corundum with a soln. containing the active components	$C_3H_6:NH_3:O_2:H_2O$(vapour) = 1.0:1.0:1.9:6.2, 450-500°	Conversion 60% Selectivity up to 80%	20,21,22
	Corundum	Heat treatment of alumina at 1750°. Joint pelleting with bismuth phosphomolybdate in the presence of a carrier content of 85%	Data not available		23
Iron-modified bismuth phosphomolybdate (A-112 catalyst, Japan)	Metasilicic acid gel	Joint precipitation of active compound having the atomic ratio Bi:Fe = 1:12:3:5 with metasilicic acid gel	450-500°, fluidised bed	Conversion up to 92% Selectivity 68%	23-27
Iron-modified bismuth phosphomolybdate with added lead	Metasilicic acid gel	Joint precipitation of active compound $Pb_2Bi_4Mo_{12}Fe_9P$ with metasilicic acid gel	450°, contact time 1.2 s	Yield up to 52%	28
Bismuth antimonate		Preparation of bismuth antimonate $Bi_2O_3.Sb_2O_5$	450°	Conversion 10% Selectivity 10%	29
Mixture of bismuth antimonate and molybdate		Preparation of catalyst containing 65% of bismuth molybdate and 35% of bismuth antimonate	470°	Conversion 58% Selectivity 90%	29-31
Mixture of bismuth antimonate and molybdate		Preparation of catalyst by mixing soln. of bismuth nitrate, ammonium paramolybdate, and antimony perchlorate	450-470° $C_3H_6:NH_3$:air:H_2O(vapour) = 1.0:1.0:7.0:1.0	Conversion 60% Selectivity 85%	32-36
Mixture of bismuth antimonate and molybdate	Alumina	Impregnation of carrier with soln. containing the active components. Carrier content 50-80%	Data not available		37
Mixture of bismuth antimonate and molybdate with added tin dioxide	Silica gel, 10-60%	Precipitation of bismuth antimonate on mixing $Bi(NO_3)_3$ and Sb_2O_3 solns. in HNO_3 Bismuth antimonate mixed with bismuth molybdate: SnO_2, SiO_2. $BiSbO_4:SnO_2:Bi_2(MoO_4)_3$ = 60:40:5-50	$C_3H_6:NH_3:O_2:H_2O$ = 1.0:1.0:1.4:1.0, contact time 11.2 s	Conversion 60% Selectivity 91%	38-40
Mixture of As, Mo, and W oxides		Mechanical mixture (0.1-20 wt.% As_2O_5, 1.50 wt.% WO_3, 1-50 wt.% MoO_3)	$C_3H_6:NH_3:O_2$ = 1.0:1.2:1.5-5.0, 450-500°, 480°, contact time 10-40 s, fluidised bed	Yield of acrylonitrile 58% and 60-62%	40 41-44
Mixture of As, Mo, and W oxides	Silica gel, alumina	Impregnation of carrier by aqueous soln. of Mo, As, and W compounds. Drying at 100-200° and heat treatment at 400-450°	480°, As_2O_5 introduced into gaseous mixture	Yield up to 72%	45-46
Mixture of bismuth or antimony compounds		Mixing of the compounds $Sb(VO_3)_3$ and $SbPO_4$ or $Bi(VO_3)_3$ and $BiPO_4$, treatment of mixture at 500°	450-480°	Yield 45%	47-48
Uranium-antimony catalyst		Mixing of uranyl nitrate and antimony perchlorate solns., ratio in precipitate Sb:U = 1-50:2-100	480°, contact time 5-10 s, fluidised bed	Yield 62-64%	49-51
Mixture of spent uranium oxide with antimony oxide		Catalyst 21		Yield 62%	52
Uranium-antimony catalyst	Alumina	Impregnation of carrier by soln. containing uranium and antimony salts	480°	Yield 60%	53
Antimony-tin catalysts with atomic ratio Sn:Sb = 0.1-10:1.0-20.0		Mixing of solns. of antimony and tin chloride pptn. with ammonia, heat treatment of ppt. at 500-700°	470°, contact time 4 s, $C_3H_6:NH_3:O_2:H_2O$(vapour)= 1.0:1.0:1.2:6.0	Selectivity 65% Yield 51-52%	54,55
Solid soln. of tin(IV) oxide in antimony oxide with atomic ratios Sn:Sb = 1.0:1.0 and Sn:Sb = 0.25:1.0		Mixing of solns. of antimony and tin chlorides drying at 140°, and heat treatment at 800°	480°, contact time 0.8-1.5 s, $C_3H_6:NH_3:O_2:H_2O$(vapour) = 1.0:1.0:1.5:2.0	Yield 41-42%	56,57
Iron-antimony catalyst		Preparation of iron antimonate containing 55 at.% of antimony	480°, $C_3H_6:O_2$ = 1:6	Selectivity 80-82%	58,59

Table 1 (contd.)

Catalyst	Carrier	Conditions governing the preparation of catalyst	Reaction conditions	Process parameters	References
Iron-antimony catalyst		Mixing of solns. of antimony and iron chlorides. Heat treatment of ppt. for 16 h at 650°. Atomic ratio Sb:Fe from 1:50 to 99:1	480-500°, contact time 0.5-10 s, $C_3H_6:NH_3:O_2:H_2O$(vapour) = 1.0:1.2:1.5:1.2	Conversion 74% Selectivity 70%	60,61
Iron-antimony catalyst	Metasilicic acid gel	Joint precipitation of iron nitrate and antimony chloride with silica soln. Drying at 120° and heat treatment at 750°	450-550°, $C_3H_6:NH_3:O_2$ = 1:1.2:1.2-5.0	Selectivity 70%	60-62,68
Iron-antimony catalyst	Pumice	Impregnation of pumice by solns. containing iron and antimony compounds	$C_3H_6:NH_3$:air:H_2O(vapour) = 1.0:1.1:7.5:1.0	Selectivity 80%	63
Iron-antimony catalyst with added Mo(W) and B(P)		Preparation of compound by precipitation on mixing solns. of $Fe_aSb_bMo_c.X_dO_e$, where X = P or B, a = 10, b = 5-60, c = 0.5-1, and d = 0.005-1.0	$C_3H_6:NH_3:O_2$ = 1:0.5:0.5-5.0 480°	Selectivity 80%	64-67
Iron-antimony catalyst with added vanadium		Preparation of compound with the conventional formula $Fe_aSb_bV_cX_dO_e$, where X = P or B, a = 10, b = 5-80, c = 0.01-2, and d = 0-2. Catalyst activated by heating for 2-24 h at 600° and for 20 h at 700-1000°	480-500°	Yield 60%	69-70
Tin molybdate with atomic ratio Sn:Mo = 9:1		Mixing of ammonium molybdate and tin(II) chloride soln., heat treatment of ppt. at 500°	Contact time 7 s, $C_3H_6:NH_3:O_2:H_2O$(vapour) = 1.0:1.0:1.2:1.0	Conversion 75% Selectivity 65%	71
Bismuth molybdate + TeO_2	Silica gel	Joint pelleting of bismuth molybdate and tellurium oxide with silica gel	400-500°, contact time 0.5-15 s $C_3H_6:NH_3$ = 2.0-1.0:0.6-1.0	Selectivity 85%	73
Mixture of tellurium, lanthanum (cerium), and molybdenum oxides		Mixing of lanthanum nitrate with telluric acid, heat treatment at 500°		Selectivity 70%	73
Mixture of tellurium and molybdenum oxides	Silica gel	Deposition from soln. containing active components. Drying at 120° and heat treatment at 450°	$C_3H_6:NH_3:O_2:H_2O$(vapour) = 1.0:1.0:2.0:2.5, contact time 6 s	Yield 32%	74-76
Mixture of tellurium and molybdenum oxides with added phosphorus		Mixing and evaporation of aqueous solns. of ammonium molybdate, phosphoric acid, and telluric acid. Heat treatment at 420°	480°, contact time 3 s	Selectivity 80% Conversion 70%	77-80
Vanadium molybdate	Metasilicic acid gel	Joint deposition of silica soln. with molybdenum and vanadium oxides. Heat treatment at 400-500°	$C_3H_6:NH_3:O_2:H_2O$(vapour) = 1.0:1.0:1.5:1.2, fluidised bed, 400-500°	Conversion 71% Selectivity 80%	81-83
Copper phosphate	Silica gel	Impregnation of silica gel by copper pyrophosphate or triphosphate solns.	450-480°	Conversion 40%	84
Iron and bismuth phosphates			$C_3H_6:NH_3:O_2:H_2O$(vapour) = 1.0:1.2:2.0:2.0, 480°	Conversion 70% Selectivity 68%	85
Solid phosphoric acid		Mixture of titanium, molybdenum, iron, cobalt, vanadium, bismuth, etc. phosphates	500°	Conversion 30%	86
Copper phosphate	Borophosphate	Impregnation by soln. of copper nitrate and phosphoric acid		Selectivity 67%	87
Iron-containing zeolite	NaX	Ion exchange between NaX zeolite and iron thiocyanate soln.. Degree of exchange 50%	480°	Conversion 40%	88

of hydrocarbons on the surface of the catalyst, the formation of two kinds of anionic vacancies linked to the doublet centre is necessary. Unfortunately the hypothesis of the existence of doublet centres, responsible for the selective oxidation of olefins, is based only on the chemical composition and the determination of catalytic activity and requires additional evidence.

The molybdenum–oxygen plays a major role in catalytic oxidation reactions. The Mo=O bond in various metal molybdates is more reactive than other bonds [99,100]. A similar view was expressed earlier in a study of the catalytic activity of vanadium catalyst by Tarama and Teranishi [101], who observed that catalysts containing the V=O double bond exhibit the highest activity in the oxidation of benzene.

Many investigators are now seeking various correlations between particular properties of catalysts and their relative activities with respect to a specific reaction or group of reactions. Correlations have been observed between catalytic activity and properties such as the electronic work function, electrical conductivity, the width of the forbidden gap in semiconductors, etc. However, each correlation embraces a very limited range of catalysts for which the chosen property is for some reason dominant. Moreover, this property reflects only partly the characteristics of the chemical interactions of the reactant molecules with the catalyst and with one another, which determine the catalytic effect. The most reasonable are attempts to relate catalytic activity to thermodynamic characteristics—the energies of the bonds broken and formed on formation of the activated complex in the rate-determining step [102].

However, none of these hypotheses can explain fully the mechanism of the action of complex catalysts for the oxidation of hydrocarbons. From this standpoint, it is interesting to analyse the extensive literature data on catalysts for the oxidative ammoniolysis of propene in order to elucidate the nature of the active surface and its role in the selectivity of the process.

II. SOME PROBLEMS OF THE MECHANISM OF THE OXIDATIVE AMMONIOLYSIS OF PROPENE

Several communications dealing with the mechanism of the oxidation and oxidative ammoniolysis of propene in the presence of mixed catalysts were published recently[2,3,12,103,104]. According to their results, the only rigorously proved fact is that the oxidative ammoniolysis of propene as well as its oxidation proceed via the formation of an allyl complex. The constancy of the isotope effect in the formation of acrolein and acrylonitrile[105] and also the identical reaction kinetics[106] enabled many investigators[103,105,106] to suggest that the rate-limiting stages in these two processes are the same.

The discovery of the relations governing the formation of the CN group in the oxidative ammoniolysis of various compounds enabled Rafikov and Suvorov[3,107,108] to put forward the hypothesis that in the case of organic compounds of the type RCH_3 nitriles and their amide precursors are formed mainly from aldehydes. The authors believe that nitriles can be formed also via an "amine" reaction pathway. The hypothesis concerning the role of aldehydes in the oxidative ammoniolysis of hydrocarbons has found confirmation in studies by other investigators[109-112], although some of them suggest that ammonia interacts with the carbonyl group via an aldimine mechanism[111].

On the basis of kinetic data for the individual stages in the oxidative ammoniolysis of propene, Germain and coworkers[103,104] and Callahan and coworkers[4] believe that acrylonitrile is only partly formed via acrolein, while the contributions of the "amine" and "aldehyde" pathways to the formation of nitriles as well as the escape of acrolein to the gas phase apparently depend markedly on the concentration of oxygen and ammonia in the catalyst zone and on the structure of the initial hydrocarbon. On the basis of his data obtained under the condition of a low oxygen concentration and a high water concentration, Germain suggested that acrylonitrile may be formed via a stage involving the formation of an adsorbed carbene having the structure $CH_2{=}CH{-}\ddot{C}H$.

However, the mechanism proposed by the author for this reaction was not proved unambiguously and is extremely hypothetical. Gorshkov and coworkers undertook a detailed study of the mechanism of the formation and further reaction of the intermediate and side products of the joint oxidation of propene and ammonia using the kinetic isotopic method[113], with a complete computer calculation of the mechanism of the oxidation of propene[114] and the individual carbonyl compounds[115] with simultaneous evaluation of the rate constants for the individual stages. The experimental results suggested a possible process mechanism involving a number of stages[116], according to which a major role is played by the successive reaction of certain oxygen-containing compounds formed in the interaction between adsorbed oxygen and the hydrocarbon, which are desorbed from the surface in the form of aldehydes. According to a study[117] on the adsorption of propene and acrolein at 200° and 300°C on the surface of molybdenum catalysts using infrared spectroscopy, such oxygen-containing compounds are carbonyl-containing complexes coordinated to the surface via the double bond and via the carbon atom of the aldehyde group.

A significant distinctive feature of the proposed mechanism is also the demonstration of the formation of acetaldehyde and formaldehyde, like acrolein, via an allylic compound. Since it has been shown by the kinetic isotope method[113] that the intermediate in the formation of these compounds is the same, they are probably produced on the same active centres of the catalyst surface. The different modes of reaction of the intermediate are probably determined by the different energies of the bond between oxygen and the surface of the catalyst and the number of oxygen atoms involved in the formation of the surface carbonyl-containing compound. It has also been established[114-116] that carbon oxides are formed by the subsequent oxidation partly of the surface carbonyl-containing compounds and partly of the desired nitrogen-containing products via a parallel-consecutive mechanism, with the successive pathway predominating.

Infrared spectroscopic data on the oxidation of ammonia in the presence of certain metal oxides[118] and also for its adsorption on the oxidised surface of molybdenum catalysts[119] suggest that an oxygen containing complex of the type $H_2N{-}O{-}M$, adsorbed on the surface, is the most reactive. This complex probably plays a major role in the oxidation [of ammonia ?] and possibly in the oxidative ammoniolysis of propene. Similar ideas concerning the formation of NH_2 radicals bound to the surface in the presence of molecular oxygen have been put forward in other investigations[120-122].

The study of the adsorption of propene–ammonia–oxygen and acrolein–ammonia–oxygen mixtures in different sequences on the surface of molybdenum catalysts using infrared spectroscopy and a comparison of the resulting spectra with those of allylamine and acrylonitrile adsorbed under analogous conditions was undertaken[123]. The similarity of these spectra apparently confirms the hypothesis that acrylonitrile may be formed in the oxidative ammoniolysis of propene either via an intermediate surface amine compound, produced when the adsorbed propene interacts with ammonia adsorbed on top of oxygen, or via an oxygen-containing surface complex of the carbonyl type with subsequent addition to the latter of an oxygen-containing complex of ammonia and the formation of an amide.

The results are satisfactorily consistent with the calculations[124] by the LCAO-MO method of the energy scheme for the elimination of individual hydrogen atoms and the addition of oxygen and nitrogen atoms to the hydrocarbon residues in the formation of acrylonitrile on the surface of molybdenum trioxide. It was found that the pathways leading to the formation of acrylonitrile via the intermediate formation of compounds of the carbonyl or amine type are energetically equivalent.

Thus in the interaction of propene, oxygen, and ammonia with the catalyst surface dissociative adsorption of the olefin takes place with formation of an allylic surface compound[125-127] and probably of an oxygen-containing ammonia complex[119]. The allylic surface compound can be subsequently converted into an oxygen-containing surface complex of the carbonyl type, which can be desorbed into the gas phase in the form of the aldehyde or can react further with the oxygen-containing ammonia complex to form a surface amide. Moreover, the allylic surface compound can itself react with ammonia adsorbed on top of the surface oxygen with formation of an amine surface compound.

III. THE EFFECT OF THE ELECTRONIC STRUCTURE OF LATTICE CATIONS ON THE ACTIVITY OF THE CATALYSTS

It is believed[128] that the metal ions in the crystal lattice behave as hydrocarbon adsorption centres. In connection with the hypothesis that the dissociative chemisorption of propene entails the formation of a π-complex

which is subsequently converted into a π-allyl complex[125], it is necessary to examine the effect of various metal ions on the formation of complexes with olefins and to elucidate the relation between the stability of these complexes and catalytic activity.

Olefins are known to form π-complexes with vanadium, chromium, molybdenum, and cobalt[129] and π-allyl complexes with molybdenum, tungsten, cobalt, and iron[130].

Indeed, it has been shown for iron-containing zeolites[88] that iron ions can catalyse the oxidation and oxidative ammoniolysis of propene, the selectivity of these reactions depending on the distribution of the ions in the matrix and on their oxygen environment[131,132]. Presumably propene is capable of forming π-allyl complexes with iron ions like ethylene in its adsorption on silver ions in silver-zeolites[133]. If the oxygen adsorbed on the surface of the zeolite is sufficiently mobile, as happens on alumina[134], the oxidation and oxidative ammoniolysis of propene are possible.

It has been suggested[135] that the chemisorption of propene is determined by the formation of a donor-acceptor bond with a catalyst lattice cation as a result of the withdrawal of the double bond π electrons into the vacant d orbitals of the transition metal atoms. The adsorbed molecules are then positively charged.

On the other hand, the symmetry of the antibonding olefin orbital and the transition metal d orbitals promotes their interaction[136], as a result of which the positive charge produced is partly compensated by the withdrawal of the catalyst electrons into the π orbital. On this basis, it is suggested[135,136] that the electronic structure of the metal ions determines the bonding energy of the olefin in the complex.

Application of crystal field theory to the study of the catalytic activity of transition metal oxides in various reactions[136,137] led to the observation that maximum catalytic activity corresponds to the maximum stabilisation by the crystal field with increase of the coordination number, the maximum rate of catalysis corresponding to the following elements: Cr(d^3), Co(d^7), and Cu(d^9).

Data for the extensive oxidation of propene also show that metal oxides containing chromium, cobalt, and copper exhibit the highest activity[138], i.e. there is some correlation between the rate of the catalytic reaction and complex formation.

Data have been published[71,139] concerning the change of catalytic activity in the oxidative ammoniolysis of propene in relation to the formation of acrylonitrile, carbon dioxide, and the molybdates[71] and phosphates[139] of various metals in the Fourth Period as a function of the number of unfilled d levels. Fig. 1 shows that the catalytic activity of the molybdates falls on passing from the first to the last element of the Fourth Period. The maximum rates of formation of acrylonitrile and carbon dioxide are observed in the presence of iron phosphate; the activities of cobalt, nickel, and manganese phosphates are low. The data presented in Fig. 1 evidently demonstrate that there is no correlation between the catalytic activity in the oxidative ammoniolysis of propene and the maximum stabilisation of the complexes by the crystal field. The difference between the activities and selectivities of the compounds investigated in this reaction cannot be accounted for by the presence of a number of unfilled metal d orbitals.

Moreover, the experimental data obtained under analogous conditions for the catalytic activities of various mixed oxide systems showed that the compounds formed when tin ($5s^25p^2$) and lead ($6s^26p^2$) oxides are mixed with bismuth ($6s^26p^3$) oxide do not catalyse the oxidative ammoniolysis of propene[140]. It was natural to conclude that none of the above metals are active catalysts of this process, because their cations do not contain vacant d levels. However, solid solutions of tin and antimony ($5s^25p^3$) oxides proved to be extremely active and selective catalysts of the oxidative ammoniolysis although tin and antimony atoms do not contain unfilled d orbitals either.

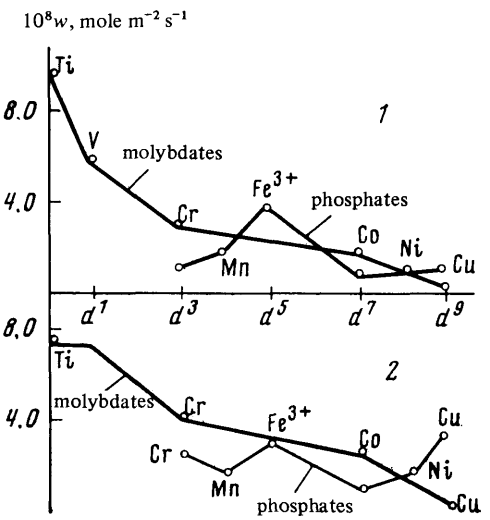

Figure 1. Dependence of the catalytic activity of molybdates[71] and phosphates[139] in the formation of acrylonitrile (1) and carbon dioxide (2) in the oxidative ammoniolysis of propene on the number of unfilled d levels in the lattice cations.

The possibility of the formation of unfilled d levels in the adsorption of oxygen on non-transition metals has been discussed in the literature[141]. For example, in the presence of oxygen silver behaves as a transition metal with this type of structure, acquiring the ability to chemisorb ethylene[142]. Oxygen binds the s electrons of silver and enables some of the d electrons to pass to the s and p levels. In this case catalysts containing, tin, antimony, and copper should be active and selective. However, it has been shown[140] that in the presence of stannates only extensive oxidation of propene takes place, while in the presence of bismuth antimonate the rate of formation of acrylonitrile is low.

Nor does the presence of cations with unfilled d levels influence the oxidation of ammonia under the conditions of the oxidative ammoniolysis of propene. The catalytic activities of various metal oxides in the oxidation of ammonia under the conditions of the oxidative ammoniolysis of hydrocarbons have been determined[143]. The maximum catalytic activity was observed in the presence of the oxides of cobalt (d^7), manganese (d^5), chromium (d^3), and copper (d^{10}), but complex catalysts containing these oxides do not exhibit an appreciable activity in the joint oxidation of propene and ammonia[140].

Thus the formation of a complex of the catalyst and the olefin requires that the catalyst contain a metal ion with a specific electronic structure. However, in the oxidative ammoniolysis of propene as well as in its oxidation[144] a correlation between the reaction rate and the stability of the metal–olefin complexes has not been observed. Such complexes are probably not the controlling intermediates in this process, oxygen being involved in its rate-limiting stage with formation of oxygen–hydrocarbon complexes.

Indeed, a Mössbauer study of the formation of a surface compound in the adsorption of propene and acrolein on the surface of an Sn–Mo–O catalyst showed[145] that the linkage between the chemisorbed organic molecule and the ion is formed via oxygen.

Moreover, as stated above, a study of the adsorption of propene on the oxidised surface of molybdenum catalysts for the oxidative ammoniolysis of propene revealed the presence of oxygen-containing complexes of the carbonyl type[117]. Oxygen also takes part in the formation of a reactive oxygen-containing ammonia surface complex.

For this reason, in the analysis of the nature of the active surface of catalysts for the oxidative ammoniolysis of propene particular attention must be paid to the type of bond between oxygen and the catalyst and to its reactivity.

IV. THE EFFECT OF THE ENVIRONMENT OF THE CATIONS IN THE CRYSTAL LATTICE ON CATALYTIC ACTIVITY

Many investigators[102,146,147] believe that the differences between the catalytic activities of oxides in oxidation reactions can be explained by the differences between the oxygen binding strengths in these oxides. The rate of oxygen isotope exchange between the gas phase and the oxide can serve as a measure of the reactivity of the oxygen in the surface layer of oxides. The mobility of oxygen in transition metal oxides frequently increases when they are mixed with oxygen derivatives of other elements. For examples, Boreskov and coworkers[148] established that potassium sulphate increases sharply the mobility of oxygen in vanadium pentoxide.

Skalkina[150] and Gel'bshtein and coworkers[151] compared the activation energies for the isotope exchange of the lattice oxygen determined for iron[149], cobalt[152], and bismuth[153] molybdates, iron and tin[154] antimonates, and molybdenum oxide[153] with the catalytic activities of these compounds in the formation of acrylonitrile by the oxidative ammoniolysis of propene. They concluded that the optimal M–O bond energy is 80–90 kcal mole^{-1}.

Such high M–O bond energies probably indicate that the lattice oxygen has a low probability of being involved in the rate-limiting reaction step, since the activation energy for the reaction does not exceed 20 kcal mole^{-1}. However, this oxygen can serve as a centre for the adsorption of the hydrogen split off in the dissociative adsorption of propene or can participate in the formation of certain other intermediates in the oxidation of propene.

Sachtler and De Boer[125] chose the rate of the partial reduction by hydrogen of various mixed catalysts as a criterion for the assessment of the lattice oxygen binding strength (ΔHM-O) in mixed oxide catalysts for the oxidation of propene, since ΔHM-O is proportional to the activation energy for the reduction reaction (Fig. 2). They estimated the rate of reduction from the quantity $10^3/T_\tau$, where T_τ is the temperature at which identical degrees of reduction are attained. Fig. 2 shows that the higher the capacity of the catalyst for reduction, i.e. the lower the metal–oxygen bond strength, the higher the degree of conversion of the hydrocarbon and the lower the process selectivity. Gel'bshtein and coworkers[155] measured the initial rate of reduction by propene of bismuth–molybdenum catalysts for the oxidative ammoniolysis of propene at 450°C and a pressure of 80 mmHg and showed that the maximum rate is observed for molybdenum oxide and the minimum for bismuth oxide. Bismuth molybdates of different compositions are reduced by the olefin at rates lower than the rate of reduction of molybdenum oxide.

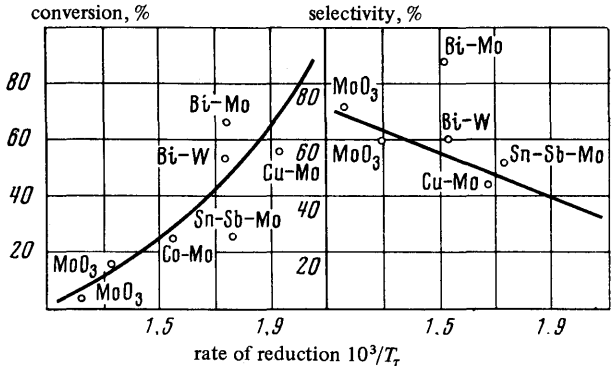

Figure 2. Dependence of the activity and selectivity of complex oxide catalysts in the oxidation of propene on their degree of reduction (T_τ is the temperature at which equal degrees of conversion are attained)[125].

Kolchin[11] also investigated this type of relation for various catalysts of the oxidative ammoniolysis of propene. Fig. 3 shows the variation of the degree of conversion and process selectivity with the rate of reduction of various complex oxide catalysts. Different relations between the rate of reduction and composition were obtained for molybdates and tungstates. Moreover, it is noteworthy that, according to Sachtler and De Boer's data[125] (Fig. 2), the activity and selectivity vary in opposition, while in another study[11] (Fig. 3) it was shown that they vary in parallel, albeit for a narrower range of catalysts. Evidently comparison of the catalytic properties of the substances for incomplete oxidation reactions with the values of ΔH_{M-O} is possible only within the limits of fairly small groups of selective oxidation catalysts and the optimal energy of the oxygen-catalyst bond is not the only factor responsible for the high activity and selectivity of the catalyst in the oxidative ammoniolysis of propene.

The energy of the bond between the metal ions forming part of the catalyst and oxygen varies as a function of the electronic structure of the ions. Mössbauer spectroscopy has shown[157] that, when the catalyst contains atoms of two different metals, the latter interact via oxygen: $M^I–O–M^{II}$. The effective charge of oxygen, i.e. the real charge within the space surrounding the oxygen atom, will depend on the difference between the electronegativities of these metals[158].

The catalytic activity of various compounds in the oxidative ammoniolysis of propene is determined by active centres of the same type and consequently is influenced

not by the bulk-phase charges but by the effective surface charges of oxygen, which depend on the difference between the electronegativities of the metal ions.

It has been shown for the oxidative ammoniolysis of propene [71] that the addition to the main oxide (of tin or iron) of another oxide containing a metal having a higher electronegativity (molybdenum or antimony) than that of the cation in the basic matrix alters the reaction pathway in the oxidative ammoniolysis of propene. Only carbon dioxide is formed in the presence of iron and tin oxides, while in the presence of solid solutions based on these oxide lattices acrylonitrile is obtained and the proportion of extensive oxidation falls. The authors conclude that the environment of the metal ion and the effective charge on the oxygen both change on formation of the solid solutions.

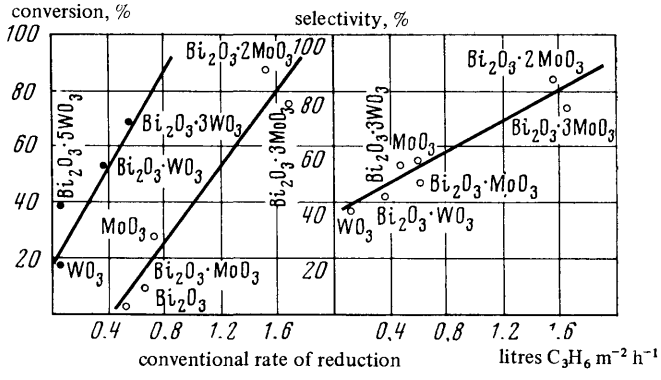

Figure 3. Dependence of the activity and selectivity of bismuth molybdates and tungstates in the oxidative ammoniolysis of propene on the rate of reduction of the catalyst [10].

In the determination of the catalytic activities of a large series of mixed oxide catalysts, Dalin et al. [159] drew attention to the fact that the highest selectivity is shown by catalysts in which there is a small difference between the ionisation potentials of the cation and the central atom of the anion. Evidently the difference between the ionisation potentials determines to some extent the amount of ionic character of the bond between the metal ion and oxygen. The isomeric shift δE of the Mössbauer spectrum, which is due to the change of the s electron density near the nucleus of the cation, can serve as a measure of the amount of ionic character of the bond.

Table 2 presents parameters of the Mössbauer spectra taken from the literature [160–162] (the isomeric shifts and the quadrupole splittings) for certain iron-containing compounds and the selectivities of the oxidative ammoniolysis of propene in the presence of such compounds. These data show that the dependence of the selectivity of the oxidative ammoniolysis on the amount of ionic character of the bond passes through a maximum. The highest selectivity is observed in the presence of iron phosphate and arsenate. A decrease and an increase of the number of s electrons in the Fe^{3+} ion both reduce the yield of acrylonitrile.

Another parameter of Mössbauer spectra, namely quadrupole splitting ΔEa, characterises the electric field gradient around the cation due to the distortion of the symmetry of the charge distribution within the crystal lattice. The electric field gradient depends on various factors, primarily on the type of bond, the crystal structure of the compound, and the electronegativity of the adjacent atoms.

Table 2. The isomeric shifts δE and the quadrupole splittings ΔEQ in the Mössbauer spectra of certain iron-containing compounds and the selectivity of oxidative ammoniolysis on their presence.

Compound	δE, mm s^{-1}	ΔE_Q, mm s^{-1}	Selectivity, %	References
$Fe_2(SO_4)_3$	1.42	0.0	9	139
Fe_2O_3	0.57	0.2	0	71
$FePO_4$	0.43	0.15	56	139
$Fe_2(CrO_4)_3$	0.34	0.38	0	71
$FeAsO_4$	0.49	0.2	50	163

Skalkina et al. [163] obtained the Mössbauer spectra of various complex oxide catalysts for the oxidative ammoniolysis of propene incorporating Fe^{3+} and Sn^{4+} ions and compared the quadrupole splitting with the activity and selectivity of the catalyst. Fig. 4 shows that the rate of extensive oxidation decreases monotonically with increase of ΔEQ, while in the mild oxidation reaction (the formation of acrylonitrile?) the rate passes through a maximum.

Since the iron(III) ion has the symmetrical electronic configuration $3d^5$, the electric field gradient at the nucleus is due solely to the external charges and is determined by the distortion of the lattice. Quadrivalent tin also has a symmetrical electronic configuration ($4d^{10}$). Thus in the given case ΔEQ characterises directly the charge distribution around the iron and tin atoms and affects the rate of reaction. For low values of ΔEQ, i.e. for slight distortions of the charge symmetry, carbon dioxide is is formed around the cation in the course of the oxidation of propene and, on further increase of ΔEQ, the formation of acrylonitrile begins. Since EM-O and qs increase with increase of ΔEQ, this can evidently be explained as follows. For low values of ΔEQ (E_{M-O} is small), a larger number of oxygen atoms enter into the reaction and extensive oxidation is observed, whereas on increase of ΔEQ a smaller number of oxygen atoms participate in the process and mild oxidation of the olefin begins. However, on further increase of ΔEQ, there is a rise in q_s also and the catalytic activity falls; the activation energy increases appreciably for these values of ΔE_q.

Evidently the differences between the ionisation potentials and quadrupole splitting both characterise the charge distribution around the cation and are probably related also to the M–O bond strength.

Apart from the oxygen adsorbed at the lattice ions, the oxygen surrounding the cation is probably also important in the oxidative ammoniolysis of propene; thus the replacement of oxygen in iron and copper oxides by sulphur and also the replacement of oxygen in vanadium pentoxide by boron, nitrogen, and carbon lead to the complete disappearance of catalytic activity in this reaction [139].

V. RELATIVE POSITIONS OF THE HYDROCARBON AND OXYGEN ADSORPTION CENTRES

According to the hypothesis of Callahan and Graselli[164], not only the electronic structure of the adsorption centres but also their number and relative positions are important for the selective oxidation of hydrocarbons. On the surfact of polycrystalline catalysts, there are planes with different indexes in which the elements entering into the composition of the catalyst are distributed with different separations.

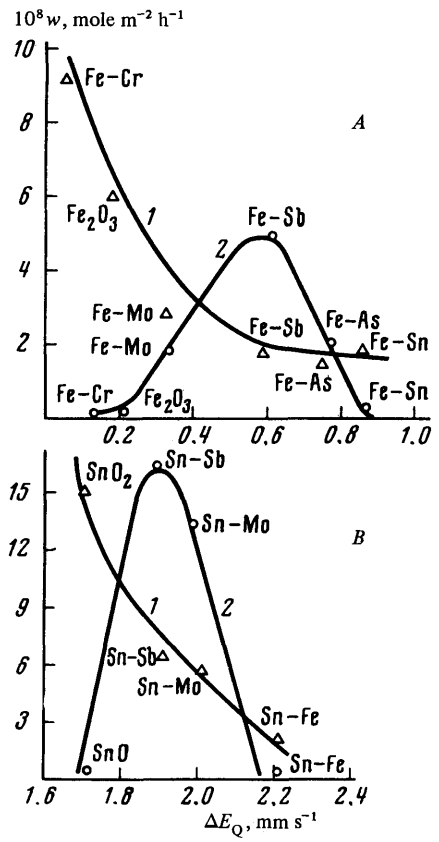

Figure 4. Dependence of the rate of formation of carbon dioxide (1) and acrylonitrile (2) in the presence of oxide catalysts containing iron (*A*) and tin (*B*) on the quadrupole splitting *E*Q (Skalkina et al.[163]).

Data are now available showing which lattice planes of the mixed oxide systems now preferentially exposed on the surface of the catalyst. These data are insufficient to analyse completely the results from the standpoint of the geometrical correspondence between the propene molecules and the atoms of the solid. However, the literature data lead to definite conclusions concerning the influence of the geometry of the active adsorption centres of the oxidative ammoniolysis of propene. Indeed, Kolchin and Gel'bshtein and coworkers showed that the most active catalysts in the Bi_2O_3–MoO_3 system usually contain compounds with the compositions $Bi_2O_3.2MoO_3$ and $Bi_2O_3.3MoO_3$ having the structures of the α- and β-phases[96,165] and that the catalytic activity of bismuth molybdate $Bi_2O_3.MoO_3$ depends on the presence of the γ''-phase structure in the crystal lattice of this catalyst[165].

It has been shown[11,165], on the basis of published data[166–168], that, on passing from molybdenum oxide to bismuth oxide and on formation of various bismuth molybdates, the distances between oxygen and bismuth and molybdenum cations are altered. For example, the distance between Mo and O in MoO_3 varies in the range 1.67–2.25 Å, depending on the position of the MoO_6 octahedra in the layer structure[167], in the bismuth molybdate $Bi_2O_3.3MoO_3$ the Mo–O distance in the tetrahedron is 1.75–1.95 Å and the Bi–O distance is 2.30–2.50 Å,[166] in the bismuth molybdate $Bi_2O_3.MoO_3$ the (Bi, Mo)–O interatomic distance is 2.35 Å, while in $2Bi_2O_3.MoO_3$ the interatomic distance is 2.45 Å.[168]

The distances between the Bi and Mo cations also change on passing from one compound to another, but in all cases are not less than the distances between the carbon atoms in the propene molecule; for this reason, the authors[11,165] conclude that the employment of a simple doublet scheme for the oxidative ammoniolysis of propene[96] on an ideal crystal is hardly valid in view of the defective structure of the catalyst surfaces.

It has been suggested[156] that the catalytic activity of compounds having the structure of the bismuth molybdates $Bi_2O_3.MoO_3$ (γ-phase) and $Bi_2O_3.2MoO_3$ (β-phase) in the oxidative dehydrogenation of n-butenes is due to the presence of Mo–O octahedra linked via their vertices within the bulk of the crystals. According to the authors, this crystal lattice structure allows the emergence onto the surface of the lateral planes of tetragonal pyramids, which leads to the occurrence of anionic vacancies associated with the molybdenum ion and these serve as the olefin adsorption centres[98].

On the other hand, in bismuth molybdates with a high bismuth content, there are vacancies on the lateral edges associated with the bismuth ion, which leads to complete oxidation. In the compound $Bi_2O_3.3MoO_3$ the Mo–O octahedra are joined via their edges and anionic vacancies associated with the molybdenum ion do not arise.

Indeed the γ-phase consists of layers of octahedra comprising molybdenum surrounded by oxygen and alternating with bismuth layers between which there is an oxygen layer[97]. Moreover, the existence of Mo–O octahedra in the structure of keochlinite has been confirmed by spectroscopic data[156].

According to crystal field theory[158], octahedral coordination leads to a greater stabilisation by the crystal field than tetrahedral coordination and for this reason compounds in which the cation is in the centre of a more or less regular octahedron catalyse many reactions.

The loss of catalytic activity by bismuth molybdates in the $\gamma \rightarrow \gamma'$ transition can be attributed to a change in the coordination polyhedron from an octahedron to a tetrahedron.

Recent structural studies[169] on individual bismuth molybdates showed that these phases are based on a face-centred pseudocubic subcell of the CaF_2 type with repeat periods of 5.4–5.8 Å, containing from MoO_2 groups, where M = W, Mo, or Bi. Since the scattering capacity of Bi and Mo atoms is much higher than that of O atoms, the above subcell should characterise primarily the distribution of the heavy atoms in the structure. Indeed, in the mineral koechlinite[167] the bismuth and molybdenum

atoms form a distorted face-centred cubic subcell in which there are four bismuth and molybdenum atoms and eight oxygen atoms.

In the range of catalyst compositions where the Bi_2O_3 content is between 0 and 50%, the subcell has vacancies corresponding to the positions of the metal atoms, when the ratio $Bi_2O_3 : MoO_3 = 1 : 1$ holds, the subcell has no vacancies, and finally in the range of compositions where the Bi_2O_3 content is between 50 and 100% the subcell has vacancies in the positions of the oxygen atoms.

Fig. 5 presents different versions of the structure, based on the data of Gal'perin and Erman [169,171], of the largest crystal faces of compounds in the Bi_2O_3–MoO_3 system. The positions of the vacancies in the distribution of bismuth atoms are indicated on the (010) face of the bismuth molybdate $Bi_2O_3.3MoO_3$ (part *a*). On the crystal faces of the compound $Bi_2O_3.MoO_3$, the vacancies are not indicated since their coordinates have not been determined. Fig. 5 shows that the structures of the largest faces of the α-, β-, and γ-phases are different and that the bismuth : molybdenum ratios also differ.

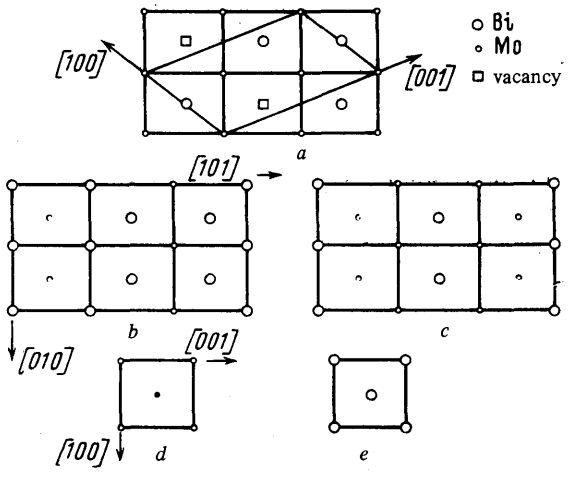

Figure 5. Distribution of metal atoms on the largest faces [144,169]: *a*) $Bi_2O_3.3MoO_3$; *b*) and *c*) $Bi_2O_3.2MoO_3$; *d*) and *e*) $Bi_2O_3.MoO_3$.

On the large (010) face of the α-phase, the presence of vacancies in the positions of the bismuth atoms increases the Bi : Mo ratio in favour of molybdenum (Mo : Bi = 1.5). On the surface of the β-phase crystals, either bismuth (1.6 : 1) or molybdenum (2.5 : 1) atoms predominate. In the γ''-phase, into which the γ-structure is converted under the conditions of the oxidative ammoniolysis of propene [11,165,170], the atoms are distributed in the same way as on the largest faces of the γ-phase (only molybdenum atoms on one face and only bismuth atoms on the other), since the expansion of the unit cell of the γ-form takes place mainly in the (100) and (001) directions, while the distances between the Bi_2O_3 and MoO_4 layers do not change significantly. Even if Bi : Mo ratios analogous to those on the faces of the α-, β-, and γ-phases hold on the surface of some of the faces of the γ'-phase, the fraction of these faces in the overall structure is small, because the γ'-phase, which exhibits the lowest catalytic activity, crystallises in the form of needles extended along the (001) axis. In the vertical band around these crystals, there are 16 faces of equal size in which both cations (Bi and Mo) are located. It is noteworthy that the presence of vacancies in the distribution of metal atoms is probably not an essential property of catalytically active phases, since they are absent from the structure of the bismuth molybdate $Bi_2O_3.MoO_3$. It is also evident that the existence of doublet centres does not play a dominant role in the activity of bismuth molybdates, because on the large faces of the catalytically active γ''-phase only Mo or Bi atoms are present.

Moreover the structural studies of Erman and Gal'perin [169,170] revealed that the length of the propene molecule and the repeat period of the sublattices of phases active in the oxidative ammoniolysis of propene are comparable. The formation of carbon–oxygen complexes probably requires the presence of a pair of identical atoms M–M with octahedral coordination and at a distance of 5.5–5.6 Å.

Comparison of the results of studies on the catalytic activities of various tin–molybdenum catalysts with the results of the phase analysis of the latter has shown [71] that, in contrast to bismuth–molybdenum catalysts, in this system catalytic activity is shown by solid solutions obtained by the substitution of both molybdenum ions in the lattice of molybdenum trioxide by tin ions and of tin ions in the lattice of tin dioxide by molybdenum ions. The solid solution based on the tin dioxide lattice with the atomic ratio Sn : Mo = 9 : 1 has the highest activity and selectivity in the oxidative ammoniolysis of propene.

Tin(IV) oxide has the rutile structure in which the cations are located at centres with octahedral coordination [172]. The replacement of a small proportion of the cations by Mo^{6+} yields a catalyst for the selective oxidation of propene. It is therefore possible that in this case, as in bismuth–molybdenum catalysts, the active centres are Mo^{6+} ions surrounded by oxygen ions with octahedral coordination.

However, in contrast to the bismuth–molybdenum catalysts, the active structure in this case is not a definite chemical compound but a solid solution obtained by the substitution of one ion by another.

In recently published detailed studies of the catalytic activity of the Fe_2O_3–Sb_2O_4 (Boreskov et al. [58]) and U_3O_8–Sb_2O_4 (Graselli and Callahan [173]) systems in the oxidative ammoniolysis of propene and the SnO_2–Sb_2O_4 system [174] in the oxidation of propene it is also emphasised that the highest catalytic activity and process selectivity are associated with the presence in the catalyst lattice of a compound having a definite structure: of iron antimonate in the Fe_2O_3–Sb_2O_4 system and of uranyl antimonate (UO_2) Sb_3O_7 in the U_3O_8–Sb_2O_4 system. In contrast to the latter, in the SnO_2–Sb_2O_4 system as for tin–molybdenum catalysts the highest activity and selectivity is shown, with a structure comprising a solid solution of antimony oxide in tin(IV) oxide. All these compounds contain Sb^{5+} ions in centres surrounded by oxygen ions with octahedral coordination [174,175].

The low activity of iron and manganese molybdates, the lattice cells of which contain, in contrast to active bismuth molybdates, MoO_4 tetrahedra between which Fe and Mn cations are distributed, can probably be explained from the same standpoint [176].

All these data show that the selectivity in the oxidative ammoniolysis of propene in the presence of various mixed oxide catalysts depends on the structure of the crystal lattice of the catalyst, which contains ions distributed at a

specific distance from one another and surrounded by oxygen ions with octahedral coordination. The accessibility of particular adsorption centres on the solid should play a major role in determining the nature of the active centres on the surface of oxidation catalysts. For example, Stone[177] believes that copper(I) oxide is more active in oxidative catalysis owing to the unusual distribution of oxygen on the faces which are preferentially exposed on the surfaces of these structures.

The low activity of iron-containing type A zeolites in relation to type X and Y zeolites, observed[131,132] in the oxidative ammoniolysis of propene, is evidently associated with the accessibility of the adsorption centres (iron ions) to the reacting molecules. In type A zeolites the size of the inlet into the large cavities is 4.2 Å, which hinders their penetration by propene molecules and hence their adsorption in the primary porous structure of this zeolite. With increase of the degree of substitution of sodium ions by iron ions, the dimensions of the octagonal oxygen inlets leading into the large cavities of the type A zeolite are somewhat altered[178] and the authors therefore believe that this makes the adsorption centre more accessible, which is probably the reason for the increased catalytic activity of the iron-containing zeolite.

VI. EFFECT OF THE ELECTRONIC WORK FUNCTION ON CATALYTIC ACTIVITY

It has been suggested[3,11,96] that in the heterogeneous oxidation of hydrocarbons the catalyst must be capable of forming a donor–acceptor bond with the organic reactant and with oxygen and also be able to transmit electrons from one molecule involved in the process to another. Depending on the mechanism of electron transfer in the solid, either the delocalised electrons of the solid or the electrons localised at the lattice cations take part in the electron exchange with the adsorbed species. As already mentioned above, in the adsorption of the reactants in the oxidative ammoniolysis of propene on the surfaces of oxide catalysts, charged oxygen-containing complexes of propene[117,135,145] and ammonia[118,119] are probably formed and therefore the rate of the process depends on their surface concentrations and the magnitude of their charges. The electron work functions of the crystals then regulate the filling of the catalyst surface by the charged intermediate species propagating the oxidation process.

It has been demonstrated in detail in a monograph[11] that, in cases where a relation is observed between the process selectivity and the electronic work function φ of the catalyst (the main characteristic of the electronic properties of the surface), it is possible to drive the oxidation of hydrocarbons in the presence of such catalysts towards partial or extensive oxidation by controlling the electronic work function of the solid. However, it has been established[179] from measurements of the conductivities of individual bismuth molybdates, which are the most active catalysts in the oxidative ammoniolysis of propene, that electrons are appreciably localised at individual lattice ions, i.e. in this case the electronic work function of the solid may play a subsidiary role in the catalytic process.

Indeed it has been shown[180,181] that, when bismuth molybdate is modified by the introduction of various additives, the electronic work functions of such catalysts hardly change. However, under these conditions their crystal lattices undergo a rearrangement, which affects the kinetic characteristics of the joint oxidation of propene and ammonia.

VII. ACIDITY OF THE CATALYST SURFACE

From an analysis of extensive experimental data for the activities of mixed oxide catalysts for partial oxidation, Roiter and Golodets[182] suggested that the stability of the activated surface complexes in the oxidation of hydrocarbons, which probably resemble salt-like formations, depends on the acid–base properties of the surface. Anphoteric properties of the catalyst surface, which ensure the ease of formation and decomposition of the salt-like complex, are particularly favourable for oxidative catalysis.

The low catalytic activity of salts of strong acids in the oxidative ammoniolysis of propene[139] compared with oxide catalysts due to the existence on their surface of mobile hydrogen atoms can probably be explained from this standpoint. The number of acid centres on the surface of these catalysts, determined by titrating them with weak bases in non-aqueous media in the presence of indicators[183,184], proved to be close to the number of acid centres on aluminosilicates (about 20 mequiv. m^{-2}, $pK \leqslant -3$).

According to Skalkina et al.[139], the presence of mobile hydrogen atoms on the surface of strong acid salts may alter the mechanism of the extensive oxidation of propene, i.e. an isopropyl carbonium ion is formed and can accelerate the subsequent conversion of the olefin molecule into final products.

In conclusion of our analysis of the published data, we may suggest that the activity and selectivity of the catalysts for the oxidative ammoniolysis of propene are determined by the structure of the oxygen-containing surface complexes of the hydrocarbon and ammonia. The active surface of the catalysts for the joint oxidation of propene and ammonia must contain active centres of the same type, the reactivity and oxygen mobility of which depend on the nature of the metal and its environment in the crystal lattice of the catalyst. Apart from the energy structure of the solid, the structure of the catalyst surface plays an important role in this reaction.

Changes in the conditions of preparation and also in the nature of the starting materials (salts, acids), which have been followed for bismuth–molybdenum[165,185], tin–molybdenum[150], and tin–antimony[174] catalysts, hardly influence the selectivity of the propene oxidation reactions.

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The Chemistry of Myoinositol

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The present state of the chemistry of myoinositol, a naturally occurring cyclitol, is discussed, with information on its stereochemistry, its physical and chemical properties, and the reactivity of the hydroxy-groups. The principal methods of preparation of various derivatives, in which the cyclitol structure is unaffected, are considered. Special attention is paid to phosphoric esters of myoinositol, which are structural units of inositol phosphatides, a most important class of naturally occurring phospholipids. Specific properties of the phosphoric esters are examined, together with problems of their stability and synthesis. A list of 169 references is included.

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I. INTRODUCTION

Myoinositol is the most widely occurring of the cyclitols (inositols, cyclohexanehexaols). Nine stereoisomeric inositols—neoinositol, *cis*-inositol, scylloinositol, myo-(*meso*-)inositol, (+)- and (−)-inositols, epi-inositol, mucoinositol, and alloinositol—are known[1]. All forms of inositols, with the exception of the (+)- and (−)-inositols, are *meso*-forms, but many of their derivatives may possess molecular asymmetry and hence exhibit optical activity. Naturally occurring optically active derivatives of myoinositol are known: (−)- and (+)-bornesitols (1- and 3-*O*-methyl-*sn*-myoinositols)†, (+)-ononitol (4-*O*-methyl-*sn*-myoinositol), (−)-liriodendritol (1,5-di-*O*-methyl-*sn*-myoinositol), galactin (3-*O*-α-D-galactopyranosyl-*sn*-myoinositol), phosphoinositides, and several other compounds have been isolated from bacterial, vegetable, and animal sources[1]. Myoinositol occurs widely in the vegetable kingdom as calcium salts of the hexaphosphoric ester (phytin)[1].

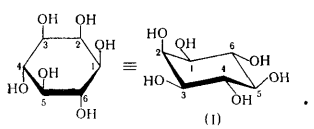
Inositols, in particular myoinositol, are suitable model compounds for the study of stereochemistry and conformational effects. Development of the chemistry of myoinositol has been stimulated also by its occurrence, as well as that of such derivatives as inosamines, in natural compounds—phospholipids, antibiotics, and several others.

Our interest in the chemistry of myoinositol arises from our prolonged concern with aspects of the synthesis of phosphoinositides and phosphoric derivatives of myoinositol, which raises the problem of the availability of definitely substituted derivatives of the latter. Each class of phosphoinositides—mono-, di-, and tri-phosphoinositides—requires its own methods of synthesis. Processes for obtaining triphosphoinositides are especially laborious, for no practicable routes are yet available; this contrasts with mono- and di-phosphoinositides, to whose synthesis definite approaches can be made.

Individual aspects of the chemistry and the biochemistry of myoinositol and its derivatives have been covered in several reviews and books[1,5-14]. The present Review does not deal with synthesis of the cyclitol structure of myoinositol, since this is an independent problem of intrinsic interest. Examples are the syntheses of derivatives of myoinositol and other cyclitols by the intramolecular aldol reaction of various compounds of D-glucose[15-21], by diene synthesis[22], by the hydroxylation of conduritols[23], etc. Research on the conversion of myoinositol derivatives into inosamines constitutes a separate field of investigation[24].

II. STEREOCHEMISTRY OF DERIVATIVES OF MYOINOSITOL AND THEIR REACTIVITY

Myoinositol (I) contains six hydroxy-groups—five equatorial and one axial[1]:



(I)

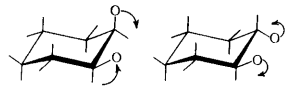
It is easy to predict by conformational analysis that the most stable conformation of myoinositol is the chair form (I), which possesses the smallest number of axial hydroxyls[25]. The chair conformation is consistent with such reactions of myoinositol and its derivatives as dehydrogenation, the formation of borate complexes, and acylation[25]. Physical data also support this conformation: derivatives exhibited an infrared absorption band at 873 ± 11 cm^{-1}, due to vibrations of equatorial C–H bonds[26]. The nuclear magnetic resonance spectra of myoinositol and its acetates[27] were also interpreted in terms of a chair conformation, and were fully consistent with the n.m.r. spectra of the corresponding hexachlorocyclohexanes[28]‡. The suggested conformation was supported also by X-ray diffraction[35] and by electron microscopy[36-38].

†A stereospecific nomenclature[2-4] is used in the Review for racemic and optically active asymmetrically substituted derivatives of myoinositol.

‡Several studies have recently been published[21,24,29-34] on the application of n.m.r. spectroscopy to the structural analysis of myoinositol and its derivatives.

Myoinositol is thermodynamically the most stable cyclitol, as is suggested by the calculated relative free energies (in kcal mole^{-1} at 25°C): myo 3.0, scyllo 3.2, (±) 3.55, (+) 4, neo 4.3, epi 4.9, allo 5.05, muco 5.1, and *cis* 8.05.[39] These values agree well with those determined from the equilibrium constants of the acid-catalysed epimerisation of isomeric inositols[40]. The possibility of the interconversion of myoinositol into other stereoisomers should always be taken into account in the preparation of various derivatives. These problems have been discussed in detail in reviews[1,14]. An example of the partial transition of myoinositol into scylloinositol is provided by the reduction of 2-myoinosose, obtained by oxidation of the axial hydroxyl[1]. Myoinositol hexa-acetate undergoes almost complete isomerisation into mucoinositol hexa-acetate when treated with liquid hydrogen fluoride[41], probably owing to the enhanced stability of intermediate acetyl-oxonium derivatives of the muco-form.

The reactivity of the hydroxyls in myoinositol is strongly dependent on the stereochemistry of the molecule, and is affected by steric hindrance. In this connection equatorial and axial substituents exhibit a difference in chemical behaviour, although the equatorial hydroxyls in myoinositol are not equivalent. But whereas differences between axial and equatorial groups in myoinositol[42] are well explained by conformational analysis and have been confirmed by numerous studies, the non-equivalence of the equatorial hydroxyls is not so usual, and each fact requires separate consideration. Attempts at such an approach have been made in reporting the chemistry of myoinositol. Many synthetic procedures, especially in the chemistry of phosphoinositides, have been based on these rules.



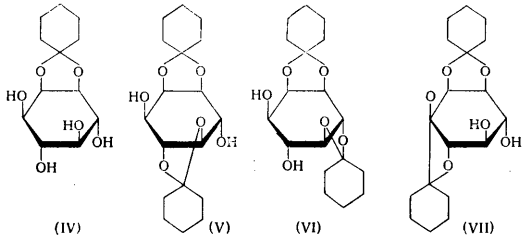
cis (II) *trans* (III)

The hydroxyls in myoinositol differ in reactivity also according as they are in *cis*- or *trans*-positions. In the undistorted chair form the distance between vicinal equatorial groups is the same as that between axial and equatorial *cis*-hydroxyls. It might have been expected, therefore, that the formation of cyclic acetals would occur equally readily with *cis*- and *trans*-hydroxyls. However, cyclisation involves formation of a new ring containing five coplanar atoms, and consequently the molecule is distorted in such a way that the two vicinal substitutents become quasi-coplanar. In all reactions requiring an approximately coplanar transition state, and not accompanied by migration of substituents, *cis* (*eq*, *ax*)-compounds react more rapidly than do *trans* (*eq*, *eq*)-compounds[43]. The chair conformation of the ring exhibits different relations towards the two types of distortion caused by bringing *cis* (*eq*, *ax*)- or *trans* (*eq*, *eq*)-substituents almost into coplanarity[36]. The former (II) is accompanied by levelling of the ring and increase in the endocyclic bond angles. Such distortion resembles incipient conformational inversion and requires no large consumption of energy. Formation of a new ring involving *trans*-hydroxyls is best explained in terms of a distorted conformation. Thus examination of hydrogen bonds has shown[44-46] that the effort to bring the two equatorial bonds (III) into the same plane entails a shortening of the interatomic distances, which distorts the chair form and therefore requires a large quantity of energy[47]. As a consequence, cyclisation takes place initially at the *cis*-hydroxyls (*ax*, *eq*), and then at the *trans*-hydroxyls (*eq*, *eq*) under more severe conditions[48]. These observations are confirmed by the formation of cyclic acetals of myoinositol.

III. ACETAL DERIVATIVES OF MYOINOSITOL AND REACTIONS BASED ON 1(3), 2-*O*-CYCLOHEXYLIDENE-*sn*-MYOINOSITOL

Studies of cyclic acetals of myoinositol are of interest for synthetic chemistry, besides the solution of stereochemical problems. Acetals have proved convenient protective groups in the chemistry of myoinositol. Originally an isopropylidene group was used to protect vicinal hydroxy-groups[43,49-55]. Myoinositol reacts with acetone in the presence of zinc chloride, and with 2,2-di(m)ethoxypropanes in the presence of toluene-*p*-sulphonic acid in dimethyl sulphoxide, to form isopropylidene derivatives. *cis*-Acetals are formed first[43,51], since they correspond more closely to coplanarity. The formation of acetals with a ketone requires that water be removed from the reaction medium. Acetone hinders the azeotropic removal of water, is unstable towards dehydrating agents, and causes side-reactions[48].

Cyclohexylidene derivatives were subsequently recommended for sugars and polyols, since they are obtained more simply than the corresponding acetonides, and moreover in the crystalline state[56]. Myoinositol is dissolved in a boiling mixture of cyclohexanone and benzene containing catalytic quantities of toluene-*p*-sulphonic acid, and water is removed by azeotropic distillation. The resulting formation of *O*-cyclohexylidene-*sn*-myoinositol derivatives —1(3), 2 (IV), 1(3), 2:4(6)5 (V), 1(3), 2:5, 6(4) (VI), and 1(3).2:3(1), 4(6) (VII)[48,57]



(IV) (V) (VI) (VII)

involved firstly the *cis*-hydroxyls (*ax*, *eq*) and then *trans*-hydroxyls (*eq*, *eq*).[48] Angyal showed[48] that a triacetal of myoinositol was formed, but this compound was not isolated.

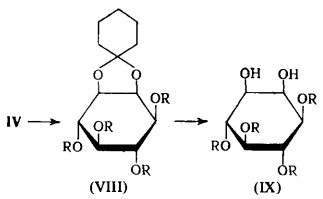
Cyclohexylidene derivatives of myoinositol are starting compounds for the preparation of phosphoinositides. A diphosphoinositide has been obtained from the diacetal (V).[58-60] Several syntheses of monophosphoinositides[61-65] have involved the use of 1(3), 4(6), 5, 6(4)-tetra-*O*-substituted derivatives of myoinositol obtained from the monoacetal (IV). Examples are the tetrabenzyl and tetra-acetyl compounds (IX: R = $C_6H_5CH_2$, CH_3CO) obtained by the benzylation or acetylation of (IV) followed by acid hydrolysis of the acetal protection (Scheme 1).[48,66] Other groups (toluene-*p*-sulphonyl (tosyl), methyl, allyl, etc.) are less suitable for these purposes, mainly because of the difficulty of their removal. Acetylation and benzylation of the acetal (IV) go to completion, so that differences in reactivity between the hydroxy-groups cannot be detected, although such conclusions may prove useful in the synthesis of polyphosphoinositides.

In this connection interesting results have been obtained for the tosylation of various derivatives of myoinositol. The action of tosyl chloride in pyridine on the mono-, di-, tri-, and tetra-tosylates (X–XVII, XIX, and XX) is represented by Scheme 2.[29] The degree of tosylation is determined by the quantity of the reagent: a large excess of tosyl chloride is required to obtain polytosyl derivatives of myoinositol. Gravimetric analysis of the tosylates obtained in various reactions leads to the reactivity sequence

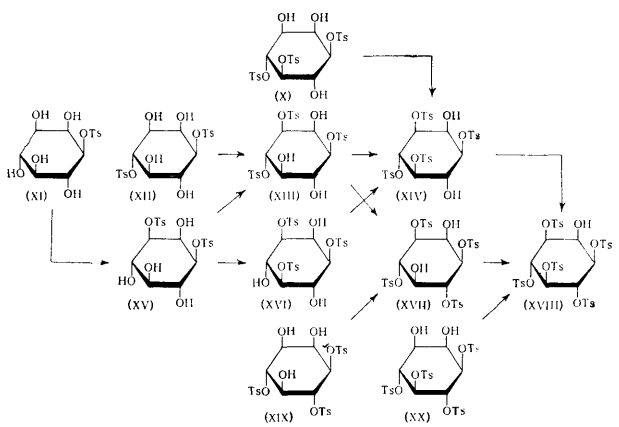
1(3)-OH>4(6)-OH>5-OH>2-OH

for the hydroxy-groups in this case.

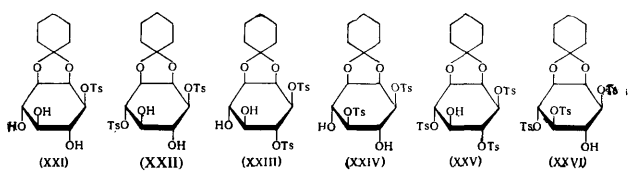
Scheme 1



Scheme 2



Similar results have been obtained for corresponding reactions with the monoacetal (IV):[30] several tosyl derivatives

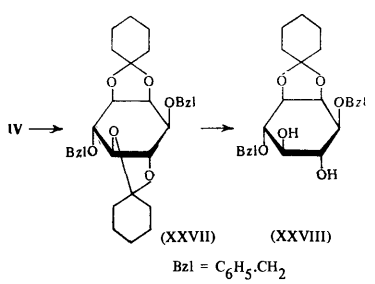


were prepared and used, after removal of the cyclohexylidene protection[31], to obtain polytosylates of myoinositol[29]. Similar reactivity of the hydroxy-groups in the monoacetal (IV) has been observed in benzoylation[33]. The derivatives (X), (XII), (XIII), (XXII), and (XXVI) are worthy of attention as starting materials for the preparation of di- and tri-phosphoinositides. However, the low yields of myoinositol tosylates, the difficulty of their isolation, and also the possibility of various transformations in work with tosyl groups[66,67] restrict the use of tosylation in the synthesis of polyphosphoinositides.

Several conclusions of the relative reactivity of the equatorial hydroxyls were drawn from an investigation of substitutions (S_N1 and S_N2) of the diacetals (V) and (VI) and their derivatives. Thus the benzylation[63,68,69], benzoylation[70], and phosphorylation[71] (S_N2) of (V) suggest that the 3(1)-hydroxyl is more reactive than the 6(4)-hydroxyl, despite the unfavourable conformational factors that the former is adjacent to a *cis*- and *trans*-acetal group, and the latter to a *trans*-group. The selectivity is due to the more strongly nucleophilic character of the 3(1)-hydroxyl. A similar phenomenon has been observed in the benzylation of (VI).[69] Selective benzoylation of the diacetal (V) formed the basis for a synthesis of a diphosphoinositide[60]. Nevertheless, these hydroxy-groups exhibit closely similar reactivity towards transesterification (S_N1).

With the diacetal (VI) this reaction showed that the 4(6)-hydroxy-group is more reactive than the 3(1)-hydroxyl, while 4 is the more active of the enantiotopic positions 4 and 6.[72,73] These hydroxyls behave similarly towards methylation[72,73]. The explanation is that position 4(6) is sterically more favourable (*trans*-OH, *trans*-acetal) than position 3(1) (*trans*-OH, *cis*-acetal).

Scheme 3



Transesterification of 1(3), 4(6)-di-*O*-cyclohexylidene-*sn*-myoinositol (XXVIII) by the ethyl chloroacetate of D-mannose indicates that the 5-hydroxyl is more reactive than the 6(4)-group. Of the two most probable diastereomers the compound with a free 4-hydroxyl is formed preferentially[63]. Examination of the stability of the *cis*- and *trans*-cyclohexylidene groups in the diacetals (V)–(VII) revealed the possibility of selective removal of the *trans*-acetal protection as sterically the less favourable[57,33,68]. This provided a method for preparing (XXVIII)[63] (Scheme 3), from which compound the preparation of triphosphoinositides can be planned.

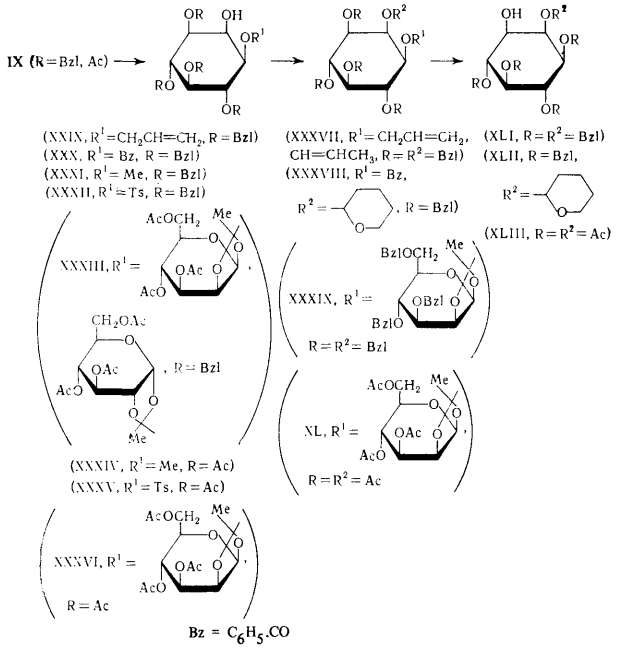
IV. PENTASUBSTITUTED DERIVATIVES OF MYOINOSITOL

A general method for obtaining monophosphoinositides is based on pentasubstituted derivatives of myoinositol having the free hydroxyl at the 3(1) position. It would therefore have been tempting to seek a selective protection for the axial hydroxyl in 1(3), 4(6), 5,6(4)-tetra-*O*-substituted derivatives. Unfortunately, it is impossible to

suggest such a group: substitution of 1(3), 4(6), 5,6(4)-tetra-*O*-substituted derivatives takes place predominantly at the 3(1) position. Benzylation[66], methylation[66], tosylation[31,74,75], acetylation[66], benzoylation[76], phosphorylation[62], and allylation[52] occur in this way. On the other hand, 2,3-dihydropyran and benzyloxymethyl chloride do not exhibit selectivity[77].

Reactions exhibiting selectivity towards an equatorial hydroxy-group can be assumed to depend on steric hindrance and to involve a transition state by an S_N2 substitution mechanism. If an ion is formed in the initial stage, on the other hand, the subsequent rapid interaction is less sensitive to steric hindrance, and such reactions (S_N1) therefore occur non-selectively. Results obtained for the transesterification of orthoacetates of D-mannose and D-glucose with 1(3), 4(6), 5,6(4)-tetra-*O*-benzyl-*sn*-myoinositol (IX: R = $C_6H_5CH_2$),[78,79] in which orthoesters of myoinositol isomeric with respect to the axial groups were isolated in considerable quantities, are significant in this connection. The absence of selectivity, despite steric hindrance to the introduction of an orthoester group at the 2-hydroxyl, becomes clear from an examination of the suggested S_N1 mechanism of transesterification[80], which is analogous to reactions with 2,3-dihydropyran and with benzyloxymethyl chloride[77].

Scheme 4

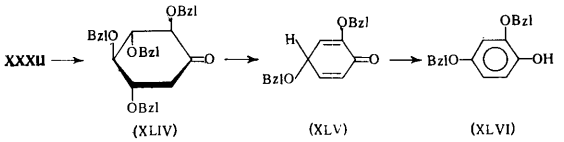


After the 3(1)-hydroxyl has been replaced, the problem is to protect the axial hydroxy-group and remove the protection from the 1(3)-hydroxyl (Scheme 4). The hydroxy-group attached to $C_{(2)}$ has been substituted by benzyl[52,61,62], acetyl[81], and tetrahydropyranyl[76] groups. 1(3), 4(6), 5,6(4)-Tetra-*O*-acetyl-*sn*-myoinositol (IX: R = CH_3CO) has not usually been employed in these syntheses, since the removal of methyl, acetyl, allyl, and tosyl groups entails deacetylation, although individual reactions[82] have been examined on this tetra-acetate. An exception is the orthoester carbohydrate protection, which makes it possible to acetylate completely the orthoester (XXXVI), and then remove the protective orthoester group without affecting the acetate groups[81]. Another factor restricting use of the tetra-acetate (IX), as well as the benzoyl derivatives to some extent, is acyl migration[83-85]. 1(3), 2,4(6), 5,6(4)-Penta-*O*-substituted derivatives of myoinositol have therefore been obtained mainly from the tetrabenzyl ether (IX: R = $C_6H_5CH_2$), from which the penta-acetate (XLIII) has also been prepared[86].

1. Tosylation–Detosylation Reactions

Tosylation of the compounds (IX: R = $C_6H_5CH_2$, CH_3CO) occurs selectively at the 3(1)-hydroxyl: tosyl chloride does not react with the sterically hindered 2-hydroxy-group[66,75]. Acetylation and benzylation of tosyl derivatives at the 2-hydroxyl (Scheme 4) followed by removal of the tosyl group might have given pentasubstituted derivatives of myoinositol with a free 1(3)-hydroxyl, but difficulties arise in such removal. Detosylation is effected with sodium amalgam in aqueous methanol at pH 5 to prevent side-reactions (deacetylation, acetyl migration, and formation of epoxides). The process takes place slowly, but varying the conditions leads to concurrent deacetylation[75].

Scheme 5



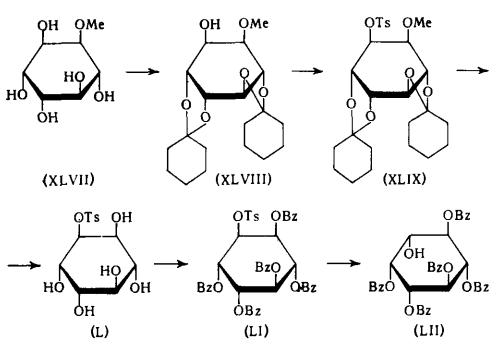
Attempts to benzylate 3(1), 4(6), 5,6(4)-tetra-*O*-benzyl-1(3)-*O*-tosyl-*sn*-myoinositol (XXXII) with benzyl chloride in the presence of alkali result in loss of the tosyl group with aromatisation of the ring. It was postulated that the reaction mechanism involved (Scheme 5) elimination of the tosyl group to give an unsaturated ketone (XLV), followed by aromatisation of the ring with formation of 2,4-dibenzyloxyphenol (XLVI).[66]

2. Methylation and Demethylation

Methyl ethers of cyclitols are of intrinsic interest, since they are widely represented in Nature[1]. They are used in the chemistry of myoinositol to establish the structure of its derivatives[71-73,78,79]. Methods of methylation are distinguished by standardisation of the conditions (methyl iodide and silver oxide) and are suitable for various derivatives of myoinositol[49,87], in which the 3(1)-hydroxyl is methylated first[66,74]. Other methods for methylating such compounds are also known (diazomethane and boron trifluoride)[88], when the 1(3)-hydroxyl is methylated more slowly than the 4(6)- and 5-groups, and the axial 2-hydroxyl does not react at all.[84]

Methyl ethers are little used as protection because of the severe conditions for demethylation by hydriodic and hydrobromic acids. Carbohydrate chemistry has recently seen the development of demethylation by means of boron trihalides (fluoride, chloride, and bromide), which form complexes with the ethereal oxygen, permitting nucleophilic cleavage of the O–CH_3 bond [89]. This method was first used in the chemistry of cyclitols by Gero [90] to prepare 1,2,4,5,6-penta-*O*-benzoyl-*sn*-myoinositol (LII) from natural quebrachitol, 2-*O*-methyl-(—)-inositol (XLVII) (Scheme 6). Cyclohexylidene and tosyl protective groups were employed in this preparation. Demethylation by boron trichloride was accompanied by removal of cyclohexylidene groups (XLIX → L). The tosylate (L) was benzoylated under the usual conditions, and the tosyl group was removed from (LI) by the action of sodium fluoride in dimethylformamide with inversion of the previously tosylated hydroxy-group.

Scheme 6



Since the initial quebrachitol (XLVII) is optically active, the pentabenzoate (LII) possesses the same property, but unfortunately only unnatural phosphoinositides, with the phosphoric residue at position 3, can be obtained from it. Another defect of the scheme is the relative unavailability of quebrachitol (XLVII). Boron tribromide has been used to remove methyl groups from pentatosylates of (–)-bornesitol (1-*O*-methyl-*sn*-myoinositol) and (+)-bornesitol (3-*O*-methyl-*sn*-myoinositol) [74,91].

3. Preparation of Penta-acyl Derivatives of Myoinositol. Acetyl Migration. Tetrahydropyranyl Protection. Acetolysis of Benzyl Ethers of Myoinositol

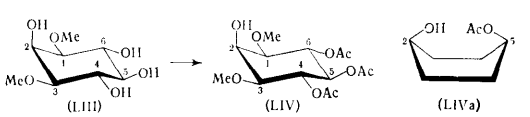
Acyl derivatives of myoinositol (acetates and benzoates) are well known. These groups are used to protect hydroxy-groups and also for the identification of derivatives. The simplicity with which acyl groups can be introduced and the great selectivity of the acylation of the 3(1)-hydroxyl attracted the attention of research workers, but these protections were then found to have substantial defects, so that they did not acquire general importance. Firstly, the ester link in derivatives of myoinositol is cleaved under conditions of hydrolysis and alcoholysis, so that it cannot be preserved during the removal of many other groups. Another disadvantage of acyl and especially acetyl groups is a tendency to migrate in the presence of bases [75,83,84].

Migration of acetyl groups in acetylated polyols has been observed previously [92–95]. In the chemistry of myoinositol attention was directed to this phenomenon in the methylation and tosylation of acetylated derivatives [49,85,96]. It is noteworthy that migration occurs when methyl iodide and silver oxide are used, but not when methylation is effected with diazomethane and boron trifluoride [83,84]. Migration is almost equally probable in *trans*- and *cis*-directions. The conformational factors responsible for the direction of these processes have not yet been determined [83,84].

The conditions governing acetyl migration have been studied in the methylation of 1(3), 4(6), 5,6(4)-tetra-*O*-acetyl-*sn*-myoinositol (IX: R = CH_3CO) and the 1(3), 3(1), 4(6), 5,6(4)-penta-*O*-acetyl derivative by the action of methyl iodide in the presence of silver oxide [83,84]. The presence of water is found to accelerate migration, which can be diminished to 25% by the addition of an anhydrous calcium sulphate, but cannot be completely suppressed because of the water produced in this method of methylation. The polarity of the solvent also influences the rate of the process: replacing dimethylformamide by chloroform in the methylation of the tetra-acetate (IX: R = CH_3CO) diminishes migration, but also lowers the yield of the methylated product. Raising the temperature accelerates methylation of the equatorial hydroxy-groups, but also increases *trans*-migration and methylation of the axial hydroxyl.

In order to avoid *trans*-migration and limit *cis*-migration in the methylation of 1(3), 4(6), 5,6(4)-tetra-*O*-acetyl-*sn*-myoinositol (IX: R = CH_3CO) it is advisable to use neutral silver oxide, a solvent of low polarity, a small content of methyl iodide, and a low temperature. However, methylation is incomplete under these conditions, and affects predominantly the equatorial position. Changing the reaction conditions in order to increase the yield entails increased migration.

Scheme 7



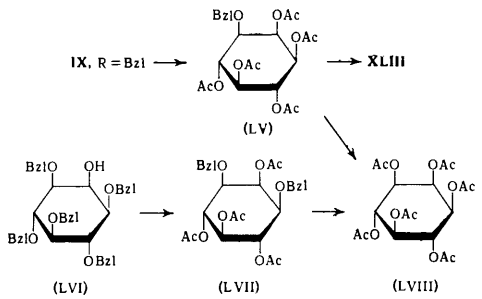
In view of possible transfers of acetyl groups round the ring, it was of interest to examine whether *trans*-ring migration—through adjacent *trans*-groups—will occur. To settle this question Angyal chose as model compound 1(3), 3(1)-di-*O*-methyl-*sn*-myoinositol (LIII, Scheme 7). [49] The axial hydroxyl remained free when this compound was acetylated, as the nuclear magnetic resonance spectra indicated that the main product was 4(6), 5,6(4)-tri-*O*-acetyl-1(3),3(1)-di-*O*-methyl-*sn*-myoinositol (LIV). The stability of the compound (LIV) in aqueous pyridine solution indicates that *trans*-ring migration is absent. These results also confirmed that myoinositol derivatives, in the present case (LIV), exist in the chair form, since in the boat form (LIVa) the 5-acetyl group is situated in a favourable position for migration to the $C_{(2)}$ atom.

Less study has been made of the behaviour of other ester derivatives of myoinositol. A benzoyl group has

been introduced at the equatorial group in 1(3), 4(6), 5,6(4)-tetra-*O*-benzyl- and -acetyl-*sn*-myoinositols (IX: R = $C_6H_5CH_2$ and CH_3CO respectively)[76,70,97] (Scheme 4). The product (XXX) was then used to obtain the 1(3), 2,4(6), 5,6(4)-penta-*O*-substituted derivative (XLII). The tetrahydropyranyl group was suggested for protecting the 2-hydroxyl in (XXX)[76]. This group had previously been used to protect primary, secondary, and tertiary alcohols[98], and several examples of its application in carbohydrate chemistry are known[99-101]. Having been the first to use it in the chemistry of myoinositol, Angyal[77] discovered the possibility of its selective removal by acid methanolysis in the presence of isopropylidene groups[102]. Unfortunately, the action of 2,3-dihydropyran is not distinguished by selectivity towards the 1(3)-hydroxyl[77]. A favourable aspect of this protection is the absence of acetyl migration when it is removed.

In spite of the difficulties caused by acetyl migration, the search for convenient synthetic methods of obtaining myoinositol penta-acetate (XLIII) was continued, since this compound forms a convenient starting point for the synthesis of an unsaturated monophosphoinositide. This problem was solved by the acetolysis of polybenzyl ethers of myoinositol[63,86,103]. Acetolysis of the tetrabenzyl ether (IX: R = $C_6H_5CH_2$) by acetic anhydride in the presence of perchloric acid at 18–20°C gives 1(3), 2,4(6), 5,6(4)-penta-*O*-acetyl-3(1)-*O*-benzylmyoinositol (LV) in 57% yield, which increases to 83% when the reaction is conducted at 0°C (Scheme 8). Acetolysis of the pentabenzyl derivative (LVI) involves formation of 2,4(6), 5,6(4)-tetra-*O*-acetyl-1(3),3(1)-di-*O*-benzyl-*sn*-myoinositol (LVII)[86].

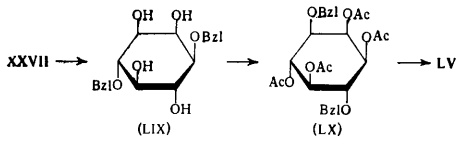
Scheme 8



The acetolysis of benzyl ethers of myoinositol (IX: R = $C_6H_5CH_2$) and (LVI) depends on steric factors. The 1(3)- and 2-benzyl groups are acetolysed more slowly than the corresponding 4(6)- and 5-groups, but this difference disappears with rise in temperature, and all benzyl groups are removed with formation of the hexa-acetate (LVIII). Acetolysis involves addition of an acetyl ion to the ethereal oxygen atom, and its rate depends on the nature and the configuration of neighbouring groups[86]: the acetoxy-group exerts greater steric hindrance than does the benzyloxy-group, and *trans*-groups impede acetolysis to a smaller extent than do *cis*-groups. It becomes clear why benzyl groups at positions 1(3) and 3(1) in the compounds (IX: R = $C_6H_5CH_2$) and (LVI) having *cis*-acetyl groups undergo acetolysis slowly. Acetolysis of the hexabenzyl ether is less selective and gives several products, among which the 1(3)-monobenzyl and 1(3),3(1)-dibenzyl derivatives (LV) and (LVII) predominate[86], which confirms the suggested reaction mechanism.

A similar process occurs in the acetolysis of 1(3), 4(6)-di-*O*-benzyl-*sn*-myoinositol (LIX), obtained from the diacetal (IV) by benzylation (XXVII) followed by removal of the protective cyclohexylidene groups (Scheme 9)[83].

Scheme 9



Hydrogenolysis of (LV) yields 1(3), 2,4(6), 5,6(4)-penta-*O*-acetyl-*sn*-myoinositol (XLIII), whose isolation may entail acetyl migration. Thus even crystallisation of the penta-acetate (XLIII) may be accompanied by migration owing to contamination with bases, and is therefore conducted in the presence of traces of acid[83,86].

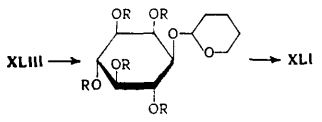
4. Pentabenzyl Ethers of Myoinositol. Allyl Protective Grouping

Benzyl ethers have found application as protective groups in the chemistry of cyclitols, in particular myoinositol, because they are stable in alkaline and acid media. They are obtained in good yields by the action of benzyl chloride or bromide in the presence of alkali[104], benzyl bromide in dimethylformamide in the presence of silver or barium oxide, and benzyl chloride in the presence of sodium hydride[105]. The benzyl group can be removed not only by catalytic hydrogenation but also by boiling with Raney nickel or reducing with metallic sodium in alcohol[86,106]. This makes the benzyl ethers convenient starting materials for obtaining monophosphoinositides. Their only disadvantage is that they cannot be used to obtain monophosphoinositides with unsaturated aliphatic acid residues.

The requirements for obtaining 1(3), 2,4(6), 5,6(4)-penta-*O*-benzyl-*sn*-myoinositol (XLI) are not satisfied by methyl, tosyl, or any ester group selectively introduced at the 3(1)-hydroxyl in the tetrabenzyl derivative (IX: R = $C_6H_6CH_2$). Allyl protection has since been successfully used for these purposes[52]. Allyl bromide, reacting mainly with the equatorial hydroxyl in the above compound (IX), gives a derivative (XXIX), which is benzylated to (XXXVII: $R^1 = CH_2.CH:CH_2$) and, after alkaline isomerisation of the allyl into the propenyl group and hydrolysis in an acid medium, is converted into (XLI)[52]. In the case of myoinositol derivatives containing acid-labile groups it has been suggested that the propenyl protection should be removed by (i) ozonolysis followed by alkaline hydrolysis, (ii) oxidation with alkaline permanganate, or (iii) the action of mercury(II) chloride in the presence of mercury[107-110]. A disadvantage of the allyl group is that it cannot be used in the presence of groups that are unstable to alkaline conditions, which applies in

particular to myoinositol derivatives with ester protecting groups. Furthermore, the conditions for isomerisation of the allyl into a propenyl group may cause aromatisation of the myoinositol ring[111].

Scheme 10



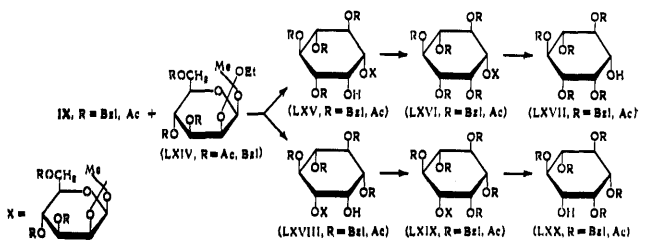
(LXI, R = Ac; LXII, R = H; LXIII, R = BzI)

Another route has recently been found[112] from the penta-acetate (XLIII) to the pentabenzyl ether (XLI). Reaction of the former with 2,3-dihydropyran gives 1(3), 2,4(6), 5,6(4)-penta-*O*-acetyl-3-*O*-tetrahydropyranyl-*sn*-myoinositol (LXI, Scheme 10), treatment of which with methanolic ammonia yields 1-*O*-tetrahydropyranyl-*sn*-myoinositol (LXII). Treatment of the latter with benzyl chloride in the presence of alkali converts it into the pentabenzyl derivative (LXIII), and removal of the oxanyl group by acid hydrolysis gives (XLI).

5. Orthoester Protective Group

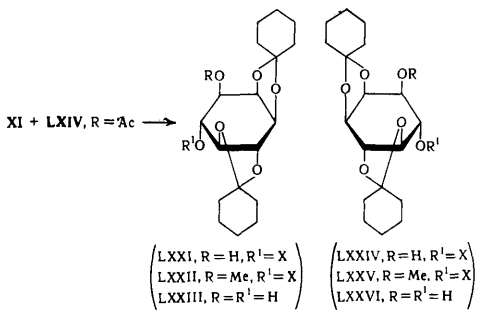
The carbohydrate orthoester group is beginning to find use in myoinositol chemistry[61,62,71-73,78,79,81,112-114]. Hitherto the main use of orthoesters has been based on their rearrangement into isomeric glycosides in the preparation of oligosaccharides[80]. The chief virtues of the orthoester group lie in the mild conditions of its introduction (transesterification with lower orthoacetates) and removal (acid hydrolysis)[80], which leave other groups unaffected. Furthermore, the diastereomeric orthoacetates of D-mannose and of myoinositol obtained from racemates of the latter differ in properties, and hence can be used to obtain optically active derivatives of an asymmetrically substituted myoinositol.

Scheme 11



D-Mannose orthoacetate (LXIV: R = CH_3CO, $C_6H_5CH_2$) has been used to prepare optically active pentabenzyl ethers and penta-acetates of myoinositol (LXVII, LXX: R = $C_6H_5CH_2$, CH_3CO—Scheme 11), which are initial compounds in the preparation of saturated and unsaturated monophosphoinositides[61,62,81,112,114]. A peculiarity of this reaction is that the 1-hydroxyl is more reactive than the 3-hydroxyl[78,81].

Scheme 12



D-Mannose orthoacetate (LXIV: R = CH_3CO) reacts with the diacetal (VI) to give the compounds (LXXI)–(LXXVI) (Scheme 12)[72,73], which, containing labile orthoester and *cis*- and *trans*-acetal groups, can be the starting points for the preparation not only of monophosphoinositides but also of di- and tri-phosphoinositides.

The orthoester protective group shows great promise in the chemistry of myoinositol, because of the simplicity of its introduction, the mild conditions of removal, and also the possibility of its use to obtain optically active derivatives of an asymmetrically substituted myoinositol.

V. PHOSPHORIC ESTERS OF MYOINOSITOL

1. Properties of Phosphoric Derivatives of Myoinositol

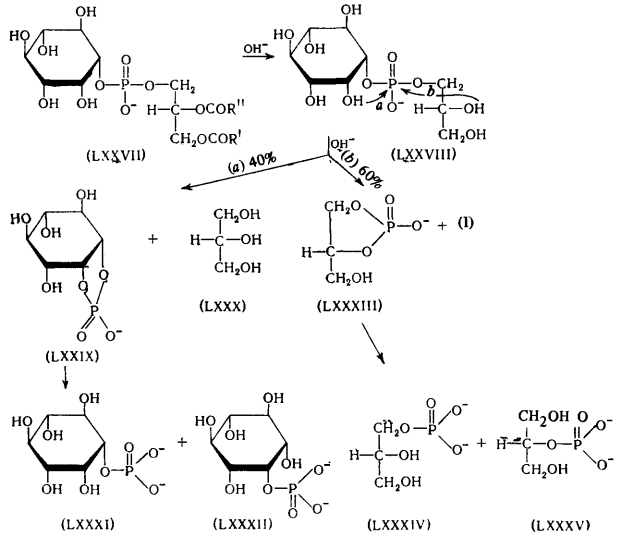
Phosphoric esters of myoinositol are polyfunctional compounds. The phosphoric groups in phosphoinositides are present in both monoesterified and diesterified forms; a triesterified form appears in the chemical reactions during preparation. Phosphoric esters of myoinositol are distinguished by lability depending on the presence of neighbouring groups. Study of the behaviour of these esters must take into account their capacity for various migrations[115-120], and therefore these properties should be allowed for in the preparation of phosphoinositides (phosphorylation, removal of protective groups).

Hydrolysis of Phosphoinositides

Diesterified phosphates of myoinositol are hydrolysed by acids and bases, the phosphates showing an appreciable tendency to cyclisation when vicinal hydroxyls are present (Scheme 13).[120-122] Such hydroxyls increase the rate of hydrolysis of phosphoric groups both in acid and in alkaline media, with formation of cyclic phosphates (LXXIX) and (LXXXIII) in the first stage. These reactions obviously involve transesterification, the cyclic phosphates being readily hydrolysed and forming the isomeric phosphates (LXXXI), (LXXXII), and (LXXXIV), (LXXXV). This is

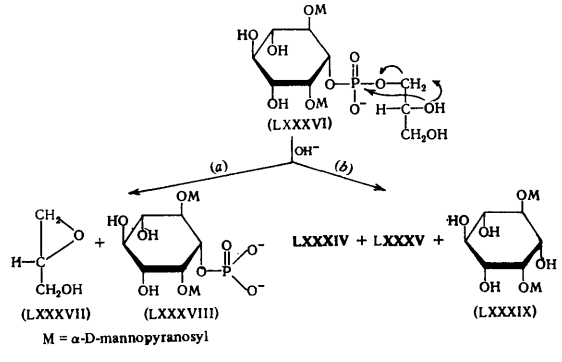
supported by results for the alkaline hydrolysis of the cyclic phosphate (LXXIX), when myoinositol 1-phosphate (LXXXI) and 2-phosphate (LXXXII) are formed to the extents of about 80–90% and 20–10% respectively, i.e. in the same proportions as in the alkaline hydrolysis of soya-bean phosphoinositides [122]. The ratio of these two phosphates shows that the bond at $C_{(2)}$ in the 1,2-cyclophosphate (LXXIX) is the more readily cleaved [122].

Scheme 13



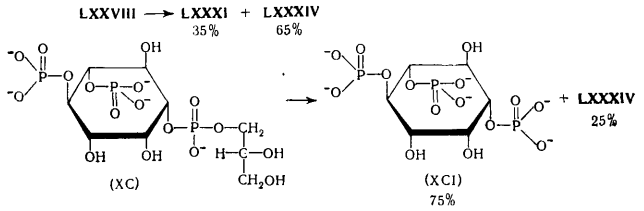
Cyclisation accompanying hydrolysis may involve functional groups both in *cis*(*ax*, *eq*) and in *trans*(*eq*, *eq*) positions. Stereochemical considerations indicate that a *cis*-diol cyclophosphate should be more stable than the *trans*-isomer, which was confirmed by Pizer and Ballou [122]. The action of dicyclohexylcarbodi-imide on *sn*-myoinositol 5-phosphate, in which the phosphate group is adjoined only by *trans*-hydroxyls, gives a series of unstable cyclophosphates, which then undergo several successive ring-openings and cyclisations, with the 1,2-cyclophosphate (LXXIX) as sole product of the reaction.

Scheme 14



The stability of deacylated dimannophosphoinositides (LXXXVI) to alkaline hydrolysis is somewhat puzzling [115–120]. The hydrolysis of these compounds is of considerable interest, since the vicinal hydroxyls attached to $C_{(2)}$ and $C_{(6)}$ are bound by a glycosidic bond with D-mannose and should not form cyclic phosphates. It might therefore have been expected that the only products of hydrolysis would be glycerophosphates, but a dimannoinositol phosphate (LXXXVIII) was also isolated on hydrolysis (Scheme 14). This fact can be explained by a different mode of degradation of the diesterified phosphate (LXXXVI), involving formation of epoxides (LXXXVII) (route *a*), which may compete with hydrolysis via intermediate formation of cyclic esters, which ultimately yield glycerophosphates (LXXXIV) and (LXXXV)—route (*b*).

Scheme 15



*Weights of hydrolysis products based on a mixture of isomers. *sn*-Myoinositol 2-phosphate and 2,4,5-triphosphate, as well as the 2-glycerophosphate, have been omitted from Scheme 15.

The ease of formation of cyclic phosphates depends very strongly on the degree of phosphorylation of the phosphoinositides [116–119]. In this connection it is interesting to compare the hydrolysis of mono- and tri-phosphoinositides (Scheme 15) [115–119,123]. Differences in the proportions of the corresponding hydrolysis products (LXXVIII) and (XC) may result from ionisation of the monoesterified phosphate groups in the triphosphoinositides, leading to distortion of the conformation of the myoinositol ring [124]. The 2-hydroxyl is then in a more favourable orientation for attack on the phosphorus, which is responsible for hydrolysis (route *a* in Scheme 13) with the formation of myoinositol triphosphate (XCI).

Migration of phosphate groups

Such migration was noticed in the isolation of glycerophosphates from lecithin and cephalin [125,126]. Hawthorne and Chargaff considered this process to be improbable in the myoinositol series in view of the large distance separating neighbouring hydroxy-groups in the chair conformation [127]. Migration of phosphate groups between vicinal hydroxy-groups in myoinositol phosphates was first observed by Posternak [128]. This phenomenon becomes appreciable at moderately low pH values [129]. The mechanism of such processes is analogous to migrations via cyclophosphates investigated in the alkaline hydrolysis of phosphoinositides (Scheme 13, route *a*) [121]. In myoinositol phosphates transfer of phosphate groups takes place when two vicinal *cis*-hydroxyls are present, whereas *trans*-migration is atypical [130].

Ballou et al.[122,131] investigated the migration of the phosphate group in *sn*-myoinositol 1-, 2-, and 5-phosphates, (−)-inositol 3-phosphate, and pinitol 4-phosphate in acid media. When 0.1 M solutions of the acid forms of myoinositol phosphates are heated to 90°C, interconversion of *sn*-myoinositol 1- and 2-phosphates is observed. The other compounds do not exhibit such properties, which indicates that autocatalytic migration of the phosphate group between *trans*-hydroxyls in hindered. It also appears possible[132] to hydrolyse monophosphoric esters of myoinositol at pH 4. Nevertheless, boiling 80% acetic acid leads to migration between the carbon atoms in positions 1(3) and 2, but not *trans*-migration; yet 1 *N* hydrochloric acid at 80–85°C causes both types of process. Under these conditions equilibrium is established between *sn*-myoinositol 1(3)- and 2-phosphates in 30 min, *trans*-migration is observed after 1 h, and all isomeric phosphates of myoinositol are detected after 8 h.[120,130,133] Thus under acid conditions transfers of phosphate groups took place between *cis*- and *trans*-positions, which governed migration round the ring.

Interconversions of myoinositol phosphates under alkaline conditions involve formation of an intermediate cyclic phosphate[134], as shown earlier. Absence of vicinal hydroxyls makes these processes more difficult owing to the low probability of formation of cyclophosphates through well separated hydroxyls, and also because of the stability of these cyclophosphates. Thus the cyclophosphate

obtained by phosphorylating *cis*-cyclohexane-1,3-diol, is not decomposed by 30% caustic soda at 100°C; ready degradation with the formation of phosphoric acid was appreciable only on treatment with 3 *N* hydrochloric acid at this temperature[134].

2. Synthetic Routes to Phosphoric Derivatives of Myoinositol

Preparation of monoesterified myoinositol phosphates

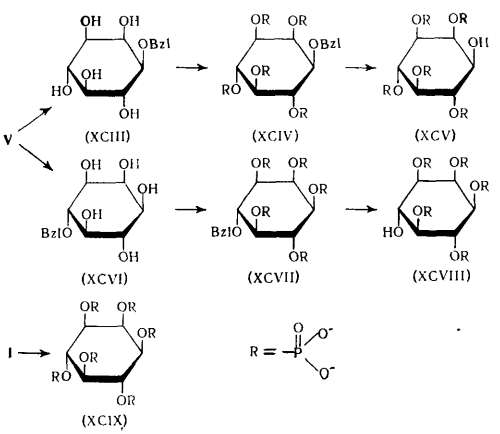
The phosphorylating agent most often used in the chemistry of monoesterified myoinositol phosphates is diphenyl phosphorochloridate, which is used at 0°C or in pyridine at 18–20°C. It is a strong phosphorylating agent, giving good yields of readily crystallisable triesterified phosphates. The phenyl groups are removed by hydrogenolysis in the presence of platinum catalysts. Phosphate migrations caused by the intrinsic acidity are avoided by isolating the myoinositol phosphates, obtained after removal of the protective groups, as their triethylammonium, cyclohexylammonium, and other salts. With as initial compounds myoinositol derivatives containing free hydroxyls at the positions to be phosphorylated, diphenyl phosphorochloridate has been successfully applied to the preparation of *sn*-myoinositol 2-phosphate[135], 1(3)-phosphate[49,52,71,112,131,136–138], 4(6)- and 5-phosphates[71,130] and 1(3), 4(6)-, 1(3),6(4)-, and 4(6),5-diphosphates[71,130]. It is interesting that, when this agent acts on D-mannose mono- and di-orthoacetates and on the diacetal (V) at 80–90°C, phosphorylation is accompanied[71] by replacement of orthoester by diphenyl phosphate groups (only phosphorylation takes place at 18–20°C), probably owing to nucleophilic attack on an orthoester oxygen atom by the activated phosphorus atom of the diphenyl phosphorochloridate with formation of a C–O–P bond. The phenomenon of removal of an orthoester group with simultaneous phosphorylation and probably acylation may find use in the synthesis of phosphoinositides.

Myoinositol monophosphates can be obtained also by the alkaline[139], acid[140], and enzymic[141–143] hydrolysis of phytin, and by the acid and alkaline hydrolysis of phosphoinositides[144,145].

The presence of a hydroxyl adjacent to the diphenoxyphosphinyloxy-group may lead to elimination of a phenyl group and migration of the phosphoric group with intermediate formation of a cyclic phosphate[118]. When the orientation of the vicinal hydroxyl is unfavourable to intramolecular phosphorylation, a bimolecular pyrophosphate may be formed. Hence the use of diphenyl phosphorochloridate for phosphorylating vicinal hydroxy-groups is not always justified.

A similar phosphorylating agent—bis-2,2,2-trichloroethyl phosphorochloridate—has recently been used to obtain monoesterified myoinositol phosphates[52]. Unlike a phenyl group, 2,2,2-trichloroethyl can be removed by the action of zinc in methyl alcohol[52]. This reagent has the same disadvantages as the diphenyl ester for obtaining polyphosphate derivatives. Dibenzyl and di-*p*-nitrobenzyl phosphorochloridates exerted a weak phosphorylating action on a secondary hydroxy-group in myoinositol[12].

Scheme 16

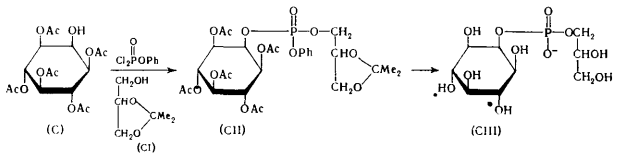


Angyal turned to polyphosphoric acid in the search for an agent for the polyphosphorylation of myoinositol derivatives[68]. However, application of this reagent to myoinositol compounds containing a benzyl, tosyl, or methyl protective group at position 1(3) results in the loss of such group with exhaustive phosphorylation. A convenient agent for these purposes was triethylammonium *N*-benzoylphosphoramidate[68], whose use completely eliminates the formation of cyclic phosphates, but involves experimental difficulties. Phytin (XCIX) and myoinositol pentaphosphates (XCV) and (XCVIII)—which may be products of the biosynthesis or decomposition of phytin—have been obtained by this method[146] (Scheme 16).

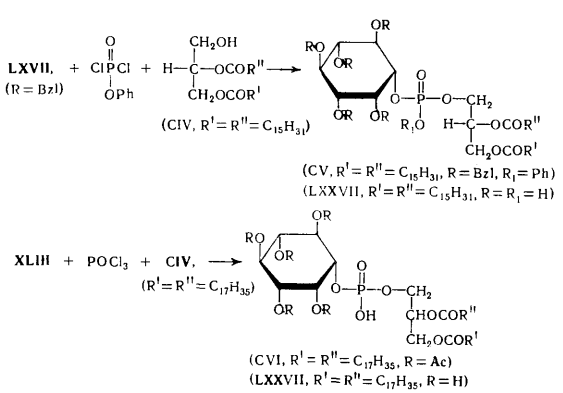
Preparation of diesterified myoinositol phosphates

Known methods of phosphorylation are used in myoinositol chemistry to form diesterified phosphate bonds[12]. Phosphorylation by means of polyfunctional chlorides of phosphoric acid presupposes the interaction of two different hydroxylated compounds followed by removal of protective groups. Thus Davies and Malkin[147] employed this method to prepare *sn*-myoinositol 2-*O*-glycerophosphate (CIII) by the interaction of *sn*-myoinositol 1(3),3(1),-4(6),5,6(4)-penta-acetate (C), phenyl phosphorodichloridate, and 1,2-*O*-isopropylideneglycerol (CI) (Scheme 17). A similar process was used to obtain the optically active monophosphoinositide (LXXVII) from the pentabenzyl derivative (LXVII: R = $C_6H_5CH_2$), phenyl phosphorodichloridate, and *sn*-glycerol 1,2-dipalmitate (CIV: R' = R" = $C_{15}H_{31}$) (Scheme 18)[61,62].

Scheme 17



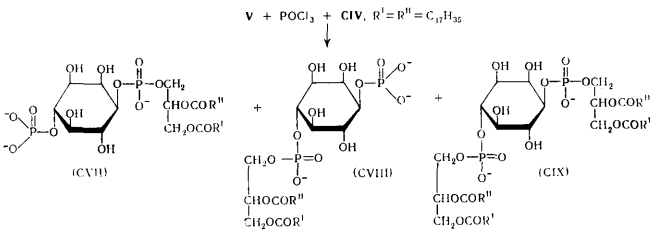
Scheme 18



Lyutik et al.[63] used phosphoryl chloride as phosphorylating agent (Scheme 18). This reacted with the 1,2-diglyceride (CIV: R' = R" = $C_{17}H_{35}$), and, without being isolated, the intermediate phosphorochloridate reacted further with myoinositol penta-acetate (XLIII). This method, unlike the previous method, can be used to obtain unsaturated monophosphoinositides. Another advantage is that the monophosphoinositide structure (CVI) is obtained as a diesterified phosphate—not the triesterified phosphate (CV)—which diminishes the number of stages in the synthesis.

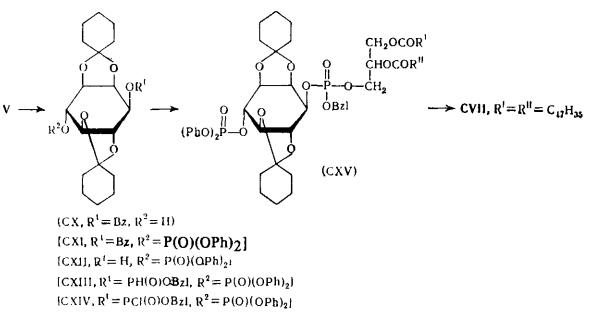
Phosphoryl chloride possesses not only advantages but also several disadvantages, which often prevent its use. Because of its polyfunctionality the phosphorylation of two hydroxylated compounds gives a large number of phosphorylated and also chlorinated products, which considerably lowers the yield of the required compound, and complicates its isolation[12].

Scheme 19



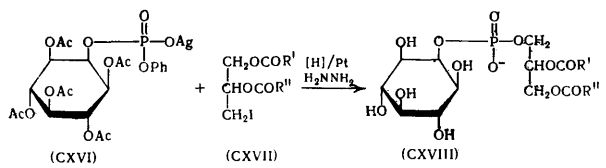
Phosphoryl chloride has been used also to produce the diesterified phosphate structure of more complicated phosphoinositides (Scheme 19)[58,59]. The above synthesis yielded not only the diphosphatidyl derivative (CIX) but also the diphosphoinositide positional isomers (CVII) and (CVIII), the latter (CVIII) having an unnatural structure. These isomers could not be separated.

Scheme 20



The above defect was overcome by using as starting material the diacetal benzoate (CX)[60], obtained by selective benzoylation of the diacetal (V) (Scheme 30)[70]. The compound (CX) was phosphorylated by means of diphenyl phosphorochloridate to form a monoesterified 4(6)-phosphate bond, and the benzoyl group was removed by the action of hydrazine hydrate (CX → CXI → CXII). A diesterified 1(3)-phosphate structure was formed by adding a phosphatidyl group by the method of mixed phosphoric anhydrides[12]: the phosphite (CXIII) was obtained by the action of the mixed anhydride of benzyl dihydrogen phosphite and diphenyl hydrogen phosphate on the derivative (CXII). The product was converted into the acid chloride (CXIV) by means of *N*-chlorosuccinimide, a new mixed anhydride was formed by the reaction of (CXIV) with diphenyl hydrogen phosphate, and this was condensed with the 1,2-diglyceride (CIV: R' = R" = $C_{17}H_{35}$) to obtain the protected diphosphoinositide (CXV), removal of the protective groups from which in the usual way gave the diphosphoinositide (CVII)[60].

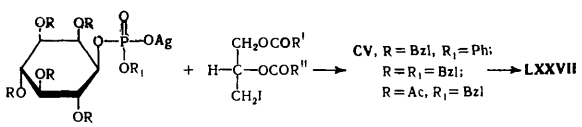
Scheme 21



(CXVI) (CXVII) (CXVIII)

The use of silver salts of substituted phosphoric acids for phosphorylation in the preparation of diesterified phosphates involves their reaction with halogen derivatives of the corresponding hydroxylated compounds. This method was first employed to obtain the unnatural monophosphoinositide (CXVIII) [148], by the action of 3-iodopropane-1,2-diyl distearate (CXVII) on the silver *sn*-myoinositol phosphate (CXVI)§ followed by removal of the protective groups (Scheme 21).

Scheme 22



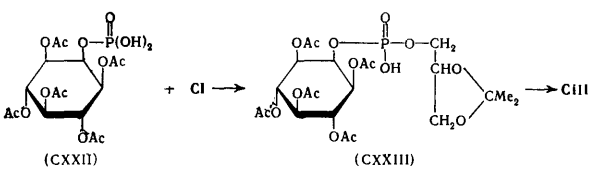
(CXIX, R = Bzl, R_1 = Ph) (CXVII, R' = R'' = $C_{15}H_{31}$;
(CXX, R = R_1 = Bzl) R' = $C_{11}H_{23}$, R'' = $C_{17}H_{33}$;
(CXXI, R = Ac, R_1 = Bzl) R' = $C_{15}H_{31}$, R'' = $C_{17}H_{33}$

The same method has been used to synthesise a natural monophosphoinositide [64,65,149] (Scheme 22), by treating the silver salts (CXIX)–(CXXI) with (CXVII). The silver salt (CXIX) was prepared by phosphorylating the pentabenzyl ether of myoinositol (XLI) with phenyl phosphorodichloridate, hydrolysing the product, and converting it into the potassium and then into the silver salt (CXIX) [52]. The silver salt (CXX) was synthesised by treating (XLI) with bis-2,2,2-trichloroethyl phosphorochloridate, removing the protective group, obtaining the dibenzyl ester by reaction with phenyldiazomethane, transforming to the sodium salt by anionic monodebenzylation, and converting to the silver salt (CXX) [149]. The silver salt (CXXI) was obtained similarly, except that myoinositol penta-acetate (XLIII) was phosphorylated with diphenyl phosphorochloridate, and the phenyl groups were then removed by hydrogenolysis [65]. This last salt (CXXI) was also prepared by treating (XLIII) with phosphoryl chloride and then with benzyl alcohol, subjecting the resulting triesterified phosphate to anionic monodebenzylation, and converting into (CXXI) [64]. The monophosphoinositide (LXXVII) containing unsaturated acid residues was obtained from (CXXI) [64,65].

The preparation of phosphoinositides by double decomposition between glycerol halogenohydrins and silver salts of phosphoric acids is distinguished by its selectivity and the high phosphorylation yields. However, it also involves many stages, as well as experimental difficulties in obtaining the starting materials, which often make it uncompetitive with other methods [12].

The reactions of monoesterified phosphates with hydroxylated compounds in the presence of condensing agents are also used to produce diesterified phosphate structures. The condensing agents act by preliminary activation of the monoesterified phosphate group [12]. Several of them are beginning to be used to obtain diesterified phosphate structures in the myoinositol series. Thus Ellis and Hawthorne synthesised the 2', 3'-dihydroxypropyl *sn*-myoinositol 1-phosphate (CIII) by condensing the phosphate (CXXII)¶ with 1,2-*O*-isopropylideneglycerol (CI) in the presence of dicyclohexylcarbodi-imide (Scheme 23) [150].

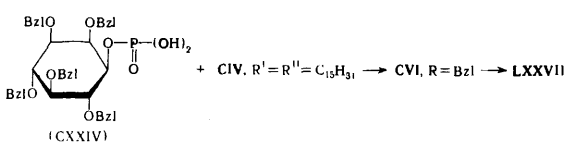
Scheme 23



(CXXII) (CXXIII)

2,4,6-Tri-isopropylbenzenesulphonyl chloride has been used to obtain the monophosphoinositide (LXXVII) from the phosphate (CXXIV) and the 1,2-diglyceride (CIV: R' = R'' = $C_{15}H_{31}$) (Scheme 24) [149]. The conversion of monoesterified into diesterified phosphates in the presence of condensing agents requires that excess of the hydroxylated compounds should be present: the use of stoichiometric quantities leads to the formation of pyrophosphate derivatives and hence a diminished yield of diesterified phosphates [150–159].

Scheme 24



(CXXIV)

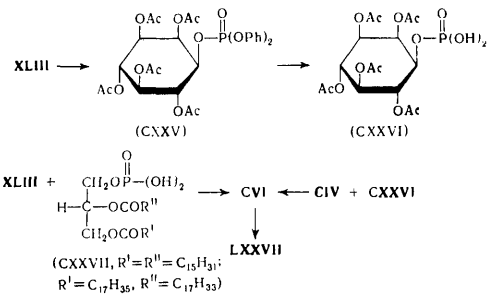
2,4,6-Trimethylbenzenesulphonyl chloride has been used in our laboratory to obtain mono- and di-phosphoinositides as optically active derivatives of natural structure or as diastereomeric mixtures (Scheme 25) [160]. Monophosphoinositides (LXXVII) have been obtained by the reaction of phosphatidic acids (CXXVII) with myoinositol penta-acetate (XLIII) or of the 1-phosphate of the penta-acetate

§The silver salt (CXVI) was prepared by phosphorylating the penta-acetate (C) with phenyl phosphorodichloridate, hydrolysing the product, isolating the potassium salt, and converting the latter into the silver salt (CXVI).

¶Compound (CXXII) was prepared by phosphorylating the myoinositol penta-acetate (C) with diphenyl phosphorochloridate and then removing the phenyl groups.

(CXXVI) with 1,2-diglycerides (CIV). A similar reaction was conducted with the phosphatidic acid (CXXVII) and the diacetal derivative (CXII) to obtain the diphosphoinositide (CVII: R' = R" = $C_{15}H_{31}$). This method is most promising for producing diesterified phosphate structures in the myoinositol series. Its virtue is that high yields of the products are obtained (almost uncontaminated with by-products) from readily available starting materials.

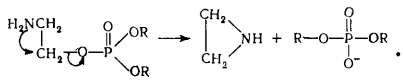
Scheme 25



Preparation of triesterified myoinositol phosphates

Various types of triesterified phosphates have already been mentioned as intermediates in the preparation of mono- and di-esterified structures. But their main interest lies in the hypothetical existence of triesterified glycerol phosphatides. It has been suggested that diesterified di- and tri-phosphoinositides are fragments of complicated lipid complexes, present in the animal brain, which may have the structure of triesters of phosphoric acid [161-165]. This hypothesis was first put forward by Collins [163]. Several hypothetical structures were suggested by Galanos and Kapoulos [164], who developed a technique for isolating lipid complexes from natural sources. According to the latter workers [164] myoinositol plays an important part in stabilising such complexes.

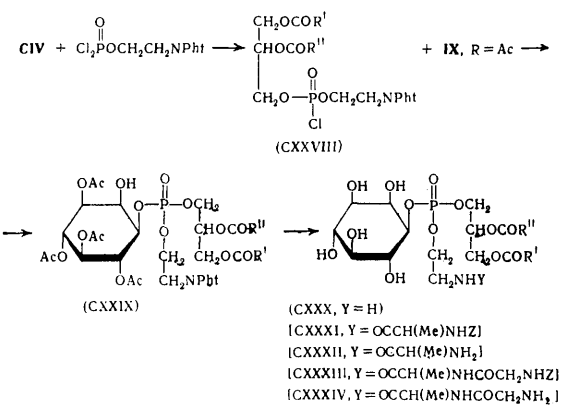
Nevertheless, other investigators [118] dispute the presence of phosphoric triesters in lipids because of instability. Reasons for the lability of triesterified myoinositol phosphates containing a vicinal hydroxyl have been discussed above. From theoretical considerations the corresponding triesters containing a neighbouring amino-group should also undergo hydrolysis with the formation of diesterified phosphate derivatives [118]:



Thus information on lipid complexes, as on triesterified phosphate structures, is inconsistent with theoretical views on the stability of such compounds studied on simple models. This problem requires further investigation, and one method may be to synthesise triesterified phosphate lipids.

Synthetic work has been done to obtain triesterified-phosphate glycerol phosphatides containing myoinositol (Scheme 26) [58,166-168]. The derivative (CXXVIII) was obtained by the action of 2-phthalimidoethyl phosphorodichloridate on the 1,2-diglyceride (CIV: R' = R" = $C_{17}H_{35}$) followed by condensation, without isolation, with the tetra-acetate (IX: R = CH_3CO), reaction occurring mainly at the equatorial hydroxyl in myoinositol [58,166]. Acetyl and phthaloyl groups were removed from the product (CXXIX) by hydrazinolysis. The resulting triesterified phosphate (CXXX) was used to synthesise phosphatido-peptides (CXXXII) and (CXXXIV) [58,167,168]—structural units in the hypothetical liquid complex of the bovine brain [164]—by condensation of the amino-group of the triesterified phosphate (CXXX) with *N*-benzyloxycarbonylalanine and *N*-benzyloxycarbonylglycylalanine followed by removal of the protective groups.

Scheme 26



The triesterified phosphate lipids—(CXXX), (CXXXII), and (CXXXIV)—are more labile than the corresponding diesterified-phosphate glycerol phosphatides [58,166-169], but their synthesis suggests that structures of this type may exist both in the free state and in natural lipids. Complexing with other natural compounds may restrict the degradation processes in triesterified phosphates studied on simple models. Final conclusions can be reached only after detailed investigation of this question.

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Formation, Structure, and Properties of Polymer Gels

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A gel is taken to be a polymer-solvent system in which the polymer, present at very low concentration, forms a quite stable three-dimensional network in the solvent. Consideration is given to the properties of gels in which the network is formed both by chemical and by physical bonds; attention is paid mainly to the second group of gels, in which variation in temperature produces a reversible transition between gel and solution. Existing views on the thermodynamic nature and structure of gels are subjected to critical analysis, and specific gel-forming systems are examined. A detailed analysis is made of the macroscopic phenomena accompanying the reversible solution-gel transition, as well as the strength, rubber-elastic, plastic, and relaxation properties of gels. A list of 399 references is included.

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I. INTRODUCTION

Many, often controversial papers have now been published on the nature and structure of gels, the laws of the transition from solution to gel-like state and the mechanism of gelation, the peculiarities of the physical and mechanical properties of gels, and also specific features of gels of polymeric and non-polymeric substances. The reasons for the appearance of different views on the nature and the sturcture of gels are firstly the disconnectedness of independently developed colloid-chemical, thermodynamic, structure–kinetic, and rheological approaches to the process of gelation, and secondly the substantial differences among the gel-forming systems themselves, from whose study various investigators have drawn their own conclusions. The Reviewers will endeavour to define what systems must be regarded as gels and what differentiates polymer gels from disperse colloidal systems and from concentrated solutions of polymers, as well as which thermodynamic, structural, and rheological changes in a coagulating system are inherent in gelation and which are characteristic only of certain classes of gelling systems.

The concept of a gel first arose in colloid chemistry[1-20]. It implied a disperse two-phase system in which particles of the disperse phase, mostly of elongated form and present in very low concentration, from a three-dimensional framework filled with a very large quantity of the dispersion medium. The framework in such systems was formed by various relatively simple compounds, crystalline or amorphous, mostly inorganic. From the start of the investigation of gels formed by compounds of high molecular weight, however, many specific features due to the nature of the polymers themselves were observed, together with the properties common to all systems of this class. The term "studen' [jelly]" appeared in the Russian scientific literature at this time. Several investigators attempted to separate the concepts of "jelly" and "gel", using various criteria. Thus systems possessing rubberlike elasticity were termed "jellies", and brittle systems were "gels"[21,22]; sometimes systems which were incapable of swelling after removal of the solvent were regarded as gels, and strongly swelling systems as jellies[21]. In other cases gels were two-phase disperse systems, while jellies were single-phase systems constituting true solutions of polymers, in which a three-dimensional network of intermolecular bonds was present between individual macromolecules[23]. However, such separation of these concepts merely introduces confusion, since, for example, systems formed by polymerisation or polycondensation in solution, in which a molecular network is certainly present, are usually termed, not "jellies", but *gels* (they are formed at a characteristic "gel" point[24]); on the other hand, jellies, formed from true solutions of polymers, may be either single-phase or two-phase systems, as we shall show below. It therefore appears to the Reviewers that, as in Ref. 25, the concepts "gel" and "jelly" must be regarded as identical, referring to the same broad range of systems, which in turn can be subdivided according to various criteria. We shall use the single term "studen'"†.

A gel is a polymer–solvent system containing a three-dimensional network of quite stable bonds of non-fluctuating character (i.e. almost unbroken by thermal motion). If such a polymer network is surrounded by the solvent (as a result of swelling of the solid polymer or diminution of the solubility of the polymer in the solution), the system is a gel independently of whether this three-dimensional framework is formed by chemical bonds or intermolecular bonds of physical nature, whether the system has been obtained without phase separation of a true solution or as a result of such separation. A gel may be either a two-component or a multicomponent system.

When gels are formed from solutions, each system is characterised by a critical concentration of gelation, below which a gel is not formed. This concentration is determined by the amphiphilicity of the macromolecules and the degree of regularity of the chemical structure of the polymer, the form of the macromolecule, the interaction between polymer and solvent, the molecular weight, and the flexibility of the polymer chain (the more flexible

† Since the above distinctions do not appear to have been made in the English language literature, "studen'" will henceforward be translated throughout as *gel* (Ed. of Translation).

the higher the critical concentration)[26]. We shall examine in greater detail below the action of all these factors on the process of gelation.

The formation of branch points in the network is accompanied by a considerable increase in viscosity, the appearance of rubberlike elasticity, and at a high polymer concentration by normal elasticity, a yield-point stress, and the capacity for retention of shape and loss of fluidity under the influence of its own weight and small stresses (as we shall see later, considerable irreversible deformations appear in gels under higher stresses). Another characteristic feature of a gel is its inability under isothermal conditions to dissolve in the solvent from which it has been formed, whatever quantity of this solvent is added[27]. Gels can be divided into two large groups depending on the nature of the bonds forming the three-dimensional network[28-30].

Gels of type I are irreversible systems with a three-dimensional network formed by chemical bonds between macromolecules, incapable of reversible fusion and coagulation, and breaking down only on degradation of the polymer itself. They include swollen three-dimensional polymers (e.g. swollen vulcanised rubbers, tanned gelatin, etc.), systems whose network has been formed by polymerisation of a monomer in solution in the presence of very small quantities of a cross-linking agent, and spatially cross-linked systems obtained in a solvent by the polymerisation or polycondensation of monomers having three or more functional groups.

Gels of type II are heat-reversible systems whose network is formed by various kinds of intermolecular bonds, obtained either by the limited swelling of solid linear polymers or from solutions of polymers by appropriate variation of the thermodynamic conditions.

II. GELS INCAPABLE OF MELTING (IRREVERSIBLE GELS)

Gels of type I containing the equilibrium concentration of solvent are equilibrium single-phase systems[31,32]; their three-dimensional network is usually regarded as macromolecular. Studies of such gels have been concentrated mainly on the thermodynamics of the swelling of cross-linked polymers in various solvents, which enables the interaction between polymer and solvent to be assessed[30,33-36]; the dependence of the swelling and the thermoelasticity of the systems on the degree of cross-linking[24] and on the polymer concentration[37-49] has also been investigated. The properties of such gels are significantly affected by whether they have been formed directly by the cross-linking of a polymer in a solvent or by the swelling of a three-dimensional system obtained with a specified degree of cross-linking in the absence of solvent[37,40,50]. On the formation of a network in solution, when the solvent concentration considerably exceeds the equilibrium value corresponding to the given degree of cross-linking, the gel is a non-equilibrium two-phase system, in which syneresis‡ takes place until the solvent has the same chemical potential within the gel and in the fluid liquid phase[31,32,51,55]. The phase ratio and the size of the structural units in gels of this type have been studied by various optical methods[37,55-58]. One of the main factors determining the properties of gels whose network has been formed in a solvent is the concentration of polymer in the system. Another important factor is the nature of the solvent, which determines both the ability of the polymer to form a supermolecular structure in solution[59,60] (in the case of poor solvents; the three-dimensional network is then also supermolecular—not molecular—in character) and the rubberlike elasticity of the resulting networks, which governs the subsequent shrinkage of the gel[61]. Both these properties play a decisive part in the forming of a polymeric solid via a stage of gelation with subsequent removal of solvent, i.e. in the so called xerogel state[62], whose structure (porosity) is completely determined by the structure of the original gel and the mode of solvent removal. The porosity of xerogels plays a very important part in their use as ion exchangers[63], and in recent years as carriers in the vigorously developing gel chromatography[59,64]. The preparation of gels having various specified porosities[65-67] requires the study of a wide range of novel gel-forming systems, solvents, and methods of cross-linking: research in this field is growing vigorously at the present time[68-70]. Such porous structures can be obtained also be evaporating the solvent from gels whose networks are formed by bonds that are physical—not chemical—in nature; the properties of such systems have been described for agar-agar[71], poly(vinyl) acetals[72], and cellulose acetate[73].

‡Syneresis is the expulsion of solvent during the compaction of particles of the disperse phase in the case of a colloidal system or during the establishment of thermodynamic equilibrium in a polymer–solvent system[51-54].

III. HEAT-REVERSIBLE GELS

We have been concerned mainly with gels in which the reversible solution–gel transition is of the greatest interest, occurring usually with change either in temperature, pressure[74], or solvent composition (addition of a precipitant, change in pH, introduction of various additives, etc.).

The properties of heat-reversible gels can be approached in various ways. Most authors consider that a gel is always a non-equilibrium heterogeneous two-phase system, since formation of a three-dimensional gel network is possible, in their opinion, only on phase separation of a single-phase solution[29,75,76]. Several authors hold the view that gels are formed without phase separation, as a result of formation of local intermolecular bonds between individual macromolecules present in true solution: gels are thus regarded as homogeneous, one-phase systems[77-79]. A number of authors think that gels may be either single phases or two-phase systems, structurally either homogeneous or heterogeneous[80-83]. It is noteworthy in this connection that the question of the phase constitution of polymeric gels is almost completely ignored in the foreign literature, where interest is concentrated mainly on the change in properties of the system with the formation of branch points of the three-dimensional network. Soviet investigators, however, pay great attention to the phase constitution of gels, and we shall examine in greater detail existing approaches to this problem.

1. Formation of Two-phase Gels with Phase Separation of a Solution

Gels of compounds of high molecular weight are regarded in colloid chemistry, by analogy with those of low molecular weight, as disperse two-phase systems, in

which particles of the solid disperse phase form a framework. Such an approach has been widely developed by the Rebinder school[84], who have worked out a detailed theory of structure formation in colloidal systems, applying generally to such diverse compounds as clays, concretes, and supersaturated solutions of synthetic and even natural polymers. A distinction is made between structure formation by coagulation and by condensation[23,84-87]: in a coagulated structure contact between the particles is effected by weak van der Waals forces, so that the system is characterised by low strength, plasticity with slight elasticity, and thixotropy; in a condensed structure strong cohesive or adhesive contacts are established between the particles, which confer durability and elasticity on the system. According to the ideas of the Rebinder school, the formation of a three-dimensional structure by means of such strong contacts between coalescing particles of a new polymer phase separating from a true solution with spontaneous formation of a colloidal system below the consolute temperature is the cause of gelation and the strengthening of the gel. Results obtained on gelation in aqueous gels of gelatin[88,89], polyvinyl alcohol[90,91], and cellulose acetate[92,93] have been interpreted in terms of the above concepts. These ideas, which are not open to doubt for gels that are typical lyophobic colloidal systems (they may also be polymer—non-solvent systems), obviously cannot be true in other extreme cases, when phase separation of the solution involves formation of two liquid phases, or when gelation is unaccompanied by phase separation. Because of the high viscosity of polymer systems, of course, and also at low interfacial energies, gels of both types can be formed, differing as little as we please. For these transition systems the actual difference between them, of course, is devoid of meaning.

It is noteworthy also that the transition from typical polymer gels (formed with liquid phase separation or without phase separation at all) to typical colloidal gels is determined by the nature of the solvent, which has a significant influence also on the flexibility of the polymer chain: as the solvent becomes poorer and the rigidity of the polymer chain increases, its ability to swell diminishes (without which a polymeric type of gel cannot be formed), and the gel becomes increasingly colloidal in nature, i.e. it becomes a two-phase system with a three-dimensional framework formed by rigid macromolecules or their aggregates, which do not swell in the solvent. The above views on the formation of a solid polymer phase may therefore apply mainly to gels of rigid-chain polymers.

According to modern views, which originated in the work of Kargin, Papkov, and Rogovin[94-96], polymers form true solutions[28], interaction between polymer and solvent being regarded as the mixing of two liquid phases[97-99]. The concept of liquid phase separation underlies Papkov's concept of gelation[29,97]§, the theoretical principles of which will be briefly considered.

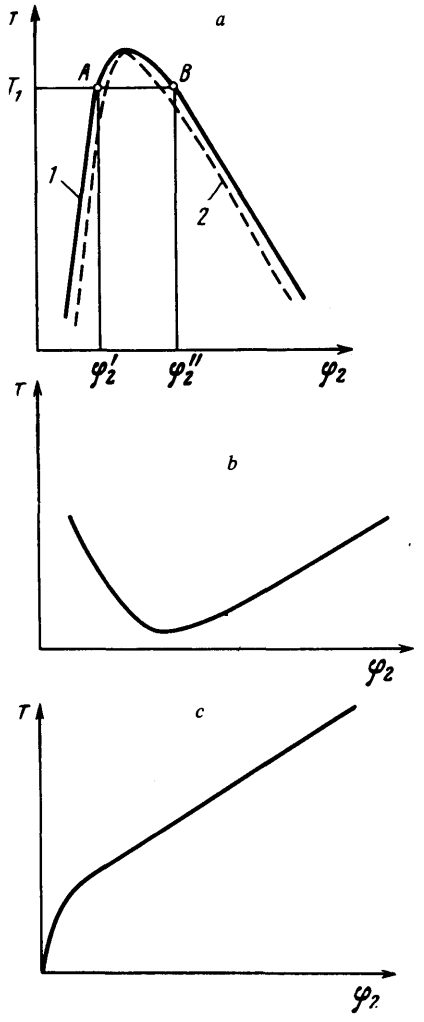

Figure 1. Equilibrium diagrams for systems with: *a*) an upper consolute temperature; *b*) a lower consolute temperature; *c*) a polymer crystallisable from solution, where T is the phase-separation temperature, φ_2 is the polymer concentration, and φ_2' and φ_2'' are the polymer concentrations in the equilibrium phases: 1) binoidal; 2) spinodal.

Gelation can occur either with a fall or a rise in the temperature depending on the type of temperature variation of solvent power[28]: gels are formed on cooling or on heating according as the systems have upper or lower consolute temperatures. Fig. 1 illustrates phase diagrams for various systems. The curve separating the regions of existence of stable single-phase and of metastable solutions is termed a binoidal (curve *1*), and that separating the regions of existence of metastable and unstable solutions is a spinodal (curve *2*). The temperatures and concentrations corresponding to the binoidal represent the conditions under which the thermodynamically stable true solution of a polymer passes into the metastable state and forms a colloidal solution containing the nascent new phase. The existence of a diagram having a consolute temperature suggests the existence of a region of phase separation of the polymer into two new, liquid phases.

§ The possibility of liquid phase separation in the formation of gels was mentioned long ago by Hardy[7,9,10], who investigated the gelatin—water—ethanol system, and showed that the single-phase solution separates into two liquid phases below a certain temperature. As these phases set further, the three-dimensional skeleton of the gel is produced by one or the other phase depending on the concentration of gelatin in the system and on its rate of cooling, which leads to a significant difference between the mechanical properties of the gels.

The diagrams are quite different in form (Fig. 1*c*) when a new solid crystalline polymeric phase separates from solution. The type of phase diagram may therefore indicate whether phase separation involves nucleation of a new polymeric solid phase or formation of two liquid phases, one of which is strongly enriched with the polymer.

According to Papkov[100] a gel is formed only in the region of phase separation if the viscosity of the concentrated polymer phase is very high, which prevents complete spatial separation of the system into two liquid phases. He therefore regards a gel as a non-equilibrium two-phase system with incomplete separation of the phases, which, in contrast to the above colloidal views on gel structure, comprise a swollen polymer forming a cellular framework with the almost pure solvent distributed in it as drops. The existence of these two phases is responsible for the presence of a gel. On Papkov's view a gel does not exist outside the region of phase separation, but a concentrated solution is present, possessing different properties—unlimited fluidity, low elasticity, etc.

Fig. 1 shows that at temperature T_1 the equilibrium state of the system corresponds to separation into two phases having concentrations φ_2' and φ_2''. Any gel of concentration below φ_2'' will therefore be a non-equilibrium system, and solvent will separate with time until the chemical potentials in the two phases become equal. Syneresis in these systems is completely analogous to that in gels which have been chemically cross-linked within the solvent (Section II). Its progress is more intense the lower the concentration of polymer in the gel, which undergoes considerable shrinkage.

Since at a given temperature the system undergoes phase separation until the concentration φ_2'' is reached, the gel obtained directly from a solution of this concentration is a thermodynamically equilibrium system[101], which means that its composition should be the same independently of the route—from the solution or by swelling of the solid polymer—by which it has been obtained. Such independence forms the basis of the plotting of phase diagrams for gelling systems: owing to the impossibility of determining the composition of a concentrated polymer phase during phase separation, points on the right-hand portion of the binoidal are determined experimentally from the equilibrium swelling of the dry polymer[89]; the left-hand portion is plotted as usual from the cloud points of the solutions[28].

Only a few experimental phase diagrams of gelling systems have been published (Fig. 2).[90,92,102,103] In most cases they are similar in shape to miscibility diagrams for partly miscible liquids. Right-hand portions of phase diagrams have been obtained experimentally from the swelling of solid films, i.e. from the view that a mixture of polymer and solvent comprises two liquid phases. However, gelation in the region of phase separation is then interpreted as emergence of the solid polymer as a new phase. As we have mentioned above, these two approaches are incompatible.

Nevertheless, the complexity of obtaining phase diagrams for gelling systems and the limited possibility of using them result from the fact that structure formation in complicated polymer systems leads to a dependence of the state of the system on the approach to it and to irreversibility of several processes. These features of polymer systems have been discussed theoretically[104,105]. It has been shown during recent years that the swelling of a polymer film also depends on the previous history, i.e. on the character of the solvent from which the film has been obtained and on its thermodynamic affinity for the polymer[60,63], on the temperature to which the solution has been preheated and on the rate of cooling, which govern the presence and character of a supermolecular structure in the film[106-109], on the concentration of the solution, which determines the proportions of intra- and inter-molecular bonds in the system and also the conformation of the polymer macromolecule[110-113], and on the temperature at which the solvent had been evaporated to obtain the film.

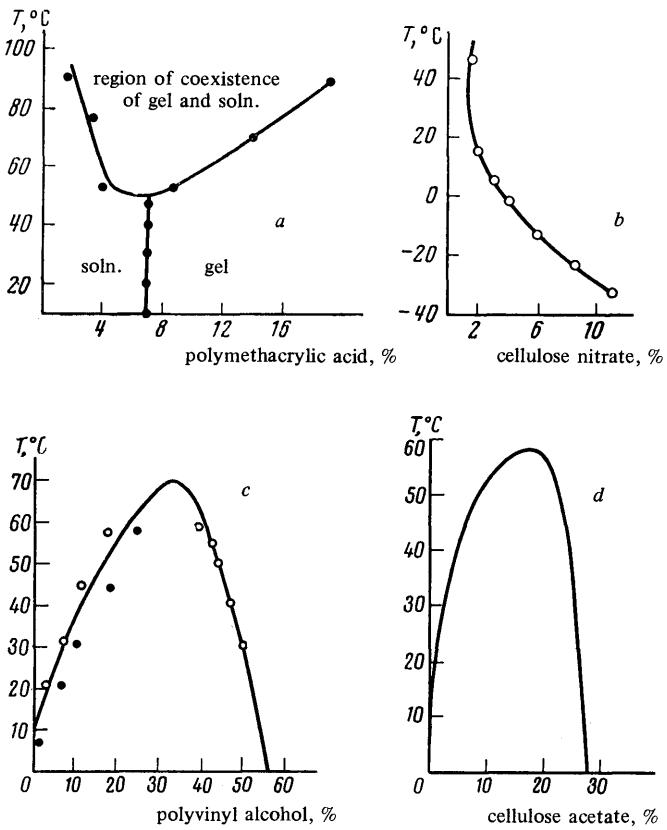

Figure 2. Experimental equilibrium diagrams for the gelling systems: *a*) aqueous polymethyacrylic acid[102]; *b*) ethanolic cellulose nitrate[103]; *c*) aqueous polyvinyl alcohol[90]; *d*) cellulose acetate—3,6-dioxaoctanol[92].

This last fact is well known for gelatin. If the solvent is evaporated at a temperature above the helix–coil transition point (considered in greater detail below), macromolecules are preserved in the loop conformation in the film; when evaporation occurs below the transition point, the macromolecules are preserved in the spiral state[114]. Furthermore, vaporisation of the solvent below the gel point of the system yields a film via a gel stage. Both these factors effect significantly the ability of the films to swell[29,115,116]. The degree of swelling of a film obtained from an aqueous gelatin gel depends very considerably on the concentration of the gel: the lower the concentration, the larger the number of cavities filled

with solvent, and the greater the swelling of the film, obtained by evaporation of this solvent, when replaced in the solvent (Fig. 3).[117]

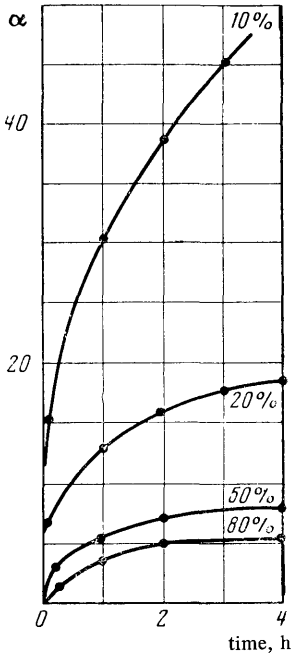

Figure 3. Dependence of swelling of film α on polymer concentration (indicated on curves) in gel from which it has been obtained[117].

For the above reasons the swelling of a film in fact depends on its previous history, and the right-hand branch of the phase diagram plotted from these values is displaced along the concentration axis (by 15–20%) depending on the various factors enumerated above[109]. As a consequence the region of phase separation in gelling systems can be determined only very roughly, and the characterisation of specific gelling systems by the temperature–concentration phase diagram is largely devoid of meaning unless the precise conditions under which it was obtained are indicated.

Two-dimensional phase diagrams are applicable only to binary systems, so that they can be used to characterise gelation only with a narrow molecular-weight distribution, when the polymer can be regarded as a single component. In this connection we must again mention the necessity of cautious use of the concept "component" in such multimolecular systems as polymers[118]. In real gel-forming systems—which are, of course, polydisperse—change in temperature is accompanied by loss of solubility initially of the higher fractions and then of the lower fractions. Gelling is therefore a multistage process[75] occurring in a multicomponent system[119], which it is illegitimate to characterise by a binary phase diagram[28,97]. The practical possibility of using such diagrams to represent gelation in polydisperse systems is due to the experimental fact that the position of the right-hand portion of the binoidal varies very little with molecular weight[120].

The investigation of gelation on narrow fractions[121-123] showed that the lower fractions play no specific part in gel formation, since it obeys the same laws in unfractionated and fractionated polymers. Fig. 4 illustrates the molecular-weight dependence of several parameters of gelation, and shows that the rigidity of the gel, as well as the melting point[124] and the "aggregation" temperature (i.e. the temperature at which viscosity begins to vary with time[125]), increases with molecular weight (in several cases only to a certain value).

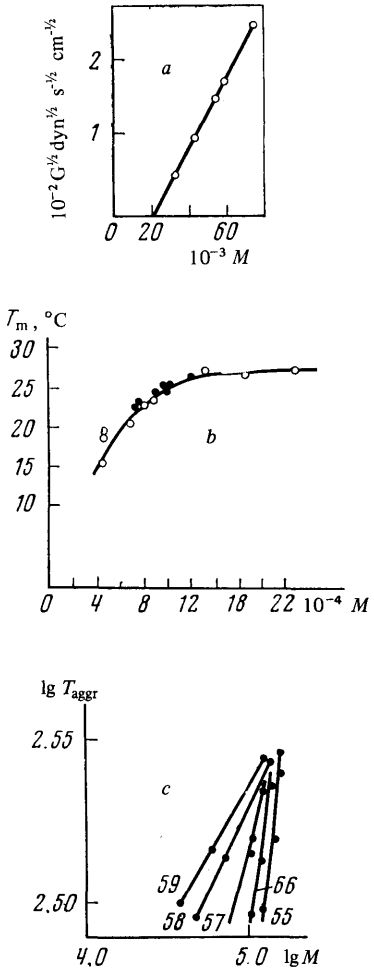

Figure 4. Influence of molecular weight of polymer on the properties of gels: *a*) modulus of elasticity G; *b*) melting point (for aqueous gelatin gels)[121]; *c*) "aggregation" temperature (for gels of cellulose acetate of varying degrees of substitution in benzyl alcohol)[125].

The above concepts on gel formation with phase separation are applicable also when the solubility of the polymer is diminished, with change not only of temperature but also of solution pH (ion-reversible gels)[112,126] and especially on introduction of a precipitant[29,127-130] (which is often encountered in the fractionation of polymers).

Under these conditions the range of existence of a gel can sometimes be determined by means of ternary diagrams[28]. In some cases not only two-phase but also multiphase systems are formed depending on the interactions of all the components[129,131,132].

2. Single-phase Gels obtained without Phase Separation

At polymer concentrations above the equilibrium value φ_2'' (Fig. 1), i.e. to the right of the binoidal, single-phase gels are formed without phase separation (Fig. 2*a*) either as the solubility of the polymer in the solution decreases or with limited swelling of linear polymers. Similarly to the swelling of network polymers, gel formation here is due to the existence of branch points in a three-dimensional network resulting from local interactions of macromolecules. Since gels are usually formed by polymers, amphiphilic in nature, in thermodynamically poor solvents, limited swelling of the polymers is evident under thermodynamic conditions such that the polymer–solvent interaction is sufficient to overcome some polymer–polymer contacts but insufficient to overcome other, stronger contacts, which form a three-dimensional network within the solvent.

Addition of excess of a lower component to an equilibrium gel cannot produce any change until the thermodynamic conditions change[27]. With rise in temperature, and also with improvement in the solvent power of the medium surrounding the gel, the number of branch points may decrease, ultimately with destruction of the gel. If the lifetime of the branch points becomes so short (owing to heating or change of medium) that the movement of macromolecules is virtually unrestricted by existing short-lived bonds, a transition will occur from the "stable" gel network to a purely fluctuational network, i.e. to a flowing liquid.

Transitions due merely to the kinetics of the formation of branch points, unaccompanied by change in the thermodynamic state of the system, are not associated with the presence of different phases, and such gels may therefore be single-phase systems. Gels comprising a single phase can be produced not only by variation of the temperature but even under isothermal conditions, with variation of the concentration during transition from the solid polymer to its dilute solution. Results obtained for such an isothermal transition in the poly(vinyl chloride)–dibutyl phthalate[133] and gelatin–glycerol[134] systems show (Fig. 5) a successive transition from vitreous to rubber-elastic state and to viscous fluid.

Rubberlike elasticity can appear only in solids possessing a three-dimensional network with sufficiently large distances between branch points, which is a necessary condition for the development of flexibility in the macromolecular segments forming the network. If the rubber-elastic state arises in solution owing to strong intermolecular bonds, i.e. because of formation of a stable three-dimensional network, the range of existence of the solution coincides with that of the gel. In solutions in which such strong bonds are not present, the rubber-elastic state is largely masked by fluidity, and the system passes from the solid polymer to a dilute solution via a concentrated-solution stage, not via a gel stage. There are then no grounds for assuming that the appearance of a rubber-elastic state as the polymer swells coincides with intersection of the binoidal, as is stated by Frenkel'[105]: i.e. rubberlike elasticity may appear equally in the one-phase and two-phase states of gels. Characterisation

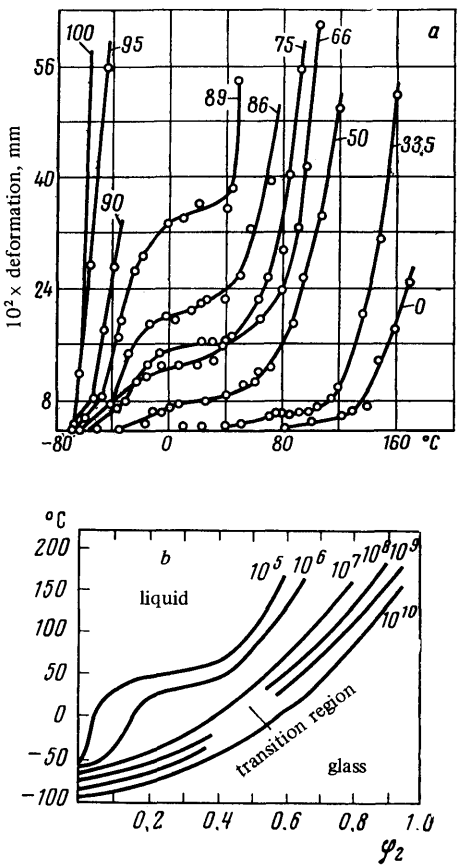

Figure 5. Isothermal transition from dilute solution to solid polymer via gelation stage: *a*) thermomechanical curves for the poly(vinyl chloride)–dibutyl phthalate system (numerals on curves denote concentrations of dibutyl phthalate)[133]; *b*) variation of modulus of elasticity of gelatin–glycerol system with temperature and concentration φ_2 (numerals on curves denote moduli of elasticity; a gel is present in the range $G = 10^5$–10^7 dyn cm^{-2}).[134]

of the gel-like state of polymers therefore requires, as stated by Papkov[29] and shown experimentally by Meerson[135], examination both of phase diagrams (which have limited applicability, as we have noted) and the concentration dependence of glass and yield points (for amorphous systems) or melting points (for crystalline systems) (Fig. 6).

The mechanism of the formation of single-phase gels of uncrystallisable polymers is analogous to vitrification of the polymers themselves[78], except that in the vitreous state bonds are formed between a considerable number of repeating units, whereas a kind of partial vitrification, i.e. formation of a small number of the strongest bonds, occurs in gels, leading to a stable network structure¶.

¶ Thus in the case of amorphous polymers gels, being systems intermediate between liquid and solid, are also intermediate between solutions and condensed systems in the vitreous state[79].

The presence of two types of intermolecular interactions—strong and weak[79]—causing the appearance of a three-dimensional network forms the basis of the gel-like state, independently of the phase state of the polymer in which it develops.

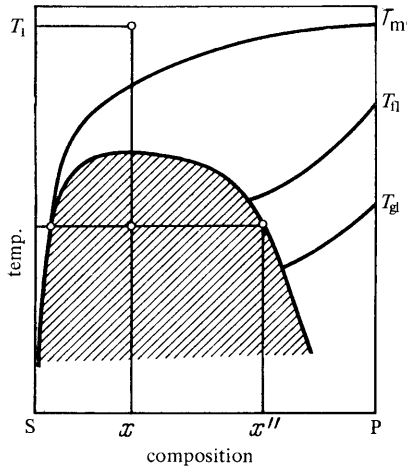

Figure 6. Concentration dependence of glass point T_{gl}, flow point T_{fl}, and melting point (S = 100% solvent; P = 100% polymer).[29]

3. Role of Crystallisation in Gelation

In contrast to the above discussion, most investigators consider that gelation is inseparably associated with crystallisation of the polymer within the solvent. This view is based firstly on the Herrmann—Gerngross micellar model[136], according to which crystalline regions (regions of parallel packing of segments of many macromolecules) form the branch points of the three-dimensional network, independently of whether the chemical structure of the polymer permits its crystallisation. It is based secondly on the fact that gelation is characteristic only of polymers whose macromolecule contains strongly interacting polar groups; such a structure leads to chain rigidity, which in the opinion of several investigators, increases the tendency to crystallisation[119,137-139]. On this hypothesis many authors assume that crystallisation accompanies gelation in polyacrylonitrile[140-142], poly(vinyl chloride)[143,144], and even random copolymers[138,145,146]. Sufficient regularity of the chain, in most cases a necessary condition for crystallisation, can hardly be achieved in ordinary statistical copolymers. In polymers and copolymers containing sufficiently extended blocks of uniform structure, however, local crystallisation is possible in solution[147], with the formation of more stable "branch points" of the gel network.

Crystallisation in solution is characterised thermodynamically by the phase diagram illustrated in Fig. 1*c*, representing the equilibrium between the pure crystalline polymer and its saturated solution. However, hardly any such diagrams have been published for specific gel-forming systems. Phase diagrams of crystallisable polymers were first obtained, for polyethylene in various solvents, by Richards[148], who showed also that, after the crystalline phase has melted completely, the system may separate into immiscible liquid phases, possibly accompanied by gelation. Thus crystalline and amorphous phase separations are independent processes, as is emphasised by Papkov[29].

The presence or absence of crystallisation is indicated also by the thermal effects and volume changes accompanying gelation[149-151] (see below) and by direct structural methods[150,152-154]. The concentration dependence of the melting points of crystallisable gels, in contrast to the corresponding relation for amorphous gels, follows Flory's equation

$$\frac{1}{T_m} - \frac{1}{T_{m_0}} = (R/\Delta H_u^1)(V_1 - \chi_1 v_1^2)(V_u/V_1) \qquad (1)$$

for mixtures of a crystalline polymer and a component of low molecular weight, in which T_{m_0} and T_m are the melting points of the polymer in the absence and in the presence of solvent, χ_1 is an interaction parameter, V_1 the molar volume of the solvent, ΔH_u the heat of fusion, v_1 the volume fraction of the solvent, and V_u the volume of the repeating unit of the polymer.

The combined application of these methods suggests that completely amorphous gels are obtained in several systems (polyacryloglycinamide in water[150,155-160], copolymers of acrylic acid, acrylamide, and acrylonitrile in water[161-163], poly(vinyl chloride) in dibutyl phthalate[143], and copolymers of methyl acrylate and methacrylic acid[164]). Nevertheless, amorphous (atactic) poly(methyl methacrylate) does not form gels in any solvent, whereas the crystalline stereoregular poly(methyl acrylate) exhibits a strong tendency to gelation because of the formation of complexes between iso-segments and syndio-segments[165-169]. The same effect is observed with polyacrylic acid[170], which forms gels only when in the isotactic form, whereas polymethacrylic acid forms gels in the amorphous (atactic) state[102,112,171-173]. The ability of several polymers to crystallise depends so strongly on the composition of the solvent that, as has been shown with polyacrylonitrile[142,174] and polyvinyl alcohol[175], they are able to give amorphous gels in some solvents, and crystalline gels in others.

When a polymer shows a strong tendency to crystallise in a solvent medium, the gels may have the character of crystalline solvates[176,177]. With intense crystallisation of the polymer the gels are devoid of the typical properties of gels, notably elastic and rubber-elastic properties: i.e. they are, rather, pastes[178] (polyvinyl alcohol in aqueous acetone[29], methanol[29], and glycerol[175], polycaproamide—formamide systems[29], and poly(alkyl acrylates) with straight-chain alcohols[176]). The other systems in which reversible gelation has been observed comprise polyvinyl alcohol in water (in the absence[179-183] and in the presence[184-186] of complexing agents) and in aqueous glycerol, diethylene glycol[124,149,187], methanol, and acetone[29], as well as in anhydrous solvents (formamide, *N*-methylpyrrolidone, and dimethyl sulphoxide[175]); poly(vinyl chloride) in dibutyl phthalate[143] and in dimethylformamide[144]; polysaccharides[188,189], alginates[190,191], pectins[192], and agaroid[193] in water; cellulose and its ethers in organic solvents[194-196]; polyacrylamide in water[197]; copolymers of vinyl chloride and methacrylic acid, acrylic acid and ethyl acrylate[198], styrene and caprolactam[199], styrene and oxiran[200], and styrene and isoprene[201] (so called "mesomorphic gels"); and gels of

cellulose and other polymers in water, obtained in a special way and containing large regions of the crystalline phase[202-205].

It is thus clear from the above account that both amorphous and crystalline gels exist: i.e. gelation often involves crystallisation, but the latter is not an inherent part of the process[163,175]. The tendency to associate gelation with crystallisation often arises from the well defined structure formation in solutions and gels of polymers, which we shall very briefly examine.

IV. STRUCTURE OF GELS

It was considered for a long time that formation of a single-phase gel involves merely the formation of a three-dimensional network of separate macromolecules[23,77,79]. However, true solutions of polymers, like solutions of liquids of low molecular weight, are inhomogeneous[28], strongly characterised by association. The presence of fluctuating association complexes is evident even in very dilute solutions and in good solvents[206-220] long before the consolute temperature. Great interest is aroused by the variation in the conformation of macromolecules during association with increase in concentration and by the dependence of this process on the flexibility of the polymer chain[221-228]. Which conformation is most favourable for gelation is also of interest[169,229].

The influence of macromolecular conformation on gelation has been studied in greatest detail on gelatin, the most widely distributed gel-forming compound. The helix—coil conformational transition, which is typical of many polypeptides and biological macromolecules, occurs in gelatin at 35°C. Gelation takes place only below this temperature, i.e. with the helical conformation of the macromolecule. When a dilute solution undergoes concentration above 35°C, with the macromolecules remaining in the coiled state, only a significant increase in viscosity occurs up to very high concentrations, with complete absence of gelation. Thus formation of the helical conformation of macromolecules and gelation are interlinked processes: i.e. the formation of intramolecular aggregates during helix formation and the formation of intermolecular bonds (branch points of the three-dimensional network) leading to gelation are due to interactions of the same nature. As we shall see below, the energy and other parameters of the gelation of gelatin are largely determined by the characteristics of the above conformational transition in the macromolecule (Section V, 1). Most other biological macromolecules do not form gels in the native state, and several of them are capable of gelation only when denatured. A favourable conformation of the macromolecule, with a considerable number of groups capable of forming intermolecular bonds facing outwards, obviously plays an important part here as well. Determination of the conformations of macromolecules in synthetic polymers involves great experimental difficulties, and therefore available data are ambiguous.

Processes preceding phase separation—aggregation and nucleation of a new phase, which appears near the consolute temperature—take place with change in temperature. However, if gelation occurs as a consequence of the formation of branch points of a three-dimensional network with change of thermodynamic conditions without phase separation, the system loses solubility and fluidity, with of course, the fixation of association complexes present at the instant of loss of fluidity. Thus, as stated by Glikman[76] for the separation of a new phase, structure formation unaccompanied by phase transition converts fluctuating association complexes present in solution into aggregates[174], i.e. into quite stable structures, the three-dimensional network within and between which is no longer fluctuating but stable in character. The viscosity of an associated true solution does not vary with time, whereas that of a solution undergoing cross-linking (a so called "gel-solution"), in which the structure of association complexes become fixed, varies considerably with time[21,75]. It appears to the Reviewers that a sharply defined transition from a solution of invariable viscosity to a solution whose viscosity varies with time does not necessarily indicate the start of separation of a new phase, as certain authors assert[33,75,88,89]. This is often evidence of the appearance of individual stable branch points of a three-dimensional network, whose formation takes a long time[21] and results ultimately either in a single-phase gel or in phase separation. Many investigators have pointed out the two-stage character of gelation (aggregation and formation of individual branch points leading to a diminution of fluidity, followed by formation of a continuous network leading to a complete loss of fluidity)[81,82,230]. The gel network would obviously be formed both inside aggregates (between separate macromolecules) and between aggregates (supermolecular structures). Theoretical aspects of the production of gels from aggregated particles have been discussed by Joly[231-233].

It may be supposed that a truly molecular network is very rarely formed in gels. It may appear either in very dilute systems or in solvents in which formation of a polymer structure is feebly developed (but these are usually thermodynamically good solvents, in which gels are seldom formed). A special case of the formation of a macromolecular network is possible in solvents possessing good affinity for the polymer but whose molecules each contain two functional groups, and can therefore act, as it were, as cross-linking agents, forming hydrogen or other intermolecular bonds between the polymer macromolecules[175].

The possibility of the formation of macromolecular and supermolecular networks in gels had already been considered by Ferry in his early papers[234,235], in which he distinguished between "coarse" and "fine" networks. He linked the different network structures with the conditions of production of the gels: the lower the temperature the less favourable the conditions for aggregation and the "finer" the networks formed. Heating the gel to near the melting point causes reorganisation with the formation of "coarser" networks. The same feature was found by Stainsby[236] from a study of the mechanical properties of gels. He stated that at low temperatures many bonds are formed of poor stability but preventing further ordering of the network, whereas near the melting point few but very stable bonds are formed, so that ordering is possible. The dependence of the structure of a gel on the temperature conditions of its formation has been confirmed also by sedimentation in an ultracentrifuge[237,238], as well as by a thermodynamic method[239], but the correctness of the latter is open to doubt.

The above considerations show that the majority of gels, including single phases, are structurally microheterogeneous systems. This is well supported by direct structural methods of investigating gels, primarily electron microscopy (with special procedures to ensure high resolution[240,241]). Results illustrated by Fig. 7 indicate that the gel networks of gelatin in water[240,242,243], as well as of cellulose diacetate in aqueous acetic acid[244] and of

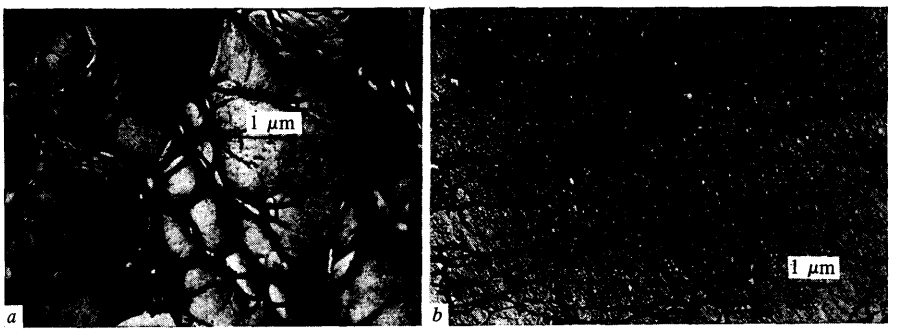

Figure 7. Electron micrographs (×8400) of gels of: *a*) gelatin in water (20% concentration);[243] *b*) cellulose diacetate in 35% aqueous acetic acid[244].

polystyrene in decalin[245], are made up of fibrillar structural units (of diameter ~1000 Å), whereas aqueous polyvinyl alcohol gels comprise globular units (diameter of globules ~1000 Å).[246-249] The electron micrographs cannot indicate, however, whether the observed structural units are at equilibrium or fluctuating in character; it must also be remembered that the presence of coarse particles in the case of polymers, *pace* Ref. 70, are quite unable to determine the phase state.

Another direct method for examining the structure of polymer solutions and gels is the scattering of light[250]. Application to concentrated solutions of polymers[251] reveals an extremal concentration dependence of scattering, which indicates that the association complexes increase in size until a fluctuating network appears in the solution, after which the scattering begins to diminish owing to the ordering of the network[252]. A similar variation is observed in coagulating systems[253,254]: the turbidity increases with aggregation, to reach a maximum on formation of the first branch points; with further increase in the latter the network becomes increasingly ordered, and the scattering of light diminishes to become independent of the number of branch points in the gel network[83,255]. The coarser scattering particles in polymer solutions and gels are therefore determined from the turbidity spectrum[56,256-259], obtained by measuring the optical density at various wavelengths of the incident light and processing the experimental results on the basis of Mie's theory[260-263]. During recent years a laser technique of measuring anisotropic small-angle scattering of polarised light has been successfully used to determine the size of the structural units of a gel[57,58,264-266]. Prins and Bueche have shown[267,268] that a random distribution of gel branch points is present over a certain concentration range and in certain solvents, but in most cases the branch points are formed by supermolecular structural units whose size varies with the temperature and with the nature of the solvent. According to this method the structural units of aqueous gels of gelatin and of polyvinyl alcohol have diameters of 3000–6000 Å, in good agreement with results obtained by electron microscopy.

The distinction between the hypothetical network and cellular structures of gels, which for a long time attracted great attention[33,269,270], disappears in considerable measure when the structural units are large. If the particles that are growing together into a network occupy a considerable volume, the space between them, filled with solvent, resembles a cell: i.e. the gel has a peculiar network–cellular structure, as is readily seen from Fig. 7. The predominance of one or other type of structure depends on the polymer–solvent system and on the concentration of the polymer. Transitions from open to closed gel structures have repeatedly been observed experimentally[93,271].

V. MACROSCOPIC PROPERTIES OF GELS DUE TO THEIR NATURE AND STRUCTURE

1. Properties characterising a Reversible Solution–Gel Transition

The temperature at which a gel passes from the rubber-elastic to a fluid state with destruction of the three-dimensional framework is termed the melting point of the gel. As this transition is somewhat diffuse, no absolute methods are available for determining the melting point; various research methods for detecting the melting of gels have been described[272-274], among which the most widely used is to measure the movement of a sphere, placed below the surface of the gel, when the temperature is slowly varied at a constant rate[275].

The gel point, i.e. the temperature at which formation of a gel first becomes possible, is usually determined as the temperature at which the viscosity of the system begins to increase rapidly (when each temperature is maintained for a given time). In all gel-forming systems the melting point is higher than the gel point. The magnitude of the difference, i.e. the hysteresis of fusion and gelation, varies within very wide limits for different gels: thus in 5% aqueous gels of gelatin the melting point is only 3 deg above the gel point[235], but in certain other gels the difference amounts to tens of and even a hundred degrees (e.g. the gel and melting points for a 5% gel of poly(vinyl chloride) in diethyl hexyl phosphate, a gel of cellulose triacetate in trischloroethyl phosphate, and a gel of polyvinyl alcohol in a 60 : 40 mixture of water and glycerol are respectively 36° and 108°C,[144] 3° and 120°C,[144] and −20° and 90°C, etc.). The hysteresis is probably due to a significant difference between the mechanisms of the formation and the fusion of a gel[114]. Formation involves a succession of many stages requiring a certain degree of supercooling and a long time, which results in a wide set of branch points in the three-dimensional network. Yet the melting of a gel has all the signs of a concerted transition, requiring the simultaneous rupture of several weak bonds followed by a rapid disordering of the chain units.

Even with infinitely slow cooling, therefore, the gel point will evidently not coincide with the melting point, as is supposed by certain authors[276], although some approach of these temperatures does occur. The difference in mechanism between formation and fusion of a gel is evident also in a difference between the energies of formation and rupture of the bonds in the network: gels of polyvinyl alcohol in various solvents show that the energy of destruction of the branch points always exceeds the energy of their formation[187,277] (since the latter corresponds experimentally to only one of the stages of gelation, whereas the former corresponds to the completely formed gel structure).

The hysteresis of melting and gel points is associated also with the often described Arisz effect[29,116,117], consisting in the dependence of the melting point of a gel on its previous history with respect to temperature. The melting point of a gel depends in several cases on the time and especially the temperature of its formation. This variation is connected firstly with different forms of cross-linking of the system at different temperatures, these determining the types and stability of the branch points formed (Section IV). The melting points of gels formed by cooling rise as the temperature of formation falls[122], but at very low temperatures of gelation (e.g. near 0°C with an aqueous gelatin gel[121]) the melting point becomes lower owing to inadequate mobility of the macromolecules involved in forming the network. Secondly, the dependence of the melting point of a gel on the conditions of its formation is determined by the completeness of the stress-relaxation processes following formation of the network[77,78].

Several quantitative approaches to the investigation of gels are based on the applicability of the theory of rubberlike elasticity and other statistical methods of polymer chemistry to the formation and properties of gels. From the analogy between the formation of a three-dimensional physical network and a network of chemical bonds within a solvent, Ferry applied to heat-reversible gels the Flory–Stockmayer theory[278], according to which a condition for formation of an infinite three-dimensional network is the relation

$$P_c = \frac{1}{\rho(\lambda_\omega - 1)} \qquad (2)$$

where λ_ω is the weight-average number of residues in the macromolecule, ρ the proportion of groups capable of forming cross-links, and P_c the proportion of these groups which actually form intermolecular bonds, i.e. the probability of cross-linking. If $\lambda_\omega \gg 1$, we have $P_c = 1/\rho\lambda_\omega$, which can be rewritten[239,279]

$$f m_{cl} = C/2M_\omega \qquad (3)$$

where m_{cl} is the molarity of cross-links (allowing for the fact that formation of a bond involves two groups) at the gel point, M_ω the weight-average molecular weight, C the concentration (g litre^{-1}) of macromolecules, and f a coefficient representing the proportion of groups capable of forming branch points that are involved, not in intermolecular, but in cyclic intramolecular bonds. Assuming that 1–2 bonds per macromolecule are required for formation of an infinite network, Ferry showed[235] that the critical concentration of gel formation by gelatin was 1%, in good agreement with experiment.

Experimental determination of the number of cross-links in the gel network and the number of groups involved in forming one cross-link is based on the equation of state

$$\tau = \alpha(d/M_0)RT\left[\left(\frac{l}{l_0}\right) - \left(\frac{l_0}{l}\right)^2\right] \qquad (4)$$

representing the relation between the stress τ and the elongation (in which $\alpha(d/M_0)RT = G$ is the modulus of rubberlike elasticity, l_0 and l are the initial and final lengths of the specimen, d is the density of the gel, M_0 is the molecular weight of the repeating unit, and α is the proportion of groups in the chain that form cross-links), deduced for three-dimensional networks from the theory of rubberlike elasticity, and the equation of swelling

$$\mu v_2 = -\ln(1 - v_2) - v_2 - \rho_2 \bar{V}_1 v_2^{1/3}/\bar{M}_c \qquad (5)$$

where μ is a polymer–solvent interaction parameter, v_2 the concentration by volume of the polymer, ρ_2 the density of the polymer, $\bar{V}_1$ the molar volume of the solvent, and $\bar{M}_c$ the molecular weight of the chain segment between branch points. It is then necessary to examine the swelling of films obtained by drying the gel (not by evaporating the solvent from a solution—Section III, 1), in which films the structure (i.e. the number and nature of the branch points) is fixed.

Most of the results calculated by using the above approach[279–284] lead to the conclusion that one cross-link is formed by many (20–30) groups, which is regarded as evidence that branch points in the gel network are formed by crystallites comprising many macromolecules. Sometimes, however, calculation shows that branch points are formed between two active groups, i.e. that association complexes are absent[155,156].

Although reasonable values are obtained in several cases for the number of branch points by transferring to cross-linked systems the theory of rubberlike elasticity developed for a macromolecular network, this theory is in large degree arbitrary and gives an idea, not of the number of real branch points in the system, but of the equivalent number in an ideal molecular network possessing the same properties as the test system†. We would like to lay special stress on this aspect, which is often overlooked.

From Eqn. (3) and the van't Hoff equation for the equilibrium formation of cross-links, Eldridge and Ferry[292] obtained the concentration dependence of the melting point T of a gel as

$$\ln C = -\frac{\Delta H}{RT} + \text{const} \qquad (6)$$

where ΔH is the energy of formation of a bond in a gel network. Pouradier established the relation

$$\frac{\Delta H}{RT^2} = \frac{1}{T} - \frac{d \lg G}{dT} \qquad (7)$$

between this energy and the temperature dependence of the modulus of elasticity of the gel[239,293]. Equations (6) and (7) enable us to determine the energy of formation (more correctly, of destruction) of branch points in a gel network. The same quantity can be determined by other methods not involving the premises of the theory of rubberlike elasticity. Firstly, it is determined as the apparent activation energy of flow (which is necessarily

† The same considerations apply also to investigation of the birefringence of gels, when the optical stress coefficient characterises the system[285–287], whereas the difference between the refractive indices, according to the theory of rubberlike elasticity, is related to the structural characteristics of the gel network[288–291].

connected with rupture of the cross-links of the gel network) from the temperature dependence of viscosity in the region of irreversible deformation of the gel (see below)[293]. Secondly, the bond energy ΔH or heat of gelation is measured by a direct thermographic or calorimetric method[294-303]. The examples of gels of gelatin, polyvinyl alcohol, and other polymers show good agreement among values of bond energies obtained by all these methods[157,175,187,299,301].

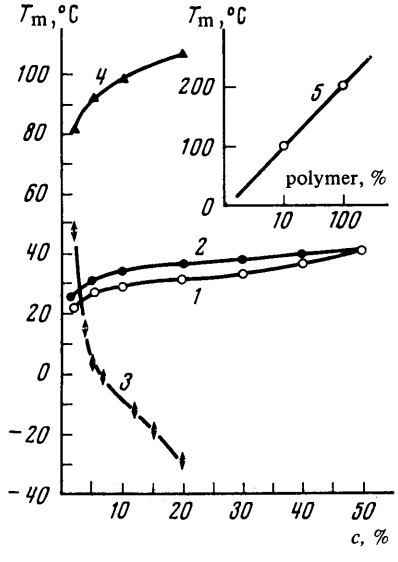

Figure 8. Concentration dependence of melting points of gels of: 1) aqueous gelatin[303]; 2) as (1) from Ref.88; 3) ethanolic cellulose nitrate[103]; 5) poly(vinyl chloride) in dibutyl phthalate[143]; 4) polyvinyl alcohol in 60% aqueous glycerol[175].

Because of the experimental simplicity ΔH is most often determined from Eqn.(6). Most of the gels investigated (gelatin, polyvinyl alcohol, poly(vinyl chloride), polyacryloglycinamide, polyacrylonitrile, etc.) exhibit proportionality between the melting point and the logarithm of the concentration. In several gels of well crystallisable polymers the melting point is proportional to the concentration (not its logarithm) in conformity with the Flory equation (Section III, 3). Equation (6) shows that the sharp concentration dependence of melting point, illustrated in Fig. 8 (curves *3–5*) for gels of poly(vinyl chloride), polyvinyl alcohol, and cellulose nitrate, and typical of the gels of most synthetic polymers, corresponds to a small energy of bonding.. Gelatin gels exhibit a quite different type of dependence (curves *1* and *2*)[303-305]: the melting point changes so little with concentration over the range 5–40% that it is often regarded as constant; the energy of formation of a bond in this region is very large, amounting to 50–200 kcal mole^{-1} depending on the conditions of preparation of the gel. The high heats of gelation and fusion of gelatin[294-303] were regarded for a long time as evidence that gelation is a phase transition of the first kind. Examination of gels of synthetic polymers of various types showed, however, that the energy of formation of a bond does not exceed 5–12 kcal mole^{-1} with amorphous polymers (which corresponds to 1–3 hydrogen bonds)[151,156,300] and 18 kcal mole^{-1} with crystallisable polymers[151,175,187]. The high heats of fusion and gelation of gelatin are due to the large helix–coil transition energy, which, as mentioned above, makes a most significant contribution to the formation and destruction of the gel. Thermogravimetric analysis with very slow stepwise heating reveals two fusion peaks, one attributed to the helix–coil transition, and the other to destruction of cross-links[302]. These peaks are preceded by an exothermic effect due to the formation of more stable bonds in the network when the gel is heated near the melting point. Calorimetric experiments show only one fusion peak[298].

The heat of the helix–coil transition has closely similar values in other proteins and polypeptides[306-309]. In cases in which these compounds form gels, e.g. with poly-(γ-benzyl L-glutamate), the heat of melting of the gels is of the same order as with gelatin[157], although slightly smaller in magnitude.

It must be remembered that heat effects in calorimetric experiments are expressed in calories per gram of the dry material, whereas energies of bonding determined by means of the Ferry–Eldridge equation are obtained in kilocalories per mole. Comparison of these quantities is difficult, since the number of bonds in a gram of the dry material is unknown.

The above considerations show that the magnitude of the heat of gelation cannot indicate that a phase transition is necessarily involved. The large heats of gelation found with gelatin and other natural polymers are explained by the large thermal effect of the intramolecular helix–coil phase transition, which cannot be separated from the heat of gelation itself. In all other gels the thermal effect is significantly lower and corresponds to the energy of formation of a few (with crystallisable polymers) or one or two (with amorphous polymers) intermolecular bonds. This can be regarded as an indication that gelation always involves structural conversion with the appearance of new branch points, the nature of which influences variation of the thermal effect within narrow limits.

The heat evolved on the formation of a small number of relatively weak bonds can be determined only in very high-sensitivity calorimeters. Hence the heat of gelation in such systems often could not be detected in the early work. In thixotropic colloidal systems formed by relatively weak van der Waals forces, in particular, the sol–gel transition occurs without a measurable thermal effect.

Analysis of the literature shows that the change in volume accompanying formation of a gel may vary. An increase occurs only when the gel is formed as a result of a chemical reaction with production of a new substance which remains in the system (e.g. the generation of hydrogen chloride in the formation of silicic acid gel)[21]. A decrease in volume on gelation has been observed with methylcellulose in water[310] and in several systems in which gelation is accompanied by crystallisation of the polymer, in particular on the gelation of polyvinyl alcohol in aqueous glycerol[149]. For a long time the volume change accompanying the gelation of gelatin was a matter of controversy[311-316]. Thus Neiman[313] assumed that the apparent change was due solely to volume relaxation (of both solution and gel) on variation of the temperature: when these factors are assessed correctly, no change in volume is detected. This view can hardly be correct, since the change in volume accompanying the helix–coil transition

and subsequent crystallisation makes a significant contribution to the gelation, and has been subjected to detailed dilatometric investigation by Flory and Garrett[317]. They discovered an appreciable, abrupt change in volume accompanying the gelation of collagen in ethylene glycol. The volume change, like other properties of a gelling system, probably depends significantly on the polymer concentration; in dilute gels and also in gels having weak intermolecular bonds, therefore, gelation takes place without a measurable change of volume. An abrupt change is evidently observed only when gelation is accompanied by rapid crystallisation of the polymer: in the absence of crystallisation, only a slight and gradual volume change takes place.

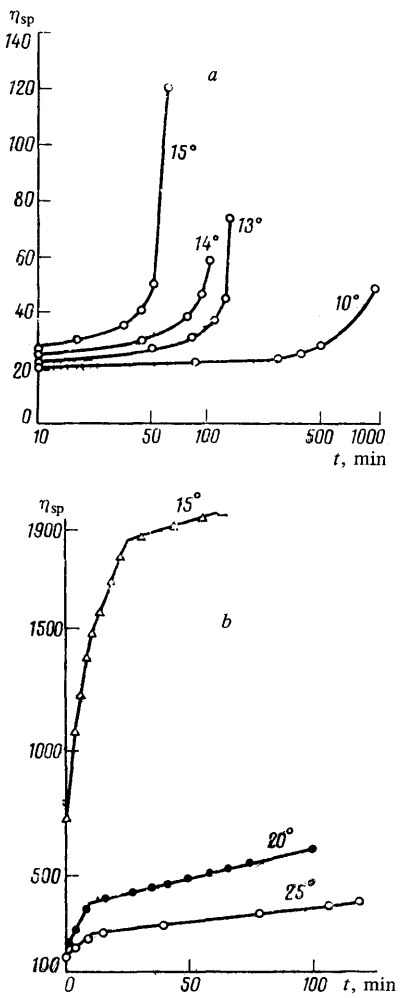

Figure 9. Variation of viscosity on gelation: *a*) cellulose nitrate in ethanol[103]; *b*) copolymer of acrylic acid and acrylonitrile in water[162].

The formation of stable branch points is most clearly evident in a change in the rheological properties of a gelling system. These properties may vary with temperature and concentration, but variation with time at constant concentration and temperature is most characteristic of gelation. Change in viscosity was for many years regarded as the most characteristic parameter of the solution–gel transition, and was studied intensively[317-324]. In several cases the viscosity isotherms have the typical shape (Fig. 9*a*) of the crystallisation isotherms of polymers[103]‡; this was used as an argument in support of the identity of gelation and crystallisation. In other cases the viscosity–time curves show several inflexions (Fig. 9*b*), which were attributed[81,180] to various cross-linking stages preceding formation of the gel.

However, the solution–gel transition is characterised not only by an increase in viscosity but also by the emergence of elastic properties in the system[11,325,326] (a reversible proportion of the deformation, a modulus of elasticity, i.e. rigidity) and a limiting shear stress[75], which increase with time§, as well as a change in the spectrum of relaxation times[327,328].

As Schwedoff emphasised, the elasticity and the viscosity of a system are not interrelated unambiguously: a system may be highly viscous and possess no shear elasticity; and conversely, the latter may be significant while the viscosity is very low. The second case is typical of dilute gels of gelatin, whose elasticity vanishes when they pass into the state of a dilute solution (melt). In contrast to dilute solutions, sufficiently concentrated solutions of polymers also exhibit elasticity, which is due to the presence of a fluctuating network (when sparse branch points are linked by flexible chain segments this is apparent as the rubberlike elasticity of solutions)[338-341]. In the gelling of a sufficiently dilute solution the increase in number and change in character of cross-links in the network lead to an increase in the rubberlike elasticity of the system; when a too dense network is present, however, the rubberlike elasticity diminishes, so that rubber-elastic deformation of a gel becomes less with increase in its concentration[342]. In concentrated solutions rubberlike elasticity is masked by flow, and adequate separation of reversible and irreversible portions of the deformation is important for a correct description of the rubberlike elasticity of solutions (as with gels and with the polymers themselves)[339,343,344]. Concentrated solutions, gels, and rubberlike polymers then exhibit closely similar moduli of rubberlike elasticity[134,339,344,345] at 10^4–10^6 dyn cm^{-2}.

Thus the rheological distinction between gels and concentrated solutions lies not in the elasticity of the former but in their yield stress[346]. Gels, like other bodies possessing a spatial framework (e.g. many disperse colloidal systems), are "quasi-Bingham" plastic solids[62]: i.e. they are characterised by a yield stress, below which they behave as solids (i.e. exhibit only elastic properties), but above as viscoelastic or viscous liquids (i.e. capable of irreversible deformation). This is evidently the decisive rheological property of gels[277,347-349], so that the long held view of gels as non-fluid systems must be regarded as incorrect. Such extremely low yield stresses were observed by Mishod in simple experiments[349] even for very

‡ A close similarity is observed also in the temperature variation of the rates of growth of cross-links and of crystal nuclei.

§ This time variation of properties, which is characteristic of a gelling system, demands that the system be brought to equilibrium—if at all possible—in order that the concentration or temperature dependence of these properties may be studied, or else that the rate of change of the properties should be taken into account.

dilute (0.2%) agar-agar gels. Later work showed that a limiting stress was absent from non-gelling concentrated solutions[345,350,351], but it also appears in filled solutions (e.g. a solution of polyisobutylene containing added particles of carbon black), in which a three-dimensional framework is formed[352].

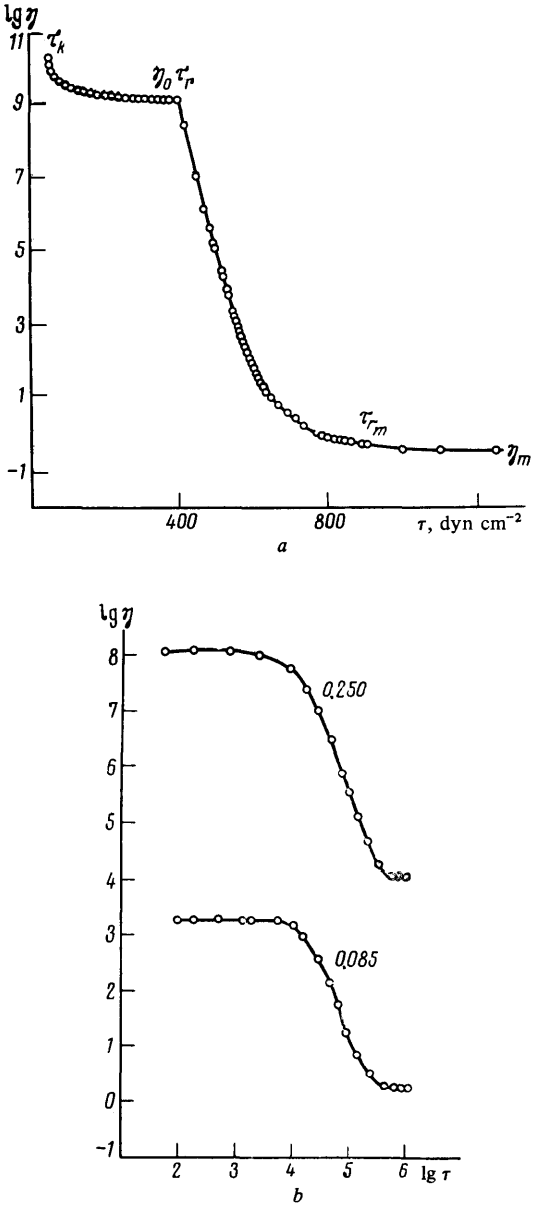

Figure 10. Variation of viscosity with shear stress in: *a*) a disperse colloidal system—an aqueous suspension of bentonite[357] (where τ_k is the limiting shear stress, τ_r the stress corresponding to the start of breakdown of the structure, τ_{r_m} the stress corresponding to complete breakdown of the structure, η_0 the maximum Newtonian viscosity, and η_m the minimum Newtonian viscosity); *b*) solutions of cellulose acetate in cyclohexane (concentrations denoted on the curves)[357].

During recent years it has become obvious that absolute limiting values do not in fact exist. According to Shurkov's theory of durability[353-355] the framework of a gel can be broken down by a sufficiently long-acting stress, even if considerably lower than the usually determined limiting shear stress. This, of course, is indissolubly connected with the development of irreversible deformations of the gel. A similar view was expressed by Trapeznikov, who considered that irreversible deformations, even in gels, could develop at any stress, and regarded the limiting shear stress as corresponding to a change in the character of the flow—Newtonian with unresolved structure below this limit, and plastic flow with resolution of the gel structure above it[356]. Shear at sufficiently high rates and stresses resolves the whole structure, and the flow again becomes Newtonian in character. Fig. 10 illustrates examples of complete rheological curves obtained both for plastic colloidal systems[357] and for concentrated solutions of macromolecular compounds[358,359]. Curves of the same type have recently been obtained also for dilute polymer gels[360] (since the limiting stress increases so much with gel concentration that it is almost impossible to realise a "quasi-Bingham" flow of gels).

Destruction of the gel structure on application of an external stress is a particular aspect of the thixotropic properties of gels[14,361,362]. In the initial stage of gel formation, when the spatial bonds have not yet become stable, thixotropy is apparent in the reversible transition of the gel into a solution under the action of external stress (and regelation after removal of the latter)[14]. Several gelling systems, however, possess dilatant properties, evident in enhanced viscosity and gelling on application of external stress, and reversible melting with decrease in viscosity after removal of the stress[363-366], which is attributed to the ordering of the structure under the influence of a mechanical field[18,347]. Among such systems are aqueous polymethacrylic acid[347], poly(methyl methacrylate) in dimethyl phthalate[366], etc. The phenomenon of rheopexy—acceleration of gelation as the external stress is increased—is often observed in such systems.

The transition from solution to gel involves a broadening of the whole relaxation spectrum[327,328,347,366]. The system retains its shape if the lifetime of the cross-links exceeds the duration of the experiment[347]. Trapeznikov therefore proposed the presence of relaxation times of 10^4—10^6 s in a polymer—solvent system, corresponding to the observation times employed in practice, as a rheological criterion of a gel, enabling it to be distinguished from a solution[367].

2. Elastic, Strength, and Relaxation Properties of Gels

The principal rheological investigations of already formed gels, like those of the polymers themselves and their concentrated solutions, reduce to the study of the static and dynamic moduli of elasticity, the dependence of stress on deformation at a constant rate of shear, creep (i.e. the development of deformation with time at a constant stress followed by relaxation of the deformation), and relaxation of stress at constant deformation, enabling relaxation times and the relaxation spectrum of the system to be estimated.

The modulus of elasticity of a gel can be determined either by static methods (under tension[368], compression[368], or shear[325,326,331,332], on change in the dimensions of the specimen in a tube[369]) or by dynamic methods (from the rate of propagation of sound waves)[370]. Good agreement

between static and dynamic shear moduli indicates the absence from the gels of relaxation times of 0.001–100 s[371]. The modulus of elasticity either increases continuously with the duration of gelation (poly(vinyl chloride)[143], polyacrylonitrile[328]) or reaches a limiting value after a very long time[88]¶. The shear modulus is proportional to the square[235] or higher powers[143,145] of the concentration of polymer in the gel, but in several cases this relation is observed only up to a certain concentration[373], above which the concentration dependence of the modulus changes. This may correspond to a change in the gel structure with increasing concentration (Section IV). With small deformations and stresses the behaviour of gels obeys Hooke's law: i.e. the modulus of elasticity is constant[374]. Under higher stresses it increases with the stress[373].

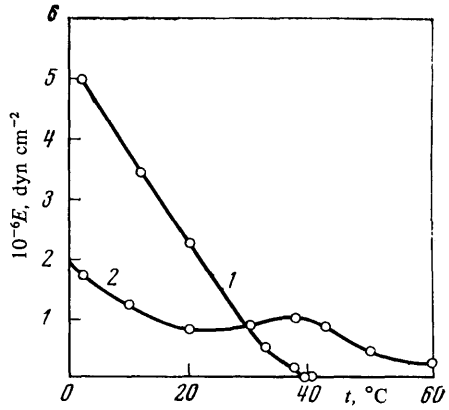

Figure 11. Temperature dependence of modulus of elasticity of gels of: 1) gelatin in water (φ_2 = 20%);[235] 2) polyvinyl alcohol in a mixture of water and glycerol (φ_2 = 10%).[373]

The temperature dependence of the shear modulus of gels indicates that in several cases their behaviour does not correspond to an entropy mechanism of elasticity. Fig. 11 shows that the shear modulus in gels of polyvinyl alcohol in aqueous glycerol increases with temperature over a considerable range (in conformity with the statistical theory of rubberlike elasticity), and only then does it decrease; whereas in gelatin gels the modulus of elasticity decreases with rise in temperature throughout the range investigated[235]. This decrease is due to the increasing rupture of cross-links with rise of temperature near the melting point of the gel, which is especially appreciable with gelatin, as the temperature range of the measurements is very limited. When a small number of chemical cross-links are introduced into a gelatin gel[375] or experiments are made under special conditions, such that the entropy mechanism of elasticity is not masked by the destruction of bonds[376-378], the shear modulus increases only slightly with rise in temperature.

¶ The modulus of elasticity, as well as other mechanical properties of gels, is determined by various aspects of their previous history: these properties differ for gels of the same concentration according as they have been obtained directly by cooling a solution or by concentrating a more dilute solution[372].

The strength properties of gels are most conveniently characterised by the limiting shearing strength[329,379], characterising the strength of the bonds forming the three-dimensional framework; rupture of these bonds precedes steady-state flow. The investigation of non-stationary régimes in concentrated solutions of polymers and gels of aluminium naphthenate has established several important laws governing these processes[379-381]. However, such a purely rheological approach is only beginning to be applied to polymer gels.

The creep of gels[382] under the influence of small shearing stresses was investigated by Rebinder and Ivanova-Chumakova, who proposed a simple method for determining the viscoelastic characteristics of gels[344,383,384].

In most gels part of the deformation is irreversible, with Newtonian flow (the viscosity of 10^6–10^9 P is independent of the applied stress). This means that gels are investigated under stresses exceeding the elastic limit, and that the flow involved in creep takes place with the structure unresolved. As the system cannot flow without the breakage of bonds forming the gel framework, however, a mechanism of chemical flow, i.e. with reorganisation of bonds under the influence of the load, must be envisaged for gels under these conditions[385,386]. Reorganisation and partial destruction of bonds in gels with rise in temperature and increase in stress also make it impossible to use reduced variable analysis in describing the creep of gels[387,388]: it is necessary to allow for reorganisation of the structure with variation in temperature, i.e. to displace the curves along not only the horizontal but also the vertical axis[389-391].

Investigations of the relaxation properties of gels by different workers have led to contradictory results. Deformation was found to be independent of frequency (between 1 and 1000 Hz) in dilute gels of gelatin (up to 20% concentration), but a frequency dependence appeared in concentrated gels[78]. The absence of long relaxation times in dilute gels was attributed to the presence of sparse local cross-links, which prevented displacement of the chains but did not ensure considerable intermolecular interaction. However, earlier[392-394] and later[395-399] investigations showed that stress relaxation occurs in extremely dilute gels (from 1% concentration) to a greater extent the higher the rate of the external constraint, and is described by the same equations as is stress relaxation in polymers and their concentrated solutions. Relaxation processes take place in gels not only by the reorganisation and interaction of chains but evidently mainly by a mechanism of destruction of old cross-links and formation of new ones under the influence of the applied stress[398]. The above discussion shows that the reorganisation of cross-links, i.e. of the gel structure, under the influence of an applied stress plays a decisive part in all mechanical properties of gels, which permits close connections to be established between such properties and the gel structure. Study of the general features of the reorganisation of the framework of gels and the mechanisms of such reorganisation is only beginning, and is extremely important for developing a theory of the deformation of all types of gels.

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Scientific views have developed appreciably since publication of the previous review on polymer gels in 1961,[26] as a consequence of the considerable progress made in investigating proteins and other natural polymers, as well as in the whole field of the physical chemistry of polymers. A deeper understanding of the properties of

gels has been gained primarily from the development of the supermolecular physics of polymers in all their states, as well as ideas on the structural reorganisation of a polymer under the influence of mechanical stress. The combination of molecular and colloid-chemical approaches has been another very characteristic feature of recent polymer chemistry and physics. In many cases the latter leads to a reinterpretation of concepts that have already become traditional, and also removes many of the contradictions which have accumulated in the investigation of gels, permitting an understanding of the occurrence of gels of different types. An important part has been played also by a deepening of our knowledge of the structure of the solvent present in a gel, and of the changes which it undergoes on the introduction of various types of additives. The general advances made in polymer science enable us to predict a rapid future development of our knowledge of the structure, properties, and possible applications of polymer gels.

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Structural Principles in the Chemistry of Heteropolycompounds

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Different types of heteropolycompounds, which are formed in solutions and can be isolated from the latter in a crystalline state, have been analysed and classified on the basis of the results of latest X-ray diffraction studies. The physicochemical and research techniques which have led to the current views on the structures of heteropolycompounds (a large class of complexes) are briefly considered. The possibilities which arise on substitution of one or several metal atoms in the coordination sphere of the heteropolycompound are examined on the basis of structural considerations. The principal trends and problems in the chemistry of heteropolycompounds are discussed. The bibliography includes 191 references.

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I. INTRODUCTION

Various views concerning the structures and nature of heteropolycompounds which have been held until recently are described fairly completely in monographs and other publications [1-4]. The present review considers the current state of the chemistry of heteropolycompounds—a large class of complexes which are formed in solution from whence they can be isolated in the solid state. The physicochemical methods and also certain problems and the principal trends in the chemistry of compounds of this class will be briefly considered.

All the heteropolycompounds examined obey the well known Pauling rules [5], which explain the properties of stable oxide structures. In all cases the fundamental unit of isopolycompounds and heteropolycompounds is the MO_6 octahedron. The octahedra are joined to one another by their vertices, edges, or faces, forming the coordination sphere around the central atom. The outer octahedra of the coordination sphere are distorted, the displacement of the metal atom leading to the formation of shortened (multiple) bonds with the non-delocalised oxygen atoms. The M–O distances are about 1.7 Å for the terminal M=O bonds, 2.0 Å for the M–O–M bridge bonds, and 2.2–2.3 Å for the M–O–X bonds, where X is the central atom; the shortest M=O bond is always in the *trans*-position to the longest bond. We may note that in all the isopolycompounds and heteropolycompounds investigated the number of such non-delocalised atoms does not exceed two [6].

The large number of physicochemical studies on aqueous solutions of these compounds has not unfortunately yielded a corresponding amount of valuable information concerning the forms in which heteropolycompounds exist.

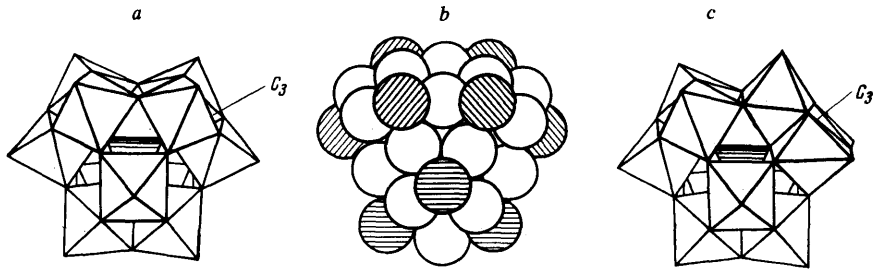

Figure 1. The structure of the anions:
a) α-$X^{x+}M_{12}O_{40}^{x-8}$; *b*) ditto in the form of close-packed spheres; *c*) β-$X^{x+}M_{12}O_{40}^{x-8}$.

Very often investigators make no assumption concerning the form with which they are dealing in solution. Although the compounds can be isolated in a crystalline form, the number of X-ray diffraction studies is fairly limited, since the large unit cell involves the determination of a large number of parameters. For this reason, work on the complete analysis of the structures of such compounds was not started unil the beginning of the 1960s.

II. STRUCTURAL TYPES OF HETEROPOLYCOMPOUNDS

Heteropolycompounds differ from the usual coordination compounds because they do not contain discrete ligands coordinated to the central atom, since the discrete MO_6^{n-} ion does not exist. Therefore one can regard the coordination sphere as one large ligand [7].

The structure of heteropolycomplexes is represented by an ideal octahedron whose vertices are occupied by oxygen atoms. Molybdenum or tungsten atoms are placed within the octahedron. The ionic radii of molybdenum(VI) and tungsten(VI) are 0.62 and 0.65 Å respectively and the ionic radius of O^{2-} is assumed to be 1.40 Å. [8]

The classification of heteropolycompounds generally adopted at present is based on the coordination number of the central atom and the number of metal atoms forming the coordination sphere [9]; attempts are being made to employ the IUPAC nomenclature for this purpose and this is the nomenclature which we shall adhere to in the present review. The overall formula, for example $H_3PMO_{12}O_{42}.nH_2O$, is usually employed to designate heteropolycompounds, because, as already stated, it is impossible to isolate an individual ligand. Sometimes formulae of the type $SiO_4W_{12}O_{36}^{4-}$ or $AlO_6Mo_6O_{18}^{9-}$ are used to indicate the coordination number of the central atom.

1. The Structure of the Anion $X^{x+}M_{12}O_{40}^{x-8}$ and Its Derivatives

The most familiar and widely investigated structure is the so-called Keggin structure [10]. The anion consists of four M_3O_{13} triplet† forming a tetrahedral cavity in which the central atom is placed (Fig. 1*a*). The general formula of the anion can be written in the form (for the 12 : 1 ratio)

$$X^{x+}M_{12}O_{40}^{x-8} ,$$

where X is the tetrahedrally coordinated central atom, which can be B, Si, P, As, Cr, Mn, Fe, Co, Cu, Zn, Ti, Zr, Ga, or H_2^{2+}. [12] The overall symmetry of the anion is T_d. X-Ray diffraction studies have been made on P^{5+}, As^{5+}, Si^{4+}, Ti^{4+}, and Zr^{4+} dodecamolybdates [8,13-20] and P^{5+}, B^{3+}, Ge^{4+}, Fe^{3+}, Zn^{2+}, Cu^{2+}, and Co^{3+} dodecatungstates [8,13,14,19-25], where the anion is claimed to have the T_d symmetry. We emphasise that the representation of the anion in the form of ideal octahedra does not take into account the fact that the oxygen atoms must be represented by large spheres. For this reason, the representation of the structure in this form (Fig. 1*a*) can create the incorrect impression that there are large open spaces within the anion. In Fig. 1*b* the anion is represented by close-packed spheres (the shaded circles represent terminal oxygen atoms). The structure is characterised by the presence of 12 M=O bonds and 24 M−O−M bridge bonds, twelve of which are almost linear and twelve are angular. The maximum M−O distance is that between the metal atom and the oxygen atom which links three metal atoms to the central atom (sp^3 hybridisation). The length of this bond depends on the size of the central atom. For central atoms of metallic type (for example Co^{III}, d^6), the tetrahedron is appreciably distorted (extended along the C_2 axis) in consequence of the Jahn−Teller effect, although the external coordination shell does not undergo appreciable changes [7]. Incidentally the Co^{3+} ion in $CoW_{12}O_{40}^{5-}$ is atypically in a tetrahedral environment.

Heteropolycompounds are formed immediately at an appreciable rate (faster on heating) in acid solutions on mixing molybdates or tungstates with the salt of the corresponding heteroelement. The acids can be isolated in a free state from highly acidified solutions by extraction with ether and also by ion exchange [1,4]. Certain metal heteropolycompounds are formed with much difficulty, since octahedral coordination is usually characteristic of the metals and the transition to tetrahedral coordination requires additional energy [26].

The large number of different hydrates of the same compound gives rise to difficulties in the preparation of truly homogeneous phases for chemical analysis and physicochemical studies. The exact amount of water is frequently fairly difficult to determine, because it can be zeolitic and is only gradually removed on dehydration [27]. The crystal structures of different hydrates of heteropolycompounds have been examined [2,28].

† The M_3O_{13} triplet, which is found in almost all the known structures of heteropolyanions, is made up of three MO_6 edge-sharing octahedra. It has been detected as a discrete unit in cluster type compounds $M_2^{II}Mo_3O_8$ in which a metal−metal bond is postulated [11]. In the heteropolyanion the M−M distance is about 3.3 Å, which rules out direct d−d interaction. However, it is quite possible in highly reduced forms of heteropolyanions.

In the crystalline state there is no direct linkage between the anions. Their packing is achieved via hydrogen bonds or via cations. Water can be completely removed by thermal dehydration (at about 300–400°C), whereupon the structure of the anion is fully retained, its stability increasing with increase of the ionic radius of the central ion [29]. All the heteropolyacids and some of their salts are very soluble in water and in oxygen-containing solvents, which can be explained [7] by the very low crystal lattice energy and by the solvation of the cations. Although the crystal lattice energies of heteropolycompounds are unknown, to a first approximation the lattice energy can be estimated as about 800 kcal mole^{-1} for $K_4SiW_{12}O_{40}$. [29]

There is no reason to doubt at present that the anion with Keggin's structure retains its high symmetry (T_d) in aqueous solutions. An X-ray diffraction study of the heteropolycompounds $H_4SiW_{12}O_{40}$ and $H_3PW_{12}O_{40}$ in aqueous solution [30,31] showed that the results agree with the existence of one form containing twelve tungsten atoms, forming a cubo-octahedron, i.e. the structure which was discovered by Keggin. Similar results were obtained for the dodecamolybdophosphate anion [30].

The determination of the diffusion coefficients of the heteropolyanions $XM_{12}O_{12}^{X-8}$ in solution showed that the anions are almost spherical, their radii are the same, and that the hydrodynamic radius of the anion is equal to the crystallographic radius of the non-solvated anion [7]. This indicates a very low degree of solvation. The addition of alkali to solutions of heteropolyacids leads to the decomposition of the anion and a slight increase of alkalinity leads to the formation of compounds with the ratio M : X = 11 : 1. [4] The formation of 11 : 1 complexes can be regarded as involving a simple elimination of one octahedron (i.e. an M=O group) from the structure of $X^{X+}M_{12}O_{40}^{X-8}$ and the charge of the anion always increases by four units. An X-ray diffraction study [28] of the salt $(NH_4)_7Na_2[GaW_{11}O_{39}(H_2O)].15H_2O$ showed that the Keggin structure persists and that gallium is in the centre of the tetrahedral cavity. The site of one octahedron is occupied by the water molecule. The formation of 11 : 1 compounds probably accounts for the hypothesis of an unjustifiably large number of dissociable protons in the Keggin structure, for example eight in molybdosilicic acid [1]. We shall not consider here the problem of the number of dissociable protons in heteropolyacids and no conclusions will be reached concerning the structure of the anion on the basis of determinations of the number of dissociable protons or the isolation of salts substituted to a high degree. In the light of structural concepts, any departure of the number of dissociable protons in an acid whose anions have the Keggin structure from the value $x - 8$, where x is the positive charge of the central atom, is caused either by the degradation of the anion or by the presence of non-salt-forming hydrogen atoms.

A greater increase in alkalinity leads to other forms with different M : X ratios. Salts containing the pentamolybdophosphate anion have been isolated [32]. The same anion was obtained in a study of multicomponent $PO_4 : MoO_4$ mixture [33], where the sodium salt was isolated and studied by X-ray diffraction [34]. The salt $Na_2H_2Mo_5.P_2O_{39}.10H_2O$ no longer belongs to heteropolycompounds, since in its anion there is no central atom, although its structure consists of five MoO_6 octahedra and two PO_4 tetrahedra. The addition of an excess of alkali (20–28 moles per mole of the anion) leads to the decomposition of the anion into simple MO_4^{2-} and XO_4^{X-8} anions. The stability of the molybdate anions varies in the series Si > (Zr,Ti) > Ge > P > As.

As early as 1941 Jahr [35] and later Chalmers and Sinclair [36] pointed out the possibility that different anions with a tetrahedral arrangement around the central atom can be formed by a simple rotation of one or several M_3O_{13} triplets by 60°, which reduces the T_d symmetry of the anion to C_{3v} or C_{2v}. Recently Yamamura and Sasaki [37] confirmed the possibility of geometrical isomerism for β-$Ba_2SiW_{12}O_{40}$ in the anion of which one W_3O_{13} triplet is rotated by 60° about the C_3 axis (Fig. 1*c*).

Heteropolycompounds with the ratio M : X = 9 : 1 or 18 : 2 have properties close to those of the 12 : 1 compounds. This series of complexes is known only with phosphorous and arsenic central atoms and they are obtained after prolonged boiling from solutions with a high excess PO_4^{3-} or AsO_4^{3-} concentration and a low acidity. An X-ray diffraction study [38] of compounds with the ratio W : P = 9 : 1 showed that the complex is made up of two fragments of the Keggin anion from the structure of which three WO_6 octahedra have been eliminated. The two 9 : 1 fragments share the resulting free vertices of the octahedra, leading to the 18 : 2 structure, which belongs to the point group D_{3h} (Fig. 2*a*). Two XO_4 tetrahedra remain separate. It is easy to imagine the formation of geometrical isomers of $X_2M_{18}O_{62}^{2X-16}$ by a simple rotation of one 9 : 1 fragment by 60°, which leads to the D_{3d} symmetry,

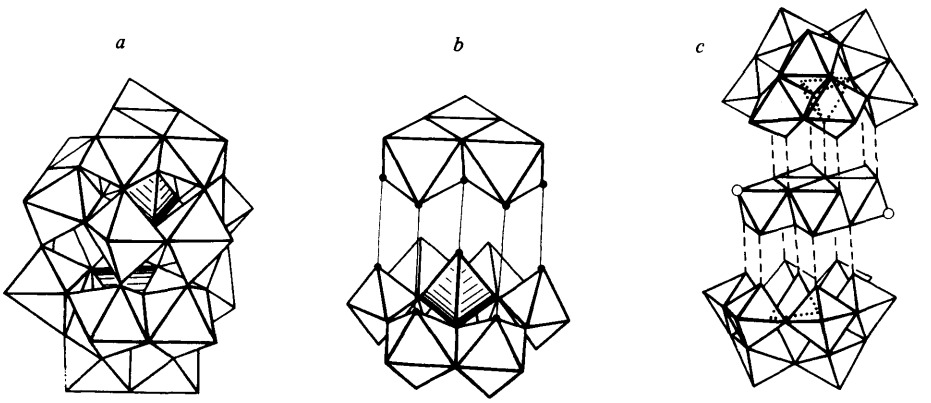

Figure 2. The structure of the anions:
a) $X_2^{X+}M_{18}O_{62}^{2X-16}$; *b*) $H_6PMo_9O_{34}^{3-}$; *c*) $P_2Co_4(H_2O)_2W_{18}O_{68}^{10-}$.

or by a rotation of W_3O_{13} triplets [39]. However, there is yet another possibility of the formation of isomers. The two fragments of the Keggin anion, each of which has lost one M_3O_{13} triplet, can share the free vertices but the two inner XO_4 tetrahedra then have a common oxygen atom (i.e. the X_2O_7 group is present) and the general formula of the anion should be written $X_2M_{18}O_{61}^{2X-14}$. There is no doubt that these geometrical isomers are possible for the molybdenum analogues.

The preparation of salts of octadecatungstodiberyllic acid, the anion of which belongs to the M : X = 18 : 2 series and has the formula $Be_2W_{18}O_{62}^{12-}$, has been described [40]. Goldman and Hargis [41], who studied the kinetics of the reduction of molybdophosphoric acid in the presence of bismuth(III), suggested the formation of a diheteropolycompound with the ratio P : Bi : Mo = 1 : 1 : 18. If this is confirmed by structural studies, the complex will be the first example of diheteropolycompounds with two different heteroelements.

It is interesting to note that a fragment of the Keggin structure was obtained recently for the first time. The anion $PMo_9O_{34}^{9-}$ (C_{3v} symmetry) was detected in the $xPO_4 : yMoO_4$ multicomponent system [33]. The sodium salt was crystallised and investigated by X-ray diffraction [42]. The structure of the anion is illustrated in Fig. 2*b*. It was also shown to persist in aqueous solutions [33].

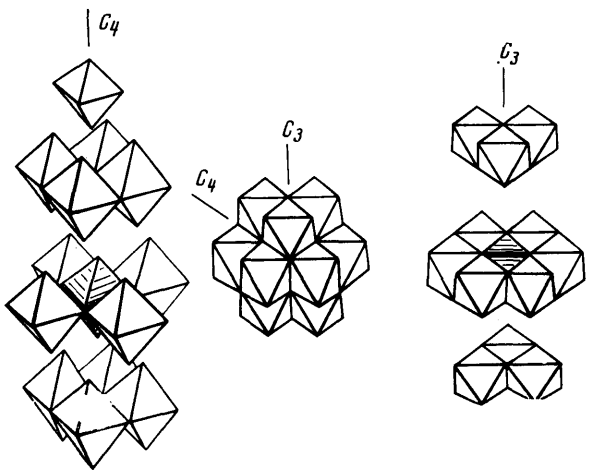

Figure 3. The structure of the $X^{X+}M_{12}O_{38}^{X-4}$ anion and its resolution along the C_4 and C_3 axes.

Another complex in which there is a fragment of the Keggin anion is $P_2Co_4(H_2O)_2W_{18}O_{68}^{10-}$ (point group C_{2h}), which has unique characteristics and whose structure has been determined [43] (Fig. 2*c*). The nickel and copper complexes belong to the same type and phosphorus can be replaced by arsenic(V). The characteristic features are the high molecular weight (4729) and the presence of the planar Co_4 group which is made up of CoO_6 octahedra in one plane; the two water molecules (represented by circles) cannot be replaced by other ligands, since they are thoroughly screened by the oxygen atoms of the neighbouring WO_6 groups. The Co_4 plane separates the two fragments of the Keggin anion from the structure of which a W_3O_{13} triplet has been eliminated. The anion may be of interest for the investigation of magnetic interactions since similar tetranuclear manganese(II), cobalt(II), nickel(II), and copper(II) complexes are unknown.

2. The Structure of the Anion $X^{X+}M_{12}O_{38}^{X-4}$ and Its Derivatives

The next group of heteropolycompounds comprises complexes whose structures are based on an octahedral arrangement around the central atom. Any of these structures can be represented as a fragment of the highly symmetrical (O_h symmetry) heteropolyanion (12 : 1) $X^{X+}M_{12}O_{38}^{X-4}$ (Fig. 3) formed by the addition of twelve MO_6 octahedra to all twelve edges of the central XO_6 octahedron [9]. This hypothetical ion would have a very low negative charge and for a high-valent central atom such as either Mo^{VI} or W^{VI} would have a zero or positive charge. However, in the case of vanadium the overall charge of the anion becomes $x - 16$; this structure has been proposed [44] for the anion $MnV_{13}O_{39}^{9-}$, the thirteenth VO_6 octahedron occupying the site between the four VO_6 octahedra on the C_4 axis (Fig. 3*a*). A preliminary X-ray diffraction study showed that the structure has tetragonal symmetry. The structure of the compound $MnV_{14}O_{40}^{8-}$ (D_{4h} symmetry), in which the fourteenth vanadium atom is in the *trans*-position relative to the thirteenth vanadium atom, was determined recently [45].

A known group of heteropolycompounds with an octahedral arrangement around the central atom comprises hexamolybdenum and hexatungsten compounds [12] (M : X = 6 : 1) with the general formula $X^{X+}M_6O_{24}^{X-12}$, where X^{X+} = Te^{6+}, I^{7+}, Al^{3+}, Cr^{3+}, Fe^{3+}, Co^{3+}, Rh^{3+}, Ga^{3+}, or Ni^{2+}. The structures of tellurium(IV) and chromium(III) hexamolybdates, which belong to this class, have been determined by Evans [46] and Perloff [47]. An incomplete X-ray diffraction study [25] confirmed this structure for the $NiW_6O_{24}^{10-}$ anion. The elimination of two M_3O_{13} triplets from the hypothetical ion on the C_3 axis (Fig. 3) leads to a structure consisting of seven octahedra, one of which is the central XO_6 octahedron. All the octahedra share their edges and are located in the same plane. The structure has the D_{3d} symmetry (Fig. 4*a*). The central XO_6 octahedron undergoes a slight trigonal distortion. The heteropolycompounds of triply-charged ions contain six protons firmly linked to the oxygen atoms of the central XO_6 octahedron. For this reason, the formula of the anion can be written as $X(OH)_6M_6O_{18}^{X-6}$.

The inclusion of six protons in the formula of the anions aroused a majory controversy, because these are non-salt-forming protons. Baker and coworkers [48,49] and then Rollins and Earley [50] had to resort to the hypothesis that dimeric forms of the anion exist in order to reduce the number of oxygen atoms and hence diminish the atomic charge of six units. However, in hexamolybdogallate(III) three water molecules are removed at a fairly high temperature, which indicates their unusual situation [51]. Subsequently Baker and coworkers [25] had to abandon these views, particularly since the ^1H NMR spectra of salts of 6 : 1 heteropolycompounds revealed the presence of six hydroxy-groups [52]. On the basis of this example, we should like to emphasise yet again the necessity for a critical approach to the interpretation of the results and also the desirability of employing several physicochemical methods to confirm one's conclusions.

Fig. 4*b* illustrates the structure of $CrMo_6O_{24}^{9-}$ with close-packed oxygen atoms (the terminal atoms are represented

by shaded circles), the metal ions being distributed within the octahedral cavities formed. The $Co_2Mo_{10}O_{38}^{8-}$ ion, whose structure has been determined by Evans and Showell[53], is related to these 6:1 complexes. The anion is formed from two $CoMo_6O_{24}^{9-}$ groups after two MoO_6 octahedra have been removed. By combining two 5:1 fragments and rotating one of them through 180° in relation to the other about the edges of the central octahedron (Fig. 5*a*), one obtains an anion with D_2 symmetry, which is consequently capable of having optical isomers. Quite recently these two isomers were isolated with the aid of the tristetramminecobalt ion[54]. In all probability this anion as well as the anions with the 2:18 ratio (Fig. 2*a*) are the only examples of true diheteropolycompounds.

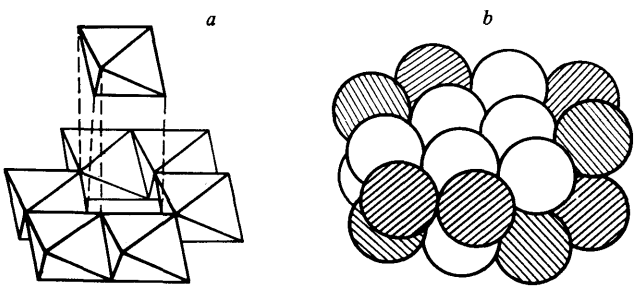

Figure 4. The structure of the anions: *a*) $X^{X+}M_6O_{24}^{X-12}$; *b*) ditto in the form of close-packed spheres.

Other examples of an octahedral arrangement about the central atom are provided by the manganese(IV) and nickel (IV) 9:1 complexes[55] whose structures are obtained by the removal of three octahedra from the six octahedra located in a plane perpendicular to the C_3 axis of the hypothetical anion $XM_{12}O_{38}$ (Fig. 3), which leads to the D_3 symmetry of the anion (Fig. 5*b*). Baker and Weakley[56] showed by cryoscopic measurements in Na_2SO_4 that the anion is monomeric. The acid prepared by ion exchange proved to be fairly unstable, but the number of its dissociable protons was found to be close to the calculated value.

3. The anions $X^{X+}W_{10}O_{36}H_2^{X-10}$

Peacock and Weakley[57] obtained a series of lanthanide heteropolytungstates with the ratio W:Ln = 10:1. It is interesting that all the lanthanides have the same coordination number, which is fairly unusual for this series of elements. The structure of decatungstocerate(IV) was determined[58] (Fig. 6). It contains the residues of two $W_6O_{19}^{2-}$ anions[59] and resembles the $W_{10}O_{32}^{4-}$ anion[60] (Fig. 7), the two halves of which make an angle of 45°. The heteropolycompounds XW_8O_{28}, where X = Ce^{IV}, Th^{IV}, or U^{IV}, have been isolated for elements with high coordination numbers[61,62], but subsequently their formulae were written as $XW_{10}O_{36}$,[63] and they probably belong to the same structural type.

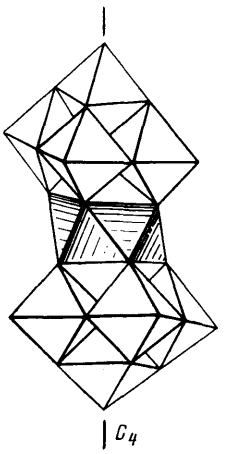

Figure 6. The structure of the $X^{X+}W_{10}O_{36}^{X-12}$ anion.

4. The Structure of the $X^{4+}Mo_{12}O_{42}^{8-}$ Anion

The anion of the 12:1 molybdoceric acid $CeMo_{12}O_{42}^{8-}$ belongs to the last known type of heteropolycomplexes. On the basis of the undoubtedly high number of dissociable protons and the high ionic radius of Ce^{4+}, Baker et al.[64] suggested that the structure of the anion should differ

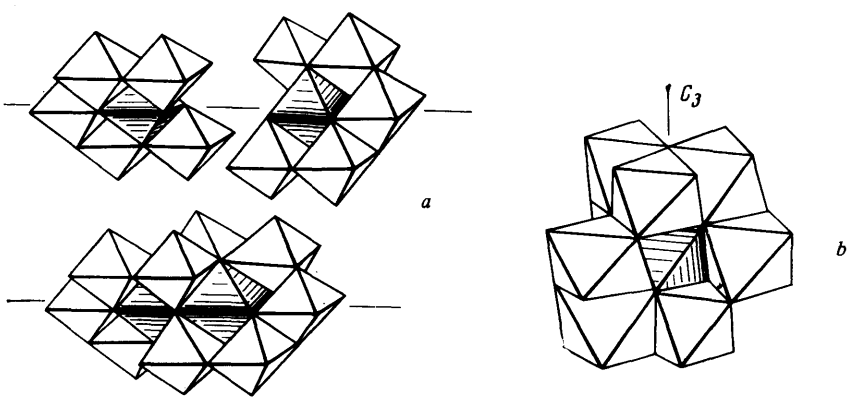

Figure 5. The structures of the anions: *a*) $Co_2Mo_{10}O_{38}^{8-}$; *b*) $X^{4+}Mo_9O_{32}^{6-}$.

significantly from the Keggin structure. A preliminary X-ray diffraction study[65] revealed two characteristic features of this anion: an eicosahedral arrangement about the central atom and face-sharing of pairs of MO_6 octahedra (Fig. 8) (T_i symmetry), observed for the first time in the structures of isopolycompounds and heteropolycompounds. The similarity of the properties[66] and X-ray diffraction data[67] show that the individual heteropolymolybdenum acids of quadrivalent cerium, thorium, uranium, and neptunium[68] have the same structures.

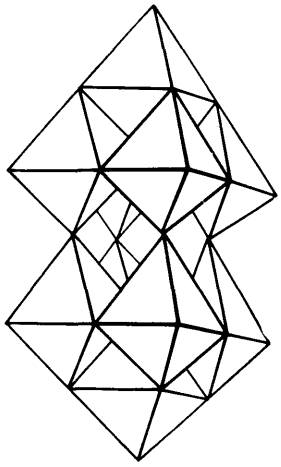

Figure 7. The structure of the $W_{10}O_{32}^{4-}$ anion.

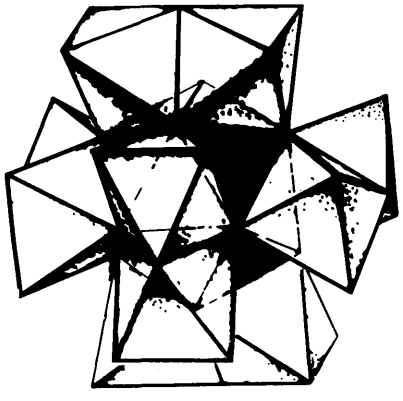

Figure 8. The structure of the $X^{4+}Mo_{12}O_{42}^{8-}$ anion.

5. Other Anions

Flynn and Stucky[69] made an X-ray diffraction study of the salt $Na_{12}[Mn(Nb_6O_{19})_2].5H_2O$. The anion consists of two isopolyanions $Nb_6O_{19}^{8-}$ coordinated to the Mn^{4+} ion (Fig. 9), so that the oxygen atoms form an octahedron about the Mn^{4+} ion and the overall symmetry of the anion becomes D_{3d}. However, in this case not all the Nb atoms are joined to the Mn^{4+} ion, and although its structure resembles $CeW_{10}O_{36}$ (Fig. 6), the complex is not intermediate between isopolycompounds and heteropolycompounds.

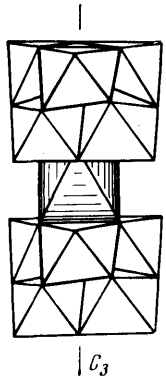

Figure 9. The structure of the $Mn^{4+}(Nb_6O_{19})_2^{12-}$ anion.

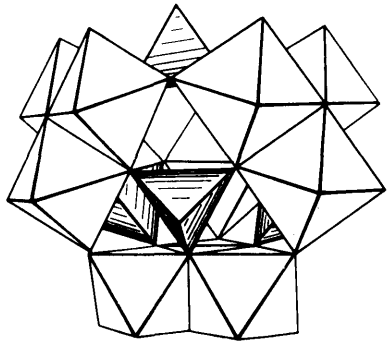

Figure 10. The structure of the $As_4Mo_{12}O_{50}^{8-}$ anion.

In 1973 Nishikawa and Sasaki[70] determined the crystal structure of $(NH_4)_4H_4As_4Mo_{12}O_{50}.4H_2O$ (Fig. 10). The anion has the T_d symmetry and resembles the Keggin structure turned inside out. The four Mo_3O_{13} triplets are joined via their vertices, forming the anion $Mo_{12}O_{46}^{20-}$ to which four AsO_4 tetrahedra are linked. At the centre of the anion there is a cavity (radius 1.43 Å) formed by eighteen oxygen atoms.

III. METHODS FOR THE INVESTIGATION OF HETEROPOLYCOMPOUNDS

There is at present no well founded theory which would account for the mechanism of the formation of heteropolycompounds, apart from a few hypotheses[71]. It is very difficult even to determine whether the process takes place in stages, the intermediate forms being fairly stable and long lived, or whether the intermediate compounds are unstable and the process can have a chain mechanism.

At any rate the intermediate compounds have not been isolated and characterised in the case of heteropolycompounds unless of course one formally includes among these the 6 : 1 compound (Fig. 4) as an intermediate before the formation of the 9 : 1 complex (Fig. 5*b*) with an octahedral arrangement about the central atom.

Moreover even for isopolycompounds it is not evident how the complex structure is produced by a simple addition of MoO_6 octahedra to the pre-existing framework. For example, it is regarded as fully proved that acidification of the MoO_4^{2-} ion [72] does not lead to the formation of intermediate species (the heptamolybdate anion [73] $Mo_7O_{24}^{6-}$ is formed at once and only then the octamolybdate anion [74] $Mo_8O_{26}^{4-}$ and the structure of the latter is not obtained by the simple addition of a single MoO_6 octahedron to the heptamolybdate framework but involves a rearrangement of the anion), but the causes of this are unknown.

In studies on the relaxation of isopolymolybdate solutions [75,76] it has been suggested that acidification of MoO_4^{2-} results in a rapid transition of molybdenum from tetrahedral configuration to an octahedral configuration with subsequent condensation of the octahedra.

In all probability the tendency of molybdenum, tungsten, and vanadium to form shortened M=O bonds, leading to a weakening of the M–O bonds in the *trans*-position, is responsible for the interaction of several octahedra. The formation of these double bonds leads to certain differences in the structures. A structure of the type XMo_6O_{24} has been suggested for the heptamolybdate (Fig. 4), but the structure of the isopolymolybdate is such (C_{2v} symmetry) that all the molybdenum atoms in it are equivalent, i.e. all the MoO_6 octahedra undergo identical distortions, whereas in the XMo_6O_{24} structure all the bonds in the XO_6 octahedron are equivalent and in MoO_6 they are different.

Furthermore, in many instances the molybdenum analogues of $XO_4W_{12}O_{36}^{x-8}$ do not exist, because the Mo–O bonds are weaker than the W–O bonds, and the $Mo_{12}O_{36}$ framework cannot maintain the X^{x+} ion in a tetrahedral arrangement. Although many examples of anions with the same structures have been observed in the chemistry of molybdenum and tungsten, in certain cases the heteropolyanions are different, for example the structure of cerium heteropolytungstate differs appreciably from that of the dodecamolybdocerate ion (Figs. 6 and 8).

The formation of heteropolycompounds is largely determined by the ability of the metal ions, comprising the coordination sphere, to polymerise and the structure of the complex depends on the nature of the central atom. However, cases are known where the conditions of the synthesis determine the coordination number of the central atom. For example, depending on the proportions of the initial reactants, the acidity of the solution, and time, it is possible to obtain complexes with the ratios M : GaIII = 6 : 1 (D_{3d} symmetry of the anion) and 12 : 1 (T_d symmetry) having octahedral and tetrahedral arrangements about the central atom [77].

The thermodynamics of the formation of polynuclear species having different shapes (the compact hexaniobate [78] $Nb_6O_{19}^{8-}$, the swollen heptamolybdate [73,79] $Mo_7O_{24}^{6-}$, or the loose bulky paratungstate [80] $W_{12}O_{42}^{12-}$) is virtually unknown. For this reason, studies [81–83] undertaken to determine the activity and osmotic coefficients of anions belonging to the 6 : 1 and 12 : 1 series merit attention.

There are many equilibrium states in the chemistry of solutions, which involves a time factor since equilibrium is very frequently established slowly, particularly in the case of molybdenum. It is sometimes impossible to compare the results of different studies, since the experiments were carried out under different conditions which are difficult to compare. Moreover it has been shown that the concentration and composition of the supporting electrolyte are very important and that the electrolyte can in turn influence the charge and dimensions of the anion. Therefore the results of studies in which the concentration of the supporting electrolyte did not exceed 3 M proved to be promising.

The existence of heteropolycompounds with the Keggin structure in different forms in equilibrium with one another, one of which (the metastable form) is converted into the other (the stable form), is well known. This equilibrium is influenced by the state of the initial tungsten and molybdenum ions, as shown clearly for dodecatungstosilicic and dodecatungstogermanic acids [84]. Depending on the sequence in which the solutions of the initial reactants are mixed, different forms are obtained:

$$\mathrm{Si(Ge)} + \mathrm{WO_4^{2-}} \xrightarrow{(H^+)} \alpha\text{-isomer (11 : 1 or 12 : 1)},$$

$$\mathrm{WO_4^{2-}} + \mathrm{H^+} \rightarrow \mathrm{HW_6O_{21}^{5-}} \xrightarrow{\mathrm{Si(Ge)}} \beta\text{-isomer (11 : 1 or 12 : 1)},$$

and in the case of silicon the conversion of the β-form into the α-form is very slow even on heating.

Much importance was attributed earlier to results obtained by certain methods which are not theoretically well founded. For example, diffusion coefficients were measured for many years [85] and then linked to the ionic weight of the polymeric form on the basis of the familiar Riecke relation. It was not until 1960 that Baker and Pope [86] published the results of a fairly simple but clear-cut experiment in which it was shown that the diffusion coefficients of the isomorphous anions $SiW_{12}O_{40}^{4-}$ (ionic weight 2875) and $SiMo_{12}O_{40}^{4-}$ (ionic weight 1820) are equal. This of course led to the conclusion (which was apparent previously) that the diffusion coefficients depend only on the ionic radius but not on the ionic weight.

Arbitrary interpretation of the results of thermogravimetric analysis and of other methods led to the assertion that heteropolyacids with the Keggin structure have a large number of dissociable protons [1] and doubts were actually cast on the results of X-ray diffraction analysis. In this connection it is useful to consider briefly the methods used to investigate heteropolycompounds. Evidently none of the individual methods can provide an unambiguous answer as to the nature of the existing forms of heteropolycompounds.

The first method used to determine the stoichiometric coefficients of the complex formation reaction products was quantitative analysis. More than 100 year ago, Marignac [87] carried out a major crystallographic and quantitative analytical study of complex compounds which were subsequently called heteropolycompounds. Here we must emphasise the importance of chemical analysis in relation to compounds where one of the metal atoms forming the coordination sphere is substituted by another metal atom, since in this case incorrect conclusions have been reached concerning the structures of the resulting compounds. For example, Baker and McCutcheon [88] reported the discovery of a new class of compounds, which they called diheteropolycomplexes, with the ratios M : X : Y = 12 : 1 : 1, where Y is a transition metal. Subsequently other studies were published [89], where the preparation of similar compounds was claimed. However, later these views were revised [28,90] and evidence was obtained showing that the second heteroatom substitutes one tungsten (or molybdenum) atom in the coordination sphere, the Keggin structure remaining unchanged. The discrepancy between the analytical results for the 11 : 1 and 12 : 1 compounds is

very small (11 : 1 = 12 : 1.09) and therefore the results of chemical analysis alone may prove to be unreliable.

In the potentiometric determination of the number of dissociable protons in heteropolyacids it is always necessary to take into account the possibility of the decomposition of the anion on increase of pH. Souchay [3] was able to show that a slight increase of the alkalinity of a solution of heteropolyacids leads to the formation of the anions of unsaturated heteropolyacids:

$$PMo_{12}O_{40}^{3-} + OH^- \rightarrow PMo_{11}O_{39}^{7-} + MoO_4^{2-} \text{ (or } Mo_6O_{24}^{6-}).$$

Therefore, in order to avoid the decomposition of the anion, Keller et al. [91] determined spectrophotometrically the degree of ionisation of heteropolyacids. These results show that the number of dissociable protons in heteropolyacids with the Keggin structure is small.

The spectrophotometric method (the molar ratio and isomolar series procedures) and also the method based on the variation of the pH of solutions as a function of the amount of heteroatoms introduced are widely used to determine the stoichiometric coefficients in complex formation reactions [92]. However, the interpretation of the results is fairly difficult and frequently indefinite so that it is difficult to determine reliably the equivalence point for high ratios such as 12 : 1. For this reason, the conclusions based on these data must be approached with much caution.

The method of salt cryoscopy, based on the decrease of the $Na_2SO_4.10H_2O \rightarrow Na_2SO_4 + 10H_2O$ transition temperature in the presence of various ions, is frequently used to determine the degree of condensation [56,77,93-95]. It was shown with the aid of this method that the hexamolybdochromate, hexamolybdoaluminate, and hexamolybdogallate ions as well as the 11 : 1 : 1 complexes (Co–Ga, Mn–Ga, Cr–Ga) are monomeric and that decomposition products are absent. A recent thermodynamic examination of this method [96] showed that it has a reasonable theoretical basis. The method involves a number of difficulties: (1) the necessity to know the exact H^+ and HSO_4^- concentrations, since they contribute to Δt and (2) the impossibility of extrapolation to infinite dilution when Δt varies with concentration. The application of certain methods requires extrapolation to infinite dilution in order to create nearly ideal conditions. Analysis of light scattering and ultracentrifugation data showed [97-99] that large anions bind the counterions from the salt medium to a considerable extent. In solutions where concentration influences the position of equilibrium, such extrapolation is impossible. Light scattering and equilibrium ultracentrifugation as well as sedimentation (methods which supplement one another) make it possible to establish the effective ionic weight of the anion in solution, usually the dominant ion, provided that the solutions are monodisperse and provided that the degree of polymerisation of the solutes is not influenced by dilution. Light scattering data [97] showed that, in solutions with the W : P = 12 : 1 and 9 : 1 ratios, there are monomeric and dimeric species respectively, i.e. W : P = 18 : 2. The results of sedimentation [100] and ultracentrifugation [101] studies on dodecamolybdophosphoric acid showed that it is fairly unstable and forms an anion with the ratio Mo : P = 11 : 1.

Ion exchange is used not only for preparative purposes (for the synthesis of heteropolyacids in a free state) but also permits an indirect determination of the ionic charge and also the stability of heteropolyanions. However, the determination of the charge of the anion yields no information about its structure, since the anion, which can formally have a large charge, frequently binds counterions from the supporting electrolyte and its overall effective charge does not exceed −6.

The origin of the absorption bands in the ultraviolet spectra of heteropolycompounds has been hardly considered [102-108]. There is no doubt that the absorption bands with extinction coefficients of the order of 10^4-10^5 are due to electron transfer from orbitals localised mainly at oxygen atoms to orbitals localised at the metal atoms forming the coordination sphere. The nature of the ultraviolet spectrum changes appreciably as a function of the structure of the anion and its symmetry [107]. A decrease of symmetry leads to the splitting of the absorption bands [104]. The similarity of the ultraviolet spectra constitutes satisfactory confirmation that the structures of the anions are the same [105]. A purely qualitative employment of ultraviolet spectra enabled Strickland [106] to detect isomeric forms of the dodecamolybdosilicate anion and to investigate the kinetics of their interconversion.

The absorption spectra of aqueous solutions in the region of $d-d$ transitions have been used to investigate the coordination and also to determine the degree of oxidation of both the central atom and of the metal ions entering into the coordination sphere [109,110]. $Na_3CrO_6Mo_6O_{18}.H_6$ (D_{3d}), the luminescence spectra of which are observed even at room temperature, has unusual spectroscopic properties [111]. This phenomenon is unknown for other chromium(III) complexes. On the basis of the calculated and experimental absorption bands in the visible spectra of solutions of dodecamolybdouranic and dodecamolybdoneptunic acids, it was shown that uranium [67] and neptunium [68] in these compounds are in the +4 oxidation state. It is noteworthy that in all instances the absorption bands due to the metal ion in the coordination sphere are appreciably more intense than in the spectra of the usual complexes. Comparison of the absorption spectra of solutions of compounds of the type $MXW_{11}O_{40}H_2^{n-}$ with the reflection spectra of crystalline specimens shows that the environment of the metal ions in the structure of the anion remains unaltered [109]. The study of the absorption spectra of lanthanide heteropolytungstates [59] permitted the determination of the coordination of the Ln ion.

The hyperchromic effect observed in the reduction of one or several metal atoms forming the coordination sphere, i.e. the formation of heteropolyblues, is due to the valence change $MV \rightarrow MVI$, [112] since the usual $d-d$ transitions have much lower extinction coefficients at $\nu \simeq 10-14\,000\ cm^{-1}$. This effect has been used in analytical practice for the quantitative determination of certain elements.

Redox titration and also magnetic measurements have been used for the direct determination of the degree of oxidation and the site of the metal ion in the heteropolycompound.

An anomalous magnetic behaviour of certain heteropolycomplexes was pointed out [28] in 1966. When two cobalt atoms (bivalent and tervalent) were present in the heteropolyanion, an intense intraionic paramagnetic interaction was observed and the magnetic susceptibility of the compound changed by only 13% between −143° and +23°C. This was also noted [89] for the complex $FeNiW_{11}O_{40}H_3^{6-}$. Quite recently these complexes as well as certain others [113] were used to investigate the spin–spin interaction between the paramagnetic ions forming part of the structure of the anion. It was emphasised that the heteropolyanions constitute a very interesting and convenient model in which the second metal atom always occupies a site with the same arrangement of oxygen atoms around it. It has been shown for the 12 : 1 copper heteropolycompound,

which is a convenient model for the investigation of electron transfer processes in copper-containing enzymes, that copper retains its tetrahedral environment in the transition $Cu^{2+} \rightarrow Cu^{+}$.[114]

The polarographic method has been used widely to investigate heteropolycompounds[84,115-124]. The conditions governing the formation of different $XM_{12}O_{40}^{X-8}$ isomers have been determined polarographically[84,117]. The electronic structures of the reduced forms (the so called heteropolyblues) are analogous to the structures of the tungsten bronzes, but there is one difference: the reduced forms are discrete (i.e. they do not give rise to polymeric species) and are soluble in water. The magnetic[121] and spectroscopic properties of reduced heteropolycompounds[108] have been investigated and it has been shown that the first electrons added are located at specific molybdenum or tungsten atoms and that as a result of further reduction the electrons introduced are located in the common delocalised orbital of the coordination sphere. Examination of the bonds in the anion with the Keggin structure (the formation of π-bonds in the coordination sphere so that the structure becomes a π-conducting system)[118] has shown that the reduction of the heteropolyanion may be compared with the reduction of polycyclic aromatic hydrocarbons with formation of the corresponding anions.

An increase of the number of electrons introduced leads to a shift of the region of stability of the heteropolyanion towards higher pH values[117]. It has been shown by X-ray diffraction that the reduced forms retain the Keggin structure[125]. In the general case 12-heteropolyphosphate anions are reduced more readily than the silicon analogues, since the charge of the latter is higher. Heteropolymolybdates have a higher oxidising capacity than heteropolytungstates.

The energies of the first charge-transfer band, observed in the ultraviolet spectra of heteropolyacids, have been correlated[103] with the reduction half-wave potential and it has been shown that the lower the first vacant antibonding orbital the higher the oxidising capacity of the heteropolyanion. The reduction of the heteropolyanions XMo_6O_{24} (D_{3d}) leads to their decomposition[124]. This example and also data for the reduction of the anions[120] $XMo_{12}O_{42}^{8-}$ (T_h) indicate differences between the structures of the anions and the environments of the molybdenum atoms. There is no unanimous view concerning the mechanism of the reduction process. Moreover it is quite probable that the employment of chemical reducing agents frequently used in analytical practice ($SnCl_2$, ascorbic acid, etc.) can lead to irreversible processes and the formation of unknown compounds with the initial heteropolycompounds. These phenomena and also the fact that, with increase of the number of electrons introduced, the maximum of the valence-change bands shifts towards shorter wavelengths, will undoubtedly affect the interpretation of the results. For this reason, studies[126] in which the reduction of heteropolyacids by an $SnCl_2$ solution was investigated quantitatively are not fortuitous.

^{1}H NMR has been widely used to determine the proton groups within the structure of heteropolycompounds[52,127-130]. It has been shown that acid protons in heteropolyacids with the Keggin structure are present in the form of H_3O^+.[127-129] Moreover, it has been established that such acids have a small number of dissociable protons. In contrast to these acids, some of the protons in heteropolymolybdoceric(IV), heteropolymolybdothoric, heteropolymolybdouranic, and heteropolymolybdoneptunic acids are present as H_3O^+ and some are present as OH^- groups, the number of dissociable protons in the acids being eight[68,129]. It has been shown for metatungstic acid, which gives rise to the anion $H_2W_{12}O_{40}^{8-}$ (T_d symmetry), that there are two protons in the tetrahedral cavity. In aqueous solutions the signal due to these protons is displaced towards lower fields by 1.0–1.4 p.p.m., relative to the water signal. This indicates a pronounced insulation of these two protons by the polytungstate shell, which can be clearly seen from Fig. 1*b*.[131]

NMR spectroscopy involving heavy nuclei (^{17}O, ^{31}P, and many others which have non-zero spins) yields valuable information about the molecular and electronic structure of the heteropolyanion[132]. The effect of the metal entering into the coordination sphere on the oxygen atoms has been traced, for example, on the basis of the chemical shifts in ^{17}O NMR of both simple and mixed heteropolyacids. The ^{27}Al NMR spectra of aluminium heteropolytungstate clearly indicate a tetrahedral arrangement of atoms around aluminium.

It is interesting that high-resolution ^{1}H NMR spectra make it possible to follow the *trans*-influence of the central atom X via the inner oxygen atom on the ligand Y in the heteropolyanions $XW_{11}CoO_{39}Y$, where Y is pyrazine[133]. ^{1}H NMR spectra in organic media[134] have shown that $XMo_{12}O_{40}^{X-8}$ exhibits a lower tendency towards the formation of hydrogen bonds than does ClO_4^-. This indicates yet again the low negative charge density (−4 over a sphere with $r = 5.6$ Å) on the surface of the anion.

The present authors' Mössbauer spectroscopic data indicate an effect by the molybdate and tungstate spheres on the iron(III) nucleus in the $SiM_{11}O_{39}Fe(H_2O)^{5-}$ ions, which have the same structures. This is correlated with ESR data for the same complexes[135]. ESR has been used to investigate the reduced $PW_{10}V_2^{IV}O_{40}^{5-}$ anions. It was shown that two vanadium(V) atoms are reduced to vanadium(IV) and that they occupy two non-equivalent positions in the structure of the anion, because the local crystal fields of the anion are directed at different angles with respect to the magnetic field[136].

Vibrational spectroscopy has not been widely used to investigate the molecular structures of heteropolyanions in view of their fairly considerable complexity, although a number of studies dealing with this problem have been published[137-143]. Vibrational spectroscopy can be very useful for the identification of the structures of new hitherto unknown compounds, since each type of structure of heteropolycompounds gives rise to fairly characteristic spectra in consequence of the differences in the structure of the anion. The employment of Raman spectroscopy, particularly with a laser source, permits the identification of the species present in solution, as has been done for vanadium, molybdenum, and tungsten isopolycompounds[142] and also heteropolyacids with T_h (Kazanskii et al.[141]) and T_d (Kazanskii[143]) symmetries. It was established that the structure of the heteropolyacids found in crystalline specimens persists also in aqueous solutions. Raman and infrared spectroscopy of the ether adducts of certain heteropolyacids[140] confirmed the retention of the structure of the anions in ether without any decomposition. The effect of the charge of the central atom X^{X+} is clearly shown in the Raman spectra of the heteropolyanions $XM_{12}O_{40}^{X-8}$ (i.e. there are *trans*- and *cis*-effects on the positions of the vibrational bands A_1 of the terminal M=O and bridging M–O–M groups). With decrease of x, the stability of the terminal M=O bonds falls[143].

Together with ^{1}H NMR, infrared spectroscopy is frequently used to investigate the nature of the water in heteropolycompounds[144,145].

Among other methods, which are purely qualitative, mention may be made of dialysis, which is used to determine the dimensions of the anions, and of chromatography, which has been employed to separate certain heteropolycompounds [146].

Interesting prospects arise in connection with the application of X-ray electronic spectroscopy to the study of the electronic structures of heteropolyanions. X-Ray electronic spectra of the inner $3d_{3/2}$ and $3d_{5/2}$ electrons of heteropolymolybdates and normal molybdates have been obtained [147]. The changes in charge distribution in the valence shell, occurring when the valent state of the atom is altered, influence all the inner levels and the results indicate a decrease of the positive charge on the molybdenum atoms in heteropolycomplexes compared with MoO_4^{2-}. According to X-ray electronic spectra [148], the binding energy of phosphorus $2p$ electrons is higher in $PW_{12}O_{40}^{3-}$ than in $PMo_{12}O_{40}$. This indicates a decrease of the positive charge in $PMo_{12}O_{40}$, which is correlated with results obtained from ^{31}P NMR chemical shifts and the vibrational spectra of these heteropolyanions [143,148].

Presumably much information about the electronic structures and charge distribution within and on the surface of heteropolyanions will be obtained from the photoelectronic spectra of the outer valence energy levels.

IV. PRINCIPAL TRENDS IN THE CHEMISTRY OF HETEROPOLYCOMPOUNDS

Apart from continued interest in the theoretical problems of the molecular electronic structure, the present state of the chemistry of heteropolycompounds is also characterised by the development of the synthesis of mixed and diheteropolycomplexes. Since the coordination sphere is made up of metal and oxygen atoms, heteropolycomplexes can serve as model compounds for the investigation of the chemistry of metal oxides. A wide range of physical methods can be used to investigate heteropolycompounds in a crystalline form, in aqueous and non-aqueous solutions, and in the recently discovered [133] gaseous state.

Many mixed compounds (sometimes one or several molybdenum atoms in molybdate coordination sphere are substituted by tungsten or vanadium) and diheteropolycomplexes (as defined by Baker), in which one atom of the coordination sphere is replaced by some other metal atom (usually a transition metal atom), have been obtained. They must be distinguished from true diheteropolycomplexes in which two atoms of the complex-forming agent are surrounded by the same atoms, which form the coordination sphere (cf. Figs. 2*a* and 5*a*).

We assigned to mixed compounds the complexes in the coordination spheres of which molybdenum, vanadium, or tungsten may be present jointly in the highest oxidation states in proportions of 11 : 1. The formation of these compounds is due to the general tendency of the ions of these elements to link up into polymeric structures. The resulting compounds are mainly complexes having the Keggin structure. Other known types are the mixed molybdotungstates $(NH_4)_4NiMo_{6-n}W_nH_6$, where $n = 0-6$ (Kokorin and Dimant [149]); the acids have been obtained from these salts in a free state.

We may quote several examples where one or several tungsten (or molybdenum) atoms in the coordination sphere are replaced by a vanadium atom. Much work has been done in this field by Kokorin and coworkers [150-168], who investigated the conditions governing the formation of heteropolycomplexes with different degrees of substitution of M by vanadium atoms. The corresponding acids were isolated, for example $H_4PMo_{11}VO_{40}$, $H_5PMo_{10}V_2O_{40}$, and $H_6PMo_9V_3O_{40}$, which decompose at different rates with increase of pH. The synthesis of vanadomolybdenum acids with substitution of up to ten molybdenum atoms, for example of the anion $PV_{10}Mo_2O_{40}^{13-}$, was reported recently [161].

Studies on the electron diffraction patterns of decamolybdotrivanadogermanic acid and of the powder diffraction patterns of hexamolybdohexatungstophosphoric acid [163] confirmed the retention of the Keggin structure in the substituted complexes.

Apart from studies on theoretical problems of mixed heteropolyacids (bond strengths, electronic and molecular structures, oxidation–reduction properties etc.) much effort has been devoted to the determination of the number of dissociable protons in these acids in both aqueous and non-aqueous media. A parallel is frequently drawn with the initial acids ($H_{x-8}XO_4$), although these analogies have no theoretical basis. It is clear from structural considerations that, following the substitution of one molybdenum atom by a vanadium(V) atom, the charge of the anion should increase by -1, since the structure of the anion persists, i.e. the number of oxygen atoms in the anion remains 40. The fact that the number of dissociable protons in the acids is sometimes inconsistent with this suggests instability of the anion, the occurrence of additional equilibria, and changes in the degree of dissociation of protons as the dielectric constant of the solvent is varied.

On the other hand, when a highly charged ion (for example, Zr^{4+}, Ti^{4+}, Th^{4+}, or Nb^{5+}) is introduced into a solution of heteropolyacids, the so called "ternary" complexes are formed. It has been claimed on the basis of spectrophotometric data only [169,170] that phosphorus, niobium, and oxygen form a "central molecule" (a niobium phosphate the composition of which varies with the medium and the pH) surrounded by a molybdate coordination sphere. Later the formation of a zirconium molybdophosphate complex of the same type was postulated [171]. However, subsequently it was shown [172] on the basis of the infrared spectra of solid complexes containing zirconium, titanium, and thorium that the ions of these elements substitute molybdenum in the coordination sphere with formation of mixed heteropolycomplexes. Heteropolycomplexes in which molybdenum is substituted by niobium, for example $PMo_{10}Nb_2O_{40}^{5-}$, have also been obtained and characterised [29]. Dodecamolybdovanadoselenic acid $H_6SeMo_{10}V_2O_{40}.xH_2O$ was obtained by extraction with ether and partly characterised [173].

We shall not consider the numerous studies (see the references in Spitsyn and Torchenkova's paper [174]) in which the preparation of two heteropolycompounds in solution is reported without proof of their individuality. Of the latest studies, we shall mention the isolation of salts of heteropolycompounds, in which rhenium(VI), for example, substitutes a molybdenum atom in 12 : 1 and 18 : 2 molybdophosphate anions. The free acids have been obtained from these salts by ion exchange [175]. We may note that the unsaturated heteropolyacid $H_6[CrW_{11}O_{39}H_3]$ was recently obtained in solution, although unsaturated heteropolyacids with the Keggin structure [176] are not usually formed in a free state. However, one may postulate the formation of a diheteropolycomplex the central cavity of which contains two protons.

Heteropolytungstate complexes with phosphorus(III) and arsenic(III) have been obtained [177]. The X-ray diffraction

study being carried out should reveal certain structural features of these compounds.

It was shown[28] in 1966 that the coordination sphere of the anion with the Keggin structure (Fig. 1) or the Dawson structure (Fig. 2*a*) can incorporate one transition metal atom (usually belonging to the 3*d* group) with simultaneous displacement of one molybdenum or tungsten atom and the formation of a new complex having the general formula

$$[H_hM^{m+}O_5X^{x+}O_4(Mo\ \text{or}\ W)_{11}O_{30}]^{m+x+h-14}.$$

On the other hand, if the sixth coordination site of the transition element is occupied by another ligand, then

$$[Y^{y-}M^{m+}O_5X^{x+}O_4(Mo\ \text{or}\ W)_{11}O_{30}]^{m+x-y-13}$$

or

$$\{Y^{y-}M^{m+}O_5[(P^{5+}\ \text{or}\ As^{5+})O_4]_2(Mo\ \text{or}\ W)_{17}O_{58}\}^{m-y-10}$$

where Y is a monodentate ligand which occupies the site of a non-delocalised oxygen atom; this can be ammonia, pyridine, pyrazine, a halide ion, etc. For a bidentate ligand, there is a possibility of the binding of two anions via this ligand and of the formation of a compound heteropolycomplex in the form of a dumbell whose molecular weight exceeds 6000. The existence of such complexes, which may incorporate a wide range of ligands and different metal atoms, greatly extends the range of complexes under consideration. The inclusion of the metal ion M^{m+} in the coordination sphere via five oxygen atoms leads to a possible overlapping of different atomic orbitals, which is reflected in unusual values of the Racah parameters and unusual magnetic properties and electrical conductivities of the anionic framework. From the standpoint of the investigation of the spectroscopic properties of the injected heteroatom (Baker's definition), these heteropolycomplexes constitute a very convenient model, since the metal ion always has the same environment and only a change in the type of ligand and also the influence of the coordination sphere can affect the spectra. The existence of this new group of compounds has been demonstrated by the following methods: (1) by the analysis of the recrystallised pure products in which the ratios Y : M : X : Mo(W) were 1 : 1 : 1 : 11 (this must be confirmed by determining the molecular weight from the results of crystal-chemical studies); (2) by ion-exchange experiments, which showed that the resin in the K^+-form does not contain M^{m+}; (3) by determining the degree of oxidation of M^{m+} by oxidation-reduction titration; (4) by magnetic measurements; (5) by cryoscopy in $Na_2SO_4.10H_2O$; (6) by studying the absorption spectra of both solutions and solid heteropolycomplexes in the region of $d-d$ transitions; (7) by polarography; (8) on the basis of the isomorphism of the crystals.

The central atom X^{x+} can be P^{5+}, Sr^{4+}, Ge^{4+}, H_2^{2+}, Co^{2+}, B^{3+}, Fe^{3+}, and Zn^{2+} and the metal M entering into the coordination sphere[178-187] can be Co^{2+}, Co^{3+}, Ga^{3+}, Fe^{3+}, Ni^{2+}, Zn^{2+}, Mn^{2+}, Mn^{3+}, Cr^{3+}, and Al^{3+}; the molybdenum analogues are less stable. Complexes with doubly charged metal ions are stable at pH ~ 4, but the corresponding acids have not been obtained, since, on being passed through a cation exchanger in the H^+-form, they split off M^{2+} and only the initial 12 : 1 heteropolyacids were produced. For triply and more highly charged ions, the new heteropolycompounds are fairly stable in acid media, M^{3+} ions are not split off in the presence of the cation exchanger, and for this reason the acids have been obtained in a free state. Derivatives of the $X_2MW_{17}O_{61}^{n-}$ anion, in which X = P^{5+} or As^{5+} and one tungsten atom is substituted by a metal ion (Mn^{2+}, Co^{3+}, Ni^{2+}, or Zn^{2+}), have also been investigated; the properties of these compounds are analogous to those of the complexes $MXW_{11}O_{40}^{n-}$.

Apart from the above data for the formation of the new class of heteropolycompounds which have the Keggin structure and the reactions in which they are synthesised (these can be classified as complex formation reactions), we shall consider cases where the second heteroatom cannot enter the inner sphere and remains on the surface of the anion. When conditions for the formation of anions of the type $XW_{11}O_{39}^{n-}$ or $XW_{17}O_{61}^{n-}$ are created (pH ~ 4–6) and the solution contains a cation with a large radius, for example a lanthanide ion (Ln radius = 1.0 Å), a complex with the ratio An : Ln = 2 : 1 is formed. The $XW_{11}O_{39}^{n-}$ anion provides four electron-donating sites, which are produced following the elimination of one metal atom from the coordination sphere; the lanthanide ion can retain two anions. The coordination number of the lanthanide is 8. On the basis of structural considerations, it is difficult to expect other possibilities in the formation of the complex apart from the manganese(IV) complex (Fig. 9), in which the Nb_6O_{19} ligands provide bridging oxygen atoms as electron-donating atoms. It is quite likely that the formation of compounds of this type is not typical for heteropolyanions having the Keggin structure and a low charge. All other oxygen atoms in the structure of the 12 : 1 anion (T_d) are sterically unsuitable for the formation of compound heteropolycomplexes.

The formation of complexes by the dodecamolybdocerate ion with the cations of lanthanide elements, thorium, niobium, tantalum, and other metals has also been established[67,188-191]. For example, the interaction of erbium chloride with molybouranic acid[67] led to the formation of a complex with the ratio Er : An = 2 : 1. However, compounds with the ratio Er : An = 4 : 3 were isolated in a solid state. It was shown that MO_6 is not split off in this case. The structural features of the $UMo_{12}O_{42}^{8-}$ anion are such that on the surface there are three terminal oxygen atoms of the three combined octahedra, which can make up the coordination polyhedron around the Er^{3+} ion. The erbium ion tends to "saturate" its coordinating capacity by forming complicated structures. This is also observed for $XW_{11}O_{39}^{n-}$ (An). The An : Ln = 1 : 1 complex has not been isolated, although its stability constant is much higher than that of the complex $LnAn_2$. In this case, as in many others, the problem must be solved by X-ray diffraction. With the introduction of modern diffractometer and high-speed computers, one may hope that these problems will be successfully solved.

In a brief review we naturally could not cover many literature sources, since our aim was to write a critical review and not a simple compilation of research results. Here we have presented general relations based on the latest X-ray diffraction studies, on which the understanding of many problems in the chemistry of heteropolycompounds depends.

In addition we endeavoured to show that, although heteropolycompounds were discovered more than a hundred years ago, their chemistry constitutes a fruitful and interesting field for both physicochemical research and for the investigation of new synthetic possibilities.

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Silicon Tetrafluoride Adducts

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The review deals with the compositions, properties, structures, and thermodynamics of silicon tetrafluoride adducts with organic molecules containing electron-donating nitrogen, oxygen, phosphorus, or sulphur atoms. Particular attention has been paid to reactions involving the conversion of the adducts of nitrogen-containing bases into fluorine-containing compounds with a covalent silicon-nitrogen bond. The comparative estimates of the electron-accepting properties of silicon tetrafluoride and other silicon tetrahalides obtained by different workers are discussed.
The bibliography includes 126 references.

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I. INTRODUCTION

In the manufacture of simple superphosphate a considerable amount of fluorine-containing compounds, mainly silicon tetrafluoride, which is the principal potential source of industrial fluorine[1], are released into the gas phase. Evidently this is why there has been no weakening of interest in various aspects of the chemistry of silicon tetrafluoride, which was discovered almost 200 years ago.

Among the numerous aspects of silicon tetrafluoride chemistry, particular attention has been devoted to the study of its complex-forming capacity: silicon tetrafluoride, which is very inert with respect to exchange reactions, enters readily into addition reactions with organic electron-donating molecules (R), forming adducts with the composition $SiF_4 nR$ (n = 1 or 2). Very many original studies have been made on silicon tetrafluoride adducts but in monographs on the chemistry of silicon and fluorine these compounds are either not considered at all or ar discussed very briefly. Even in reviews[2,3] on the chemistry of silicon complexes the problem is given very scanty attention.

This review constitutes a first attempt at a systematic and general account of the available literature data on the composition, properties, and structures of silicon tetrafluoride adducts. Account is taken of almost all the original studies on the chemistry of silicon tetrafluoride adducts published up to 1st June, 1973. In accordance with the definition of an adduct proposed by Cotton and Wilkinson[4], we shall consider solid compounds of definite composition formed by silicon tetrafluoride with organic molecules containing an electron-donating nitrogen, oxygen, phosphorus, or sulphur atom, which have been isolated in a pure state.

II. STOICHIOMETRY

Under normal conditions, silicon tetrafluoride is a colourless gas; its melting point is −90°C.[5] It has been established by electron diffraction[6] that gaseous silicon tetrafluoride has the symmetry of a regular tetrahedron with an Si–F distance of 1.54 ± 0.2 Å. In the ground state tetrahedral silicon tetrafluoride has the electronic configuration $(1a)^2(1t_2)^6(2a)^2(2t_2)^6(1e)^4(3t_2)^6(t_1)^6$.

Calculations have shown[7] that the 3*d* atomic orbitals of the central silicon atom in the silicon tetrafluoride molecule are populated to a large extent, which is evidence for a significant involvement of the orbitals in the formation of chemical bonds. Despite the presence of an electron octet, the silicon atom in the molecule is capable of increasing its coordination number from four to six by utilising two of the five vacant 3*d* orbitals and it has been noted[8] that σ-bonding with participation of the silicon 3*d* orbitals is due mainly to the presence of highly electronegative groups located at this atom. From this standpoint, silicon tetrafluoride should behave as an "ideal" silicon halide for the formation of complexes with electron-donating molecules via σ-bonding with expansion of the silicon octet.

The simplest compound of this type is the adduct $SiF_4.2NH_3$, which is a white powder; it was synthesised at the beginning of the past century[9]. It was established later[10] that, on mixing dry SiF_4 with an excess of dry NH_3, only one compound with the composition $SiF_4.2NH_3$ is formed in the solid phase; it sublimes *in vacuo* at 60–65°C and does not undergo ammonolysis even on heating in an excess of ammonia up to 300°C. In contrast to the tetrafluoride, the remaining silicon tetrahalides form with ammonia compounds having the composition $SiX_4.6NH_3$ (X = Cl, Br, or I).[11]

Aliphatic amines react with silicon tetrafluoride like ammonia. Adducts of silicon tetrafluoride with trimethylamine (Me_3N) have been investigated in greatest detail. It has been reported[12] that silicon tetrafluoride reacts with trimethylamine to form a white solid compound $SiF_4.Me_3N$, whose vapour pressure is 45 mmHg at room temperature and 0.1 mmHg at 78°C. The existence of this compound was subsequently confirmed by Berg[5]. However, Wilkins and Grant[13] discovered two compounds in the SiF_4–Me_3N system: $SiF_4.Me_3N$ and $SiF_4.2Me_3N$†, whose existence has been confirmed from the vapour pressure–composition isotherm and by cryoscopic measurements. Both adducts are white crystalline substances, which sublime congruently at atmospheric pressure and melt congruently at higher pressures. Subsequently Schnell[14] reported that the adduct

†Henceforth we shall refer to these adducts as a 1 : 1 and 1 : 2 type respectively.

$SiF_4.2Me_3N$ is deposited as a dense white precipitate when silicon tetrafluoride is passed into a solution of trimethylamine in petroleum ether. When a benzene solution of trimethylamine is used, the product is the compound $SiF_4.Me_3N$, which is readily soluble in benzene, carbon tetrachloride, petroleum ether, and carbon disulphide, while the 1 : 2 adduct is much less soluble in these solvents.

Subsequent investigations[15] confirmed Schnell's conclusions, but the SiF_4–Me_3N system proved to be the only one so far for which the existence of adducts of two types may be regarded as finally proved. Information has also been published on the synthesis of dimethylamine adducts of the 1 : 2 and 2 : 3 types[16], but subsequently these results were not confirmed. Hagen and Callaway[11] showed that dimethylamine forms with silicon tetrafluoride only an adduct of the 1 : 2 type. Methylamine, whose adduct $SiF_4.2MeNH_2$ has been investigated in fair detail, reacts with silicon tetrafluoride similarly[11,17,18]. The synthesis of the compounds $SiF_4.Am$ and $SiF_4.2Am$ (Am = mono-, di-, and tri-ethylamines and mono-, di-, and tri-ethanolamines) has been reported[19].

Alicyclic amines (piperidine, pyrrolidine[20], and aziridine[21]) also form 1 : 2 adducts with silicon tetrafluoride. The earlier data concerning the synthesis of 1 : 2 adducts with ammonia, methylamine, dimethylamine, trimethylamine, pyrrolidine, and piperidine were confirmed recently[22] and the hitherto unknown compounds $SiF_4.2NH_xR_{3-x}$ ($x = 1$, R = Et, n-Pr, or n-Bu; $x = 2$, R = Et, n-Pr, n-Bu, i-Bu, or t-Bu) and $SiF_4.2NMe_xEt_{3-x}$ (x = 0–2), obtained by the direct interaction of the reactants in the gas or liquid phase, were described. On the basis of these data, the authors[22] concluded that the formation of 1 : 2 adducts is characteristic of the silicon tetrafluoride–aliphatic monoamine systems and data[2] concerning the formation of a 2 : 3 methylamine adduct are explained by the hydrolysis of the 1 : 2 adduct by atmospheric moisture. One must agree with this conclusion, since the range of amines employed by Aylett et al.[22] and other investigators[11,17–21] was sufficiently large to extend the observed behaviour to the entire series of aliphatic amines.

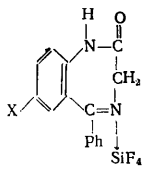
Aliphatic diamines react with silicon tetrafluoride as bidentate ligands, forming 1 : 1 adducts. Ethylenediamine reacts with silicon tetrafluoride in this way, forming a solid white adduct, which sublimes at 225°C and 0.2 mmHg[24]. Adducts of the 1 : 1 type have also been described for piperazine[21] and a number of tetramethylalkylenediamines of the type $Me_2N(CH_2)nNMe_2$, where n = 1, 2, 3, 4, or 6.[25] It is striking that hydrazine reacts with silicon tetrafluoride like the monoamines, forming a white non-hygroscopic compound $SiF_4.2N_2H_4$, which sublimes congruently at 100°C and decomposes on heating above 200°C.[23] Owing to its low molecular dimensions, hydrazine is probably unable to occupy two coordination sites at once about the silicon atom and for this reason behaves as a monodentate ligand. The behaviour of phenylhydrazine, which behaves as a bidentate ligand forming a 1 : 1 adduct with silicon tetrafluoride[21], is therefore incomprehensible. Since there are reliable data concerning the composition of the $SiF_4.2N_2H_4$ adduct[23], which were confirmed by other results[17], we believe that the observed[21] composition of the phenylhydrazine adduct requires an additional test.

Proceeding now to the consideration of the stoichiometry of the adducts of nitrogen-containing heterocycles, we may note that this problem has given rise to the greatest degree of disagreement. An example is provided by the controversy concerning the composition of the silicon tetrafluoride adduct with pyridine (Py). As early as 1888, Comey and Smith[26] described a white compound $SiF_2.2Py$ in powder form, obtained by passing silicon tetrafluoride through a benzene solution of pyridine and noted that it decomposes rapidly. Pyridine is evolved at the same time and a compound close in composition to $2SiF_4.3Py$ is produced. These observations were subsequently confirmed by Wannagat and Schwarz[27], but a final conclusion about the individuality of the compound $2SiF_4.3Py$ was not reached. Thus, taking into account the data[28,29] concerning the existence of the compound $SiF_4.Py$ in the silicon tetrafluoride–pyridine system, three types of adducts have been described altogether. On the other hand, the majority of investigators have reported the existence of only one adduct of the 1 : 2 type[30–33]. In order to resolve the above contradictions, Guertin and Onyszchuk[20] investigated the direct interaction of the two reactants in the gas phase, used for the synthesis a solution of pyridine and ether, and also applied the tensimetric titration method. In all of the above instances they obtained a solid white product of composition $SiF_4.2PY$, which sublimes congruently *in vacuo* at 60–80°C. They emphasised[20] that the method of synthesis of the 2 : 3 [26] and 1 : 1 [28,29] adducts was most carefully repeated, but in all cases only one compound $SiF_4.2Py$ was obtained. On the basis of their results, Guertin and Onyszchuk concluded that other workers who reported the formation of the 1 : 1 and 2 : 3 adducts failed to take into account the loss of pyridine as a result of the hydrolysis of $SiF_4.2Py$. Aylett et al.[22] subsequently agteed with this conclusion. They studied the silicon tetrafluoride–pyridine system in the range of temperatures from 196°C to room temperature and in all cases obtained the compound $SiF_4.2Py$, which melts at 189°C (170–180°C according to Guertin and Onyszchuk[20]) in a sealed capillary. However, Aylett et al.[22] also succeeded in obtaining compounds of other compositions by means of special procedures, but all these proved to be unstable and slowly lost silicon tetrafluoride, forming the adduct $SiF_4.2Py$. Thus we believe that the problem of the stoichiometry of the adducts in the silicon tetrafluoride–pyridine system may be regarded as finally solved in favour of the formation of only one stable compound of the 1 : 2 type.

There was a similar controversy in yet another instance. Thus Comey and Jackson[16] drew attention to the fact that, although pure quinoline does not react with silicon tetrafluoride, when the latter is passed through a benzene solution of quinoline the product is an acicular deposit of $2SiF_4.3C_9H_7N$, which sublimes without decomposition. These results were disproved by Wannagat and Schwarz[27], who pointed out that quinoline does not react with silicon tetrafluoride and the adduct described by Comey and Jackson[16] is quinolinium hydrofluoride formed as a result of the hydrolysis of silicon tetrafluoride when moist quinoline is employed. However, this report was also rejected by Gutmann et al.[21] who reported that, when a benzene solution of quinoline is employed, a 1 : 2 adduct is formed. Subsequently Wannagat et al.[34] reinvestigated the silicon tetrafluoride–quinoline system and confirmed the conclusions of Gutmann et al.[21], stating that their earlier results were erroneous. It is appropriate to mention here also the extremely interesting study by Schnell[35], according to whose results the interaction of isoquinoline with silicon tetrafluoride yields a 1 : 2 adduct. The same investigator reported[14] the existence of the adduct $SiF_4.2\beta\text{-}MeC_5H_4N$, but he presented no data concerning the conditions of the synthesis and properties of this compound.

In general one may assume that the formation of 1 : 2 adducts is characteristic of nitrogen-containing hetero-

cycles as well as of aliphatic and alicyclic amines. Only 2,4-dimethylpyridine and 8-hydroxyquinoline, for which Muetterties[29] described 1 : 1 adducts, constitute an exception to this general rule. The addition of a second amine molecule probably does not occur in this case owing to steric hindrance. The finding that complex polyatomic species, such as 1,4-benzo-2-diazepinium ions, also form 1 : 1 adducts with silicon tetrafluoride[36] supports this hypothesis:



(X = Me, Cl, NO_2) .

Judging from infrared spectroscopic data[36], the tertiary nitrogen atom and not the amide group is responsible for a coordination in these compounds.

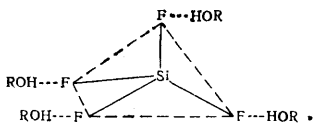
As expected, all the heterocyclic diamines investigated hitherto (2,2′-bipyridyl[21,37,38], 4,4′-bipyridyl[39], and 1,10-phenanthroline[30]) form 1 : 1 adducts with silicon tetrafluoride. Aromatic diamines behave similarly. Among these, the adduct of *o*-phenylenediamine has been most completely investigated. The compound SiF_4.*o*-PDA‡ was obtained for the first time by Gutmann et al.[21], whose finding was subsequently confirmed by Harris and Rudner[40] and also by the authors of the present review[41]. The latter showed that 1 : 1 adducts are also formed by *m*- and *p*-phenylenediamines. All the compounds were obtained by passing gaseous silicon tetrafluoride through benzene solutions of the corresponding diamines. It is therefore surprising that a precipitate is not formed on treating a benzene solution of 3,3′, 4,4′-tetra-aminobiphenyl with silicon tetrafluoride[40], although under the same conditions benzidine, which has a similar structure, gives rise readily to a 1 : 1 adduct[42].

In general the problem of the stoichiometry of the adducts of silicon tetrafluoride with aromatic diamines involves no disagreements, which cannot be said of the adducts of aromatic monoamines, although historically these adducts were in fact the first to attract attention. As early as 1888, Comey and Jackson[16] obtained white or slightly coloured compounds of composition $2SiF_4.3Am$ (Am = aniline, *p*-bromoaniline, *p*-chloroaniline, *p*-toluidine, *o*-toluidine, diphenylamine, and *NN*-dimethylaniline) and described in detail their properties. Later Gutmann et al.[21] showed that, on passing gaseous silicon tetrafluoride through benzene solutions of *p*-chloroaniline, *p*-aminophenol, β-naphthylamine, and *p*-aminobenzoic acid at room temperature, cryptocrystalline 1 : 2 adducts are formed in all cases, but *o*-nitroaniline gives rise to the compound $SiF_4.H_2NC_6H_4NO_2$.

It has also been reported that 1 : 2 adducts are formed by *NN*-dimethylaniline[29], *o*-aminophenol, and 2-amino-4-chlorotoluene[40]. On the other hand, when silicon tetrafluoride was passed through boiling benzene solutions of the initial amines, 1 : 1 adducts of *p*-anisidine[43] and α-naphthylamine[44] were obtained and at room temperature products of the 2 : 3 type were synthesised.

Unfortunately, information about the influence of the conditions of synthesis and of the structure of the initial amine on the composition of the adduct formed in silicon tetrafluoride–aromatic amine systems is extremely limited, so that the general conclusions of Aylett et al.[22] appear to be insufficiently well-founded.

It is noteworthy that the investigations[16,21,29,40,43,44] have been carried out using solutions of the amines in aprotic solvents, mainly benzene, in which silicon tetrafluoride is almost insoluble[45]. The situation is different when aliphatic alcohols, in which silicon tetrafluoride dissolves readily, are employed. Under these conditions, the products[46,47] are the complexes $SiF_4.4ROH$ formed as a result of strong hydrogen bonding[49]§:



We established that in alcoholic solutions aromatic amines (Am) react with silicon tetrafluoride as follows[50-52]:

$$SiF_4 \cdot 4ROH \rightleftarrows SiF_4 + 4ROH , \quad (1)$$

$$\underline{SiF_4 + 2Am \rightleftarrows SiF_4 \cdot 2Am , \quad (2)}$$

$$SiF_4 \cdot 4ROH + 2Am \rightleftarrows SiF_4 \cdot 2Am + 4ROH , \quad (3)$$

with formation of a precipitate consisting of the adduct $SiF_4.2Am$ (Am = aniline, *p*-aminophenyl difluoromethyl sulphone, *m*- and *p*-nitroanilines, *o*- and *p*-aminobenzoic acids, *m*-trifluoromethylaniline, *p*-aminoazobenzene, *o*-, *m*-, and *p*-anisidines, *o*-, *m*-, and *p*-aminophenols, *p*-bromoaniline, *p*-chloroaniline, *o*-, *m*-, and *p*-toluidines, *p*-phenetidine, diphenylamine, and *N*-ethylaniline). In this case the proportions of the initial reactants influence appreciably the rate of complex formation, which makes it possible to employ the proposed technique in the investigation of the kinetic parameters of the reaction.

As a result of higher steric hindrance in the case of the tertiary amines *NN*-dimethyl-, *NN*-dipropyl-, and *NN*-dibutyl-anilines and *NN*-dimethyl-*p*-toluidine, these amines do not form solid products with silicon tetrafluoride either in alcoholic or benzene solutions[52]. *o*-Aminobenzenethiol behaves analogously, although, as mentioned above, under analogous conditions *o*-aminophenol forms a compound with the composition $SiF_4.2H_2NH_6H_4OH$.[40]

Apparently the only known adduct of silicon tetrafluoride with amides is the compound $SiF_4.2Me_2NCHO$, obtained by passing silicon tetrafluoride through a benzene solution of *NN*-dimethylformamide[53,54]. It has also been reported that acetamide absorbs about one quarter of a mole of silicon tetrafluoride with formation of a white solid product[55], while formamide[54] and urea[16] decompose under the influence of silicon tetrafluoride even at room temperature. In contrast to aliphatic amides, aromatic amides, for example chloroacetamidobenzophenones in which the nitrogen atom is conjugated with the π-electron system of the benzene ring, do not form any solid product with silicon tetrafluoride[36]. In this case steric hindrance cannot be of decisive importance, because chloroacetamidobenzophenones are models of 1,4-benzodiazepin-2-ones, which, as mentioned above, form 1 : 1 adducts with silicon tetrafluoride.

On the basis of the results of early studies[45,55], it was believed for a long time that silicon tetrafluoride is incapable of coordination with molecules containing an electron-donating oxygen atom. Muetterties[29] described

‡PDA = phenylenediamine.

§Borodin et al.[48] investigated the silicon tetrafluoride–ethanol system by ^{19}F NMR, but were unable to reach definite conclusions concerning the structure of the alcohol complex of silicon tetrafluoride.

"weak complexes" of silicon tetrafluoride with acetylacetone and tropolone and noted that these complexes are unstable even at room temperature. It has also been reported that under certain conditions silicon tetrafluoride promotes the dissociation of the C–O bond in epoxide molecules [56], but in this case adducts were not isolated. It has been established only in recent years that silicon tetrafluoride reacts with certain oxygen-containing donors (methylene and trimethylene oxides, tetrahydrofuran, tetrahydropyran, and methyl ether), forming white solid 1 : 2 adducts [57,58], which are stable only at room temperature.

According to Guertin and Onyszchuk [58], the adducts of pyridine, dimethylamine, triphenylphosphine, and tricyclohexylphosphine oxides [59] and dimethyl sulphoxide [60] as well as the dimethylformamide adduct described above should also be classified as compounds in which the oxygen atom is responsible for the formation of the coordinate bond. All these compounds react vigorously with silicon tetrafluoride, forming 1 : 2 adducts, which, like the dimethylformamide adduct, are white cryptocrystalline substances insoluble in ether, toluene, benzene, etc. The compounds are much more stable than the adducts of alicyclic ethers. Thus the adduct of dimethyl sulphoxide sublimes congruently at 107–111 °C, while $SiF_4.2Ph_3PO$ and $SiF_4.2(C_6H_{11})_3PO$ decompose with liberation of the initial reactants at 158–161° and 167 °C respectively. The above differences between the stabilities can probably be explained by the increase of the electron-donating capacity of the oxygen atom as a result of the shift of the electron density of the phosphorus, sulphur, or nitrogen atom linked to oxygen. This explanation is supported by the finding that solid products are not formed in the case of diphenyl sulphoxide [61], in which such conjugation should be much weaker than in dimethyl sulphoxide.

The first attempt to synthesise an adduct with an Si ← P coordinate bond was unsuccessful: trimethylphosphine (Me_3P) does not react with silicon tetrafluoride at 25 °C. [62] Subsequently Beattie and Ozin [15,63] obtained at low temperatures the compounds $SiF_4.Me_3P$ and $SiF_4.2Me_3P$. However, the attempt to obtain triphenylphosphine adducts were unsuccessful even on cooling the reaction mixture to −96 °C. [64]

Together with the adducts of "simple" molecular donors, compounds of silicon tetrafluoride with complex ligands—dicyanobis-(1,10-phenanthroline)iron(II) (A) and dicyanobis-(4,7-diphenyl-1,10-phenanthroline)iron(II) (B)—of compositions $SiF_4.A$, $2SiF_4.A$, and $SiF_4.B$ have been described; they are cryptocrystalline powders, very sensitive to atmospheric moisture [65]. Another example of an adduct of silicon tetrafluoride with a complex ligand is the compound $SiF_4.Pt(PPh_3)_2$, colourless crystals of which have been obtained by treating a benzene solution of tris-(triphenylphosphine)platinum(0) with silicon tetrafluoride at room temperature [64]:

$$(Ph_3P)_3Pt + SiF_4 \rightarrow (Ph_3P)_2Pt \cdot SiF_4 + Ph_3P \ . \qquad (4)$$

III. PROPERTIES

Like the initial silicon tetrafluoride, its adducts are readily hydrolysed by water with the formation of the hexafluorosilicate ion, which is characteristic of silicon tetrafluoride [10,23,34,35]:

$$3(SiF_4 \cdot 2Am) + 2H_2O \rightarrow 2(AmH)_2SiF_6 + SiO_2 + 2Am \ . \qquad (5)$$

The quantitative experiments of Aylett et al. [22] showed that the hydrolysis of $SiF_4.2NH_3$ and $SiF_4.2MeNH_2$ is described by the equation for first-order kinetics and that the rate constants at 25 °C are 1.0×10^{-3} and 1.9×10^{-3} s^{-1} respectively. For other adducts, there are only qualitative data, on the basis of which Aylett et al. [22] arranged the 1 : 2 adducts in the following sequence in terms of their resistance to hydrolysis¶: $NH_3 > MeNH_2 \sim EtNH_2 > > i\text{-}BuNH_2 > Me_2NH \sim Et_2NH > Me_3N \sim EtMe_2N \sim Et_2MeN \sim \sim Et_3N$ and $Me_3N > C_5H_5N$. When the adduct reacts with hydrofluoric acid, only the fluorosilicates of the corresponding base cations are formed, for example those of hydrazinium [23] or pyridinium [20]:

$$SiF_4 \cdot 2Am + 2H_3O^+ + 2F^- \rightarrow \underset{\downarrow -2H_2O}{2AmH^+ + SiF_6^{2-}} + 2H_2O \qquad (6)$$
$$(AmH^+)_2SiF_6^{2-} \ .$$

More powerful electron pair acceptors (anhydrous hydrogen chloride and boron trifluoride) are probably capable of displacing silicon tetrafluoride quantitatively from its adducts, but such reactions have been described only for $SiF_4.2C_5H_5N$ (Wannagat et al. [66]) and $SiF_4.2M_2H_4$ (Aggarwal and Onyszchuk [23]). At room temperature gaseous boron trichloride displaces silicon tetrafluoride from its adducts with bis(triphenylphosphine)platinum [67]:

$$(Ph_3P)_2Pt \cdot SiF_4 + BCl_3 \rightarrow (Ph_3P)_2Pt \cdot BCl_3 + SiF_4 \ . \qquad (7)$$

The reactions involving the substitution of one amine by another in the adducts have been studied in much greater detail. The first such reaction was reported by Gutmann et al. [21], who found that, on treatment with dry ammonia, the adduct $SiF_4.2(CH_2)_2NH$ decomposes with liberation of free aziridine:

$$SiF_4 \cdot 2(CH_2)_2NH + 2NH_3 \rightarrow 2(CH_2)_2NH + SiF_4 \cdot 2NH_3 \ . \qquad (8)$$

A similar reaction takes place when the hydrazine and pyridine adducts are treated with free ethylenediamine [20]:

$$SiF_4 \cdot 2C_5H_5N + H_2N(CH_2)_2NH_2 \rightarrow SiF_4 \cdot H_2N(CH_2)_2NH_2 + 2C_5H_5N \ . \qquad (9)$$

Aylett et al. [22] found that for the adducts of aliphatic amines the initial bases can be arranged in the following sequence in terms of their relative strengths in the substitution reaction: $NH_3 \gg MeNH_2 > PhNH_2 > Me_2NH > > Me_3N$; $MeNH_2 > Et_3N$. A similar sequence had been established also for aromatic amine adducts. The substitution of one amine by another takes place almost quantitatively via the mechanism

$$SiF_4 \cdot 2Am + 2Am' \rightarrow SiF_4 \cdot 2Am' + 2Am \ , \qquad (10)$$

in the following sequence on treatment of the adduct of a weaker base by a stronger base: benzylamine > *p*-anisidine, *p*-toluidine > aniline > *p*-chloroaniline, *p*-bromoaniline > *p*-aminoazobenzene > *p*-aminobenzoic acid > > *p*-nitroaniline, i.e. the possibility of the substitution reaction is determined in this case by the basicity of the initial amine [68].

Among other known reactions of silicon tetrafluoride adducts, dehydrofluorination is of particular interest as a method of converting the adducts into simple fluorine-containing compounds with a covalent silicon–nitrogen bond: F_3SiNR_2 (fluorosilylamines) and $(F_3Si)_2NR$ (fluorosilazones). Compounds of this kind are formed as a result of the loss of one or two molecules of hydrogen fluoride on heating the adducts of primary or secondary amines to 200 °C in the presence of powerful reducing agents, for

¶Only the base is indicated.

example $LiAlH_4$, B_2H_6, $NaBH_4$, LiH, $NaNH_2$, Al, or Mg [69-71]:

$$SiF_4 \cdot 2HNR_2 \xrightarrow{-HF} F_3SiNR_2 + HNR_2 , \quad (11)$$

$$SiF_4 \cdot 2HNR_2 \xrightarrow{-2HF} F_2Si(NR_2)_2 , \quad (12)$$

$$2(SiF_4 \cdot 2H_2NR) \xrightarrow{-2HF} (F_3Si)_2NR + 3H_2NR . \quad (13)$$

On further heating of the adducts of primary amines to 300–400°C in the presence of the above reducing agents, more far-reaching reactions take place and polymeric compounds of the type $(-F_2SiNR-)_n$ are formed. Their chains are made up of alternating difluorosilyl and substituted imino-groups [70,71]:

$$SiF_4 \cdot 2MeNH_2 + 2NaNH_2 \rightarrow (-F_2SiNMe-) + 2NaF + 2NH_3 + MeNH_2 . \quad (14)$$

Harris and Rudner [40,72,73] found that the adducts of primary amines readily split off hydrogen fluoride on treatment with tertiary amines, for example trimethylamine, triethylamine, or ethyldi-isopropylamine, with formation of cyclosilazanes and the corresponding pentafluorosilicates:

$$RNH_2 + 2R_3N + 3SiF_4 \rightleftarrows \frac{1}{n}(RNSiF_2)_n + 2R_3NH^+SiF_5^- \quad (15)$$

or of the ammonium salts of other fluorosilicic acids, for example with the anion $Si_2F_{11}^-$:

$$RNH_2 + 2R_3N + (m+1)SiF_4 \rightleftarrows \frac{1}{n}(RNSiF_2)_n + \frac{2}{m+1}(R_3NH^+)_{m+1}Si_mF_{(5m+1)}^{-(m+1)} \quad (16)$$

depending on the structure and properties of the tertiary amine used in the reaction. The reaction proceeds in benzene solution in an atmosphere of silicon tetrafluoride at room temperature, under milder conditions than the analogous reactions of the adducts of phosphorus pentafluoride [74] or boron trifluoride [75].

The above equations (15) and (16) provide a fairly general scheme for the reactions occurring in the dehydrofluorination process, whose mechanism has been hardly investigated. One can only presume that in these processes the dehydrofluorinating agent is not the tertiary amine itself but its adduct, since in all the published instances [40,72,73] the fluorosilicates of the corresponding bases and not the hydrofluorides are formed together with cyclosilazanes. This hypothesis is also supported by the employment of the adduct $SiF_4.Me_3N$ as a dehydrofluorinating agent in the synthesis of polyfluoroalkylketens and polyfluoroalkylsulphenes [76]. It has been noted that the fluoride ion liberated as a result of dehydrofluorination is bound firmly to the adduct, as a result of which the process becomes irreversible.

Fluorine-containing silicon–nitrogen compounds can also be obtained by the direct interaction of silicon tetrafluoride with alkali metal amides, for example with sodium bis(trimethylsilyl)amide [78] or lithium alkylamides [79]. It has been believed for a long time that the aminolysis of an Si–F bond in silicon tetrafluoride proceeds only in the presence of dehydrofluorinating agents. At the same time, the aminolysis of an Si–F bond occurs when primary amines act on alkylfluorosilanes [80] and phenylfluorosilanes [81-83], so that a similar reaction is presumably feasible also for silicon tetrafluoride. In this connection particular interest attaches to the report by Aylett et al. [84]†, who found that fluorosilylamines can be obtained by heating the adducts of certain alkylamines without using any dehydrofluorinating agents. It is recommended that the adducts be heated in a sealed tube in the presence of an excess of silicon tetrafluoride at 100–200°C. Trifluorosilylamines are formed from the adducts of secondary amines:

$$SiF_4 \cdot 2R_2NH \rightarrow F_3SiNR_2 + R_2NH_2F \quad (17)$$

and the excess SiF_4 is combined with formation of the corresponding hexafluorosilicate:

$$2R_2NH_2F + SiF_4 \rightarrow (R_2NH_2)_2SiF_6 . \quad (18)$$

Pentafluorosilicates are hardly formed in this reaction. When primary amine adducts are heated, the situation is complicated because of the formation of products with a tendency towards further dehydrofluorination and disproportionation. It has been noted [84] that the yield of the corresponding hexafluorodisilazane $(SiF_3)_2NR$ depends mainly on the structure of the initial amine. Indeed the yields of the hexafluorodisilazanes obtained from the adducts of n-alkylamines (Table 1, Nos. 9–12) are much lower than for the adduct of a secondary amine—isobutylamine (Table 1, Nos. 13 and 14). In conformity with the above finding, when the adduct of t-butylamine is heated, a fairly high yield of trifluorosilylamine is produced via the reaction

$$SiF_4.2t\text{-}BuNH_2 \rightarrow t\text{-}BuNHSiF_3 + t\text{-}BuNH_3F, \quad (19)$$

since the increase of the steric effect of the substituent on passing to the t-butyl group not only increases the yield of the final product but also alters the reaction mechanism.

Table 1. Conditions governing the synthesis and yields of trifluorosilylamines and hexafluorodisilazanes [84].

No.	Adduct pyrolysed	Temp., °C	Time, h	Product	Yield, %
1	$SiF_4.2Et_2NH$(solid)	40	21.5	Et_2NSiF_3	10*
2	$SiF_4.2Et_2NH$(liq.)	110-120	4.5	Et_2NSiF_3	100*
3	$SiF_4.2Et_2NH$(gas)	175-190	7.5	...	0
4	$SiF_4.2n\text{-}Pr_2NH$(solid)	100	3	$n\text{-}Pr_2NSiF_3$	100*
5	$SiF_4.2n\text{-}Bu_2NH$(solid)	120	3.5	$n\text{-}Bu_2NSiF_3$	100*
6	$SiF_4.2C_4H_8NH$(liq.)	145	6	$C_4H_8NSiF_3$	~1*
7	$SiF_4.2C_5H_{10}NH$(solid)	120	8	$C_5H_{10}NSiF_3$	traces
8	$SiF_4.2C_5H_{10}NH$(liq.)	175-185	3.8	$C_5H_{10}NSiF_3$	16*
9	$SiF_4.2EtNH_2$(solid)	190-200	8	...	0
10	$SiF_4.2n\text{-}PrNH_2$(solid)	200	8.2	$n\text{-}PrN(SiF_3)_2$	1**
11	$SiF_4.2n\text{-}PrNH_2$(gas)	190-290	10	...	0
12	$SiF_4.2n\text{-}BuNH_2$(solid)	190-200	8.2	$n\text{-}BuN(SiF_3)_2$	2**
13	$SiF_4.2iso\text{-}BuNH_2$(solid)	190-200	8	$iso\text{-}BuN(SiF_3)_2$	10**
14	$SiF_4.2iso\text{-}BuNH_2$(liq.)	220-240	24	$iso\text{-}BuN(SiF_3)_2$	25**
15	$SiF_4.2t\text{-}BuNH_2$(solid)	190-200	8	$t\text{-}BuNHSiF_3$	60***
16	$SiF_4.2t\text{-}BuNH_2$(liq.)	220-240	24	$t\text{-}BuNHSiF_3$	86***

*Yield calculated by Eqn. (17);
**yield obtained from the conversion of the amine;
***yield calculated by Eqn. (19).

According to a patent [85], the thermal transformations of the adduct $SiF_4.2NH_3$ are particularly far-reaching, so that silicon–nitrogen films are deposited as a result of the pyrolytic decomposition of this compound. On the other hand, tensimetric measurements have shown [22] that the

†These results have been described in detail in a paper [126] published after the present review had been prepared for the press.

adducts of ammonia, methylamine, dimethylamine, trimethylamine, and pyridine dissociate almost completely into the initial reactants on heating:

$$SiF_4.2Am(solid) \rightleftharpoons SiF_4(gas) + 2Am(gas). \quad (20)$$

The diethylamine adduct melts initially and then decomposes via the mechanism

$$SiF_4.2Et_2NH(liq.) \rightleftharpoons SiF_4(gas) + 2Et_2NH(gas). \quad (21)$$

The adducts of high-boiling amines, for example of triethylamine and diethylmethylamine, decompose on heating via a somewhat different mechanism:

$$SiF_4.2Am(solid) \rightleftharpoons SiF_4(gas) + 2Am(liq.), \quad (22)$$

The last mechanism was proposed previously by the present author to describe the thermal reactions of the isomeric phenylenediamine complexes of silicon tetrafluoride [41] and was subsequently proved [68] for a number of adducts of aromatic amines with the composition $SiF_4.2Am$ (Am = *p*-nitroaniline, diphenylamine, *p*-aminobenzoic acid, *m*-aminophenol, and *N*-ethylaniline). It was reported in the same communication that the adducts of aniline, *p*-phenetidine, *p*-toluidine, *p*-chloroaniline, and *p*-anisidine dissociate on heating in accordance with reaction (20). When the adduct is heated, the amine passes to the gas phase together with silicon tetrafluoride and then interacts with the latter, reforming the adduct at lower temperatures; the adduct is deposited on the less heated components of the sublimation tube, so that the overall process resembles sublimation. In general, although the thermal reactions of silicon tetrafluoride adducts have been clearly inadequately investigated, the sum total of the results quoted permits the conclusion that the pathways and extent of these reactions are determined primarily by the structure of the initial amine.

The basicity and the structure of the initial amine are the controlling factors also in the reactions of silicon tetrafluoride adducts with alcohols and phenols. According to patent data [86], when the ammonia adduct is heated in alcohols, complete alcoholysis of silicon tetrafluoride takes place with formation of a fully substituted orthosilicic acid ester and ammonium hexafluorosilicate:

$$3SiF_4 + 4NH_3 + 4ROH \rightarrow Si(OR)_4 + 2(NH_4)_2SiF_6. \quad (23)$$

The esters of n-propyl, isopropyl, n-butyl, isobutyl, and pentyl alcohols were later obtained in the same way [87], but the possibility of employing aniline and pyridine in reaction (23) suggested in the patent quoted above was not subsequently confirmed. As mentioned previously, aniline and its substituted derivatives form 1 : 2 adducts in alcoholic solutions [52]. Silicon tetrafluoride does not undergo alcoholysis in the presence of pyridine either, although the adducts of tertiary aliphatic amines do react with alcohols and phenols in accordance with Eqns. (24) and (25):[40]

$$5SiF_4 + 4R_3N + 4ROH \rightleftarrows Si(OR)_4 + 4R_3NH^+SiF_5^-, \quad (24)$$

$$\frac{5m+1}{m+1}SiF_4 + 4R_3N + 4ROH \rightleftarrows Si(OR)_4 + \frac{4}{m+1}(R_3NH^+)_{m+1}Si_mF_{5m+1}^{-(m+1)}. \quad (25)$$

When triethylamine and ethyldi-isopropylamine are employed, the reaction proceeds with formation of pentafluorosilicic acid salts [Eqn. (24)] and in the case of triethylamine the products are salts containing the anion $Si_2F_{11}^{3-}$ [Eqn. (25)], which had not been described previously.

Dehydrofluorination is not the only method for the conversion of silicon tetrafluoride adducts into fluorine-containing compounds with a covalent silicon–nitrogen bond.

In contrast to silicon tetrafluoride, its adducts react with disilazanes and cyclosilazanes, forming the corresponding fluorosilazanes. This property of the silicon tetrafluoride adduct was established for the first time by Wannagat and Bürger [88], who obtained difluorobis(trimethylsilylamino)silazane on heating to 100°C a suspension of the adduct $SiF_4.2NH_3$ in hexamethyldisilazane:

$$SiF_4 \cdot 2NH_3 + 2(Me_3Si)_2NH \rightarrow (Me_3SiNH)_2SiF_2 + 2Me_3SiF + 2NH_3. \quad (26)$$

The adducts $SiF_4.2MeNH_2$, $SiF_4.2N_2H_4$, and $SiF_4.2C_5H_5N$ react similarly with hexamethyldisilazane, forming a mixture of fluorosilylamines of the type $(Me_3SiNH)_nSiF_{4-n}$, where $n = 1-3$.[18] Special mention should be made of the fact that, although pyridine does not in fact contain reactive hydrogen atoms, its adduct reacts with hexamethyldisilazane via the mechanism

$$SiF_4 \cdot 2C_5H_5N + n(Me_3Si)_2NH \rightarrow (Me_3SiNH)_nSiF_{4-n} + n\,Me_3SiF + 2C_5H_5N. \quad (27)$$

In this case the main product is difluorobis(trimethylsilylamino)silane ($n = 2$) and also small amounts of trifluorotrimethylsilylaminosilane and fluorotris(trimethylsilylamino)silane ($n = 3$). On heating to 120°C, the ammonia adduct reacts also with cyclosilazanes to form fluorosilazanes of the type $FMeSi(NHSiMe_2)_nF$ ($n = 1$, 2, or 3) among which an *SiSi*-difluoropolysilazane $(-F_2SiNH-)_x$ was isolated.

IV. STEREOCHEMISTRY

It has been noted above that monodentate ligands usually form 1 : 2 adducts with silicon tetrafluoride. Presumably the silicon atom passes to the sp^3d^2 hybridised state as a result of the acceptance of two electrons from the electron-donating atoms (for 1 : 1 adducts, the corresponding transition to the sp^3d hybridised state is postulated), i.e. silicon behaves similarly to transition elements. This explanation was put forward for the first time by Piper and Rochow [54], who found that the infrared spectra of the adducts $SiF_4.2NH_3$ and $SiF_4.2Me_2NCHO$ show very intense broad absorption bands with a maximum in the region of 750 cm^{-1}, which were identified as the ν(Si–F) bands of the hexacoordinate silicon atom. The authors [54] reached this conclusion on the basis of the comparison of the absorption bands corresponding to the stretching vibrations of the Si–F bonds in the ifrared spectra of gaseous SiF_4 and the octahedral SiF_6^{2-} anion. In the first case [89] these bands are observed at 1031 and 800 cm^{-1} whereas ν(Si–F) for the hexafluorosilicate ion is usually [90] in the region of 740 cm^{-1}. Subsequent studies showed that the intense absorption in the region of 740 cm^{-1} is characteristic also of other silicon tetrafluoride adducts. On this basis, it has been concluded [2,14,17,21,23,35,60,91] that the compounds investigated have an octahedral structure.

The octahedral structure has now been adopted for hexacoordinate silicon tetrafluoride compounds, but the problem of the relative positions of the ligands in the adduct molecules still remain controversial. From the examination of the octahedral model alone, different stereoisomeric distributions of the ligands are clearly possible (Fig. 1).

Beattie et al. [92] employed the infrared spectroscopic method to solve the problem of the ligand positions. They found by a [normal] coordinate analysis of the vibrations of the *cis*- and *trans*-models of the molecules of adducts of the type $SiF_4.2R$ that the infrared spectrum of the *cis*-form must be more complex: neglecting the possible band splittings, one may expect the presence in the infrared spectrum of three active high-frequency vibrations, while

only one vibration should be active in this region for the highly symmetrical *trans*-form.

Continuing these investigations, Beattie and Webster[30] identified by comparative analysis the absorption bands in the infrared spectra of the adducts $SiF_4.2Py$ and $SiF_4.2Ph_3PO$ and, on the basis of the number of these bands, concluded that both compounds obtained have the *trans*-octahedral structure. Subsequently the configurations of a number of other adducts, which are listed in Table 2, were determined similarly.

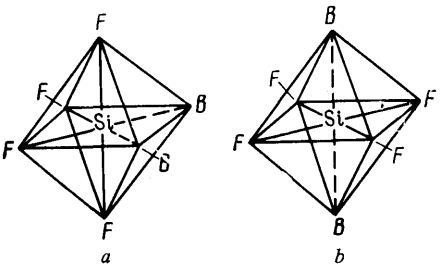


Figure 1. Configuration of hexacoordinate silicon tetrafluoride compounds: *a*) *cis*-octahedron (C_S); *b*) *trans*-octahedron (C_{2v}).

Comparative analysis of the data in Table 2 shows that the probabilities of the formation of the *cis*- and *trans*-configurations of the hexacoordinate silicon tetrafluoride compounds are almost the same. However, one must stipulate that these stereochemical differences have not so far been explained and given a theoretical interpretation.

Table 2. The results of infrared spectroscopic studies of the configurations of octahedral adducts of the type $SiF_4.2R$.

Compound	Configuration	References	Compound	Configuration	References
$SiF_4.2NH_3$	*cis*	17*, 23	$SiF_4.2N_2H_4$	*cis*	17, 23
$SiF_4.2ND_3$	*cis*	17	$SiF_4.2C_5H_5N$	*trans*	30, 93
$SiF_4.2MeNH_2$	*cis*	11, 17	$SiF_4.2Me_2NCHO$	*cis*	53
$SiF_4.2Me_2NH$	*cis*	11	$SiF_4.2Ph_3PO$	*trans*	30
$SiF_4.2Me_3N$	*trans*	15	$SiF_4.2Me_2SO$	*trans*	94
$SiF_4.2Me_3P$	*trans*	15			

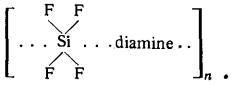
*The authors[17] also investigated the wide-band ^{19}F NMR spectrum of this adduct.

The attempt to estimate theoretically the relative stabilities of the *cis*- and *trans*-isomers of the adducts $SiF_4.2Py$ and $SiCl_4.2Py$ by an approximate parametric calculation of the energies of the $p\pi-d\pi$ bonds with additional ligands was understandably greeted with much interest. Rami and Hensen[95] examined two models in which the pyridine ligand is involved via two or one atomic p orbitals of the π type (apart from the atomic σ orbitals forming σ-bonds with the silicon atom), but they were nevertheless unable to predict the stereochemistry of the adducts investigated and noted that the choice of configuration may be determined by other causes. Moreover, as has been pointed out correctly[20,23,93], one cannot solve unambiguously the problem of the configuration of the adduct on the basis of infrared spectroscopic data alone. Even the identification of the absorption bands corresponding to $\nu(Si-F)$ is usually difficult owing to the strong absorption by the ligands and the frequency shift due to the degeneracy of the vibrations[20,30]. Moreover, gaseous silicon tetrafluoride reacts with NaCl glasses, as a result of which the intensity of the band in the region of the $\nu(Si-F)$ absorption is appreciably enhanced[96]. Analogous difficulties arise also in the analysis of the infrared spectra of other coordination compounds of this type[97].

An X-ray diffraction study has been made so far only of one adduct ($SiF_4.2Py$), the structure of which was determined with the aid of the refined three-dimensional Patterson method and three-dimensional Fourier syntheses[98]. It was shown that the configuration of this adduct is centrosymmetric and *trans*-octahedral, of the type proposed previously[30,93] on the basis of infrared spectroscopic data. Analogous *trans*-octahedral configurations have also been demonstrated for the adducts $SiCl_4.2Py$,[99] $GeCl_4.2Py$,[100] $SnCl_4.2Py$, $SnBr_4.2Py$, $SeCl_4.2Py$, and $TeCl_4.2Py$.[101]

In the case of the diamine adducts reliable data are available only for the silicon tetrafluoride compound with 2,2′-bipyridyl. The ^{19}F NMR spectrum of the adduct $SiF_4.C_{10}H_8N_2$ dissolved in chloroacetonitrile shows at room temperature two equal-intensity triplets, which enabled the authors[37] to conclude that the compound has the *cis*-configuration. A little later the validity of this conclusion was confirmed by X-ray diffraction analysis, which showed that the molecules of the $SiF_4.C_{10}H_8N_2$ adduct are monomeric with a *cis*-disposition of the bipyridyl nitrogen atoms. The Si–N distances are 1.982 and 1.972 Å and the Si–F distances are longer by 0.025 Å for the axial fluorine atoms than for the equatorial atoms. The adducts of 2,2′-bipyridyl with germanium and tin tetrafluorides have an analogous structure[38].

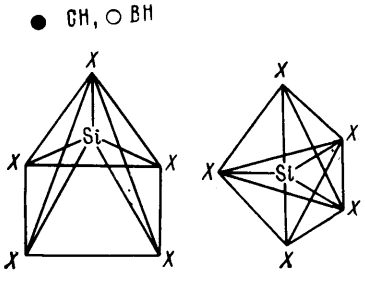
Judging from the infrared spectroscopic data, the adducts of silicon tetrafluoride with 1,10-phenanthroline[30] and ethylenediamine[23] also have the *cis*-configuration. Aggarwal and Onyszchuk[23] noted that additional evidence in support of the *cis*-configuration is provided by the fact that the ethylenediamine molecule is too small to span two coordination sites in the *trans*-configuration. Earlier Gutmann et al.[21] attributed a "polymeric" structure of the following type to the 1 : 1 adducts of diamines:



These workers also assumed the octahedral configuration of the silicon atom but they quote no additional considerations in its support. This structure was later proposed for the isomeric silicon tetrafluoride adducts with phenylenediamine on the basis of a comparison of their thermal stabilities[41]. Evidently the problem of the type of coordination of the primary diamine adducts could be solved successfully with the aid of infrared spectroscopy, but unfortunately such studies have not yet been made.

There is much less information in the literature about the structures of the 1 : 1 adducts formed by silicon tetrafluoride with monodentate ligands. As mentioned above, sp^2d hybridisation has been attributed to the silicon atom in such compounds as a result of the involvement of one of its vacant $3d$ orbitals. Linnett and Mellish[102] showed that

the most probable locations of electrons with identical spins in the $sp^3d_{z^2}$ configuration are the corners of a trigonal bipyramid. The most probable locations for the $sp^3d_{x^2-y^2}$ configuration are provided by a tetragonal bipyramid in which the four electrons located in the base are not coplanar with the central nucleus, forming an angle of approximately 105° with the nucleus and with the electron located at the vertex. The trigonal bipyramidal (D_{3h}) and tetragonal pyramidal (C_{4v}) models for a molecule of the type SiX_5 are presented in Fig. 2.


● CH, ○ BH
X
Si
X
X
X

where ΔH_1 is the enthalpy of formation of the solid adduct, ΔH_2 the enthalpy of desolvation of the ligand, ΔH_4 the crystal lattice energy determined by the dipole–dipole interaction and intramolecular hydrogen bonds, and ΔH_3 the enthalpy of formation of the adduct in the gaseous phase determined by the energy of the Si ← N donor–acceptor bond and intermolecular hydrogen bonds, if the latter exist.

Bearing in mind that the adducts investigated dissociate fully in the gas phase, Aylett et al.[22] concluded that $\Delta H_3 \ll \Delta H_4$ and that ΔH_4 is determined by the energy of the hydrogen bonds, the existence of which in the adducts of ammonia, hydrazine[17], methylamine[22], and primary aromatic amines[91] has been established by infrared spectroscopy. This conclusion agrees well with the finding that the values of ΔH^0 for the solid adducts of ammonia and primary and secondary amines differ little from one another but are appreciably higher than for tertiary amines (Table 5), although the electron-donating properties of pyridine resemble those of primary amines. The anomalous behaviour of pyridine can be readily explained on Mulliken's hypothesis[114] that the pyridine molecule can function not only as an n-donor but also as a π-donor, although the donor–acceptor bond in the adduct is formed via the nitrogen atom.

Unfortunately there are no methods so far for a direct measurement of ΔH_4. Therefore it is usually assumed that it varies little in a series of adducts with the same structures and similar molecular weights[115]. On the basis of these postulates and taking into account the results of earlier studies[32,109,111], Vandrish and Onyszchuk[110] estimated the relative electron-accepting capacities in the series of silicon and germanium tetrahalides investigated, with respect to pyridine and isoquinoline. They found that, as in the reaction with trimethylamine[108], $GeF_4 > SiF_4$, but were unable to reach any conclusions about the variation of the electron-accepting capacity in the series of silicon tetrahalides.

In view of the fundamental importance of this problem, the question of the reliability of the data merits consideration. Gur'yanov et al.[116] recently made a critical assessment of the methods described in the literature for the determination of the enthalpies of formation ΔH^0_{gas} of donor–acceptor compounds in the gas phase from the experimental heat change with the aid of a thermodynamic cycle. They noted that the hypothesis of the similarity of the crystal lattice energies is not always valid, because of difference between the enthalpies of sublimation in a series of similar compounds may be significant and comparable to ΔH^0_{gas} for these compounds[117]. Therefore, in using the heats of formation of the solid adducts as a measure of their relative stabilities, which has been done in a number of studies[109-111,113,118], very great caution must be exercised.

We believe that the attempt by Hensen and Sarholz[119] to estimate the relative electron-accepting capacities of silicon tetrahalides with respect to pyridine on the basis of the shift of the π–π^* transition band in the ultraviolet spectra of free and coordinated pyridine is even more controversial. These workers measured the ultraviolet absorption spectra of suspensions of many adducts in Nujol and found the halides can be arranged in the following sequence in terms of their electron-accepting capacity: $SiF_4 \simeq BF_3 < SiHCl_3 < GeCl_4 < SiCl_4 < SiBr_4$. On the basis of analogous measurements, the authors[39] later reported that the electron-accepting capacity with respect to 4,4′-bipyridyl decreases in the sequence $BF_3 < SiF_4 < SiBr_4$. It is noteworthy that Hensen and Sarholz's data[119] agree well with the conclusions of Wannagat et al.[111], but are in conflict with the results of later thermochemical measurements by Vandrish and Onyszchuk[110]. The latter workers also noted that a relation between the shifts in the ultraviolet spectra, the π-bonding effect, and the enthalpies of dissociation of adducts of the type $SiX_4.2Py$, formed mainly via σ bonds, has not so far been established, so that the earlier conclusions[39,119] require additional confirmation.

As mentioned above, the silicon tetrafluoride adducts with nitrogen-containing donors are much more stable than those with oxygen-containing donors (cf. Tables 5 and 6).

Table 6. Heats of dissociation of the adducts via the reaction $SiF_4.2ether(solid) \rightleftharpoons SiF_4(gas) + 2ether(gas)$ [58].

Adduct	$\Delta H°$, kcal mole^{-1}	Adduct	$\Delta H°$, kcal mole^{-1}
$SiF_4 \cdot 2(CH_2)_2O$	10.7±0.2	$SiF_4 \cdot 2(CH_2)_5O$	10.9±0.3
$SiF_4 \cdot 2(CH_2)_3O$	13.6±0.1	$SiF_4 \cdot 2Me_2O$	9.0±0.1
$SiF_4 \cdot 2(CH_2)_4O$	11.7±0.1		

Unfortunately in this case too the crystal lattice energies are unknown and the differences between the enthalpies of dissociation are too small to reach final conclusions about the relative electron-donating capacities of the ethers investigated. The most stable of the compounds listed, $SiF_4.2(CH_2)_3O$, does not decompose up to 13.6°C, while the remaining adducts exist only below 0°C.

It is noteworthy that BF_3 and GeF_4 form more stable adducts with ethers than does silicon tetrafluoride. Thus the compounds $GeF_4.2R$ (R = methyl ether, tetrahydropyran, or tetrahydrofuran) remain solid at 25°C, although in the case of epoxy-ethane the adduct decomposes at temperatures above −78°C.[57] The boron trifluoride compounds with Me_2O, $(CH_2)_4O$, and $(CH_2)_5O$ are stable liquids at 25°C, the first two distilling without decomposition[120]. The differences between the electron-accepting capacities of the above fluorides are shown particularly clearly with respect to 1,4-dioxane. Although silicon tetrafluoride does not react with the latter even at −94°C, GeF_4 forms with it a 1 : 1 adduct, which sublimes at 125°C and BF_3 forms 1 : 1 and 1 : 2 adducts, the first of which is a white powder at 25°C and the second a colourless liquid[58]. On the basis of a comparison of the behaviour of SiF_4 and GeF_4 with respect to oxygen-containing donors, Aggarwal and Onyszchuk[121] concluded that germanium tetrafluoride is a more powerful electron acceptor than silicon tetrafluoride. This can be explained by the decrease of $p\pi$–$d\pi$ binding on passing from silicon tetrafluoride to germanium tetrafluoride.

Interesting conclusions concerning the variation of electron accepting capacity in the series of silicon tetrahalides were arrived at on the basis of measurements of the vapour pressures of the adducts of SiF_4, $SiCl_4$, and $SiBr_4$ with trimethylamine and trimethylphosphine. Assuming that of two adducts which have similar structures and molecular weights, the thermodynamically more stable adduct has a lower vapour pressure, Beattie and Ozin[63] obtained the following sequences: $SiF_4 \ll SiCl_4$, $SiBr_4$ with respect to trimethylphosphine, $SiF_4 > SiCl_4 > SiBr_4$ with respect to trimethylamine, and $Me_3P \gg Me_3N$ with respect to $SiCl_4$ and $SiBr_4$. Beattie and Ozin[63]

examined the influence of steric factors, the possibility of the formation of bonds not involving the *d* orbitals, and the differences between the rearrangement energies of silicon tetrafluoride and other silicon tetrahalides, but they were still unable to show which of these factors determined the relative electron-accepting capacities with respect to each of the ligands indicated.

Silicon is a typical element of the class of "hard" acids, for which N ≫ P > As > Sb. At the same time the "hardness" of an acid is a function of the oxidation state of the central atom and depends to an equal extent on the nature of the groups linked to this atom [122]. Evidently the anomalous sequence of changes in the stability of the silicon tetrahalide adducts described above is determined by the differences between the electron-accepting capacities of the silicon atom in silicon tetrafluoride and other silicon tetrahalides ($SiCl_4$ and $SiBr_4$), which makes the study of the electron-accepting capacity of silicon tetrafluoride particularly interesting.

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The review has shown that the individual aspects of the chemistry of silicon tetrafluori have now been investigated in fair detail. This applies primarily to problems of the stoichiometry and thermal transformations of adducts with nitrogen-containing donors. The interaction of silicon tetrafluoride with oxygen-containing donors has been less thoroughly studied, although there are literature data concerning the high catalytic activity of silicon tetrafluoride in the esterification of carboxylic acids [55,123,124] and in the polymerisation of epoxides [56,125]. There are few data on the reactions of silicon tetrafluoride with other donors, for example phosphorus- and sulphur-containing donors, and also with complex ligands, which hinders a comparative assessment of the electron-accepting capacities of silicon tetrafluoride and other silicon tetrahalides. The lack of thermodynamic quantities characterising directly the strength of the Si ← N, Si ← P, etc. coordinate bonds is particularly serious, which precludes any quantitative assessment of the electron-accepting capacity of silicon tetrafluoride. On the whole, we believe that, together with thermodynamic studies, the investigation of the structures of the 1 : 1 adducts of monoamines and diamines and also fo the reactions of the adducts with formation of fluorine-containing silicon–nitrogen compounds, which frequently exhibit enhanced thermal and hydrolytic stabilities [72,88], is especially interesting at the present stage.

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Metallocarboranes

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A systematic account is given of the literature data on metallocarboranes. Particular attention is devoted to methods of their synthesis and their structures. The characteristic differences between metallocarboranes with π-linked carboranyl ligands and their π-cyclopentadienyl analogues are considered.
The bibliography includes 134 references.

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I. INTRODUCTION

A new field in the chemistry of organic derivatives of the elements arose recently and has been developing vigorously—the chemistry of polyhedral carboranes. One of the most interesting properties of compounds of this class is the ability of carboranes or products of their partial degradation to react with derivatives of transition or non-transition metals to form metallocarboranes containing metal atoms at one or several vertices of the molecule. As a rule, transition metals combine with the carborane fragment in π-type complexes, as happens in their classical cyclopentadienyl derivatives. The bond between non-transition metals and the carbon and boron atoms of the polyhedron is described in terms of many-centre bonds, the main principles of which have been described in Lipscomb's monograph[1] on boron hydrides. The vigorous development of the chemistry of metallocarboranes, particularly in recent years, led us to write the present review, since the reviews in the literature are obsolete[2-4] or deal with selected studies by individual groups of workers[5-8].

In the present review the data have been arranged systematically in terms of types of metallocarboranes. The dicarbollyl complexes of transition metals, the largest class of metallocarboranes, are discussed first. Problems associated with metallocarboranes based on π-mono- and π-hetero-carbollyl ligands isoelectronic with the π-dicarbollyl ligand are considered next. This is followed by an examination of metallocarboranes containing a transition metal (in the vast majority of cases cobalt) and π-linked ligands comprising lower carboranes. The next section deals with metallocarboranes obtained by the polyhedral expansion reaction. Metallocarboranes containing a non-transition metal in the polyhedral molecule are considered in the last section.

Particular attention has been devoted in this review to the methods of synthesis and the structures of metallocarboranes and their most interesting physicochemical characteristics are described. The review embraces all studies in 1965–1972 (and partly in 1973).

II. NOMENCLATURE

The nomenclature in the field of metallocarboranes constitutes a fairly complex problem in view of the wide variety of carborane systems behaving as ligands and the continuous appearance of new derivatives the names of which do not fit within the framework of the IUPAC rules[9]. Therefore, together with the adopted nomenclature, we shall employ the trivial nomenclature widely used in the literature, which greatly simplifies the discussion of the problem and is to a large extent consistent with the literature data. The advantage of this approach to the problem consists also in a considerable abbreviation of the names of the compounds under consideration. For example, instead of the IUPAC name "caesium 3,3′-*commo*-bis(nonahydro-1,2-dicarba-3-chroma-*closo*-dodecaborate) we shall call the compound $[(B_9C_2H_{11})_2Cr]^-Cs^+$, the "caesium salt of bis(dicarbollyl)chromium". We may note that in the IUPAC nomenclature the terms "*commo*" and "*closo*" denote a closed polyhedral system and the term "*nido*" denotes structures containing open planes or B–H–B bridging linkages. The presence of carbon atoms in the polyhedron is designated by the term "*carba*" and their number is given by the prefixes mono-, di-, etc. The number of boron atoms is designated respectively by monobora, dibora, etc. One of the most widely investigated ions employed as a π-ligand, $B_9C_2H_{11}^{2-}$, has been called "dicarbollide" and the isoelectronic ions $B_{10}CH_{11}^{3-}$, $B_9CPH_{10}^{2-}$, and $B_9CAsH_{10}^{2-}$ have been called "carbollide", "phosphacarbollide", and "arsacarbollide" respectively. The numerals before the π-ligand formula denote the position of the carbon atoms or those of carbon and an element (phosphorus, arsenic) in the carborane moiety. For example, the carbon atoms in 1,2-$B_9C_2H_{11}^{2-}$ are in the 1- and 2-positions of the dicarbollyl ligand and in 1,7-$B_9CPH_{10}^{2-}$ the carbon atom is in the 1-position and the phosphorus atom in the 7-position of the phosphacarbollyl ligand. The number in brackets before the name of the ligand denotes the position occupied by the metal in the polyhedron.

III. π-COMPLEXES BASED ON PRODUCTS OF PARTIAL DEGRADATION OF CARBORANES

1. Dicarbollyl Complexes of Transition Metals

Icosahedral carboranes $B_{10}H_{10}C_2H_2$ interact with nucleophilic agents such as alkali metal alkoxides[10-12] and amines[13,14]. This results in the removal of the boron atom from the 3-position in *o*- and *m*-carborane rings and in the formation

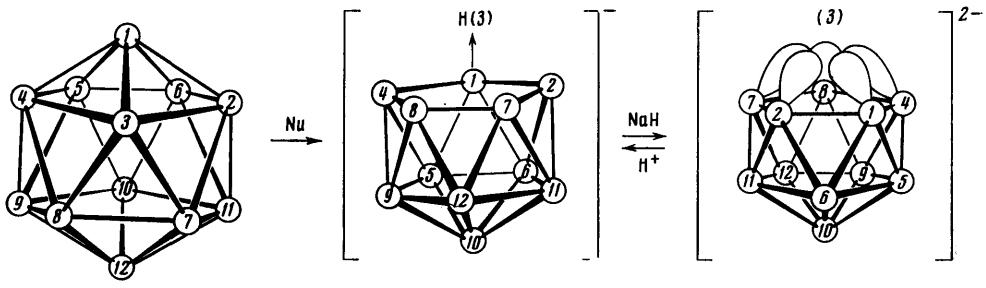


Figure 1.

of dicarbaundecaborate anions $B_9C_2H_{12}^-$. As shown for the first time by Hawthorne and coworkers[15,16], dicarbaundecaborate anions are acids which split off a proton on treatment with sodium hydride and give rise to the dicarbollide ion $B_9C_2H_{11}^{2-}$. The pK_a of the dicarbaundecaborate anion has been determined[17,18] and amounts to 21.3. Butyllithium has been used in some cases to generate the dicarbollide ion[19]. It has been shown that in a strongly alkaline medium there is an equilibrium between the dicarbaundecaborate and dicarbollide ions[16]; this has been used to obtain transition metal complexes in an aqueous medium. The (3)-1,2-$B_9C_2H_{11}^{2-}$ and (3)-1,7-$B_9C_2H_{11}^{2-}$ ions are isoelectronic with the hypothetical ion $B_{11}H_{11}^{4-}$. A structural scheme for the synthesis of dicarbollide ions is presented below (Fig. 1). Fig. 1 shows that the dicarbollide ion is a fragment of an icosahedron and consists of nine BH and two CH units. In the (3)-1,2-$B_9C_2H_{11}^{2-}$ ion the carbon atoms adjoin one another and in the (3)-1,7-$B_9C_2H_{11}^{2-}$ ion they are separated by a boron atom. According to the quantum-mechanical description of the dicarbollide ion[16], five atomic orbitals, largely sp^3-hybridised, are directed from the five atoms in the pentagonal B_3C_2 plane to the vacant position at the apex; six electrons are distributed in these orbitals. The combination of these atomic orbitals leads to one strongly bonding a_1-orbital, two degenerate bonding e_1-orbitals, and two strongly anti-bonding e_2-orbitals. Six electrons occupy the a_1- and both e_1-orbitals. In the reaction of the dicarbollide ion with transition metal salts dicarbollide complexes of the general type $(\pi\text{-}B_9C_2H_{11})_2M$ are formed. On the other hand, when the reaction is carried out in the presence of the cyclopentadienide ion, complexes of the type $[(\pi\text{-}C_5H_5)M\ (\pi\text{-}B_9C_2H_{11})]$ in some cases are formed. We shall examine the dicarbollyl complexes in terms of groups of transition metals.

A. The Iron Group

In the iron group (Fe, Ru, Os) the dicarbonyl complexes have been obtained for iron only. They were the first examples of metallocarboranes in which the transition metal is linked by a π-bond to the carborane moiety[15,20]. Hawthorn and coworkers[15,16] found that the 1,2-dicarbollide ion reacts with iron(II) chloride in tetrahydrofuran (THF) to form the bis(dicarbollyl)iron dianion $[(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Fe^{II}]^{2-}$ in which the iron atom is in the +2 formal oxidation state (FOS). This ion is readily oxidised by atmospheric oxygen to $[(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Fe^{III}]^-$ — an analogue of the ferrocinium ion. The structures of the dicarbollyliron complexes are presented in Fig. 2.

A detailed method for their synthesis in an aqueous medium has been published[21]. Iron(II) complexes are mainly obtained by the reduction of the corresponding iron(III) complexes with sodium amalgam:

$$1.2\text{-}B_9C_2H_{11}^{2-} + FeCl_3 \rightarrow [(\pi\text{-}1,\ 2\text{-}B_9C_2H_{11})_2Fe^{II}]^{2-} \underset{Na/Hg}{\overset{O_2}{\rightleftarrows}} [(\pi\text{-}1,\ 2\text{-}B_9C_2H_{11})_2Fe^{III}]^- .$$

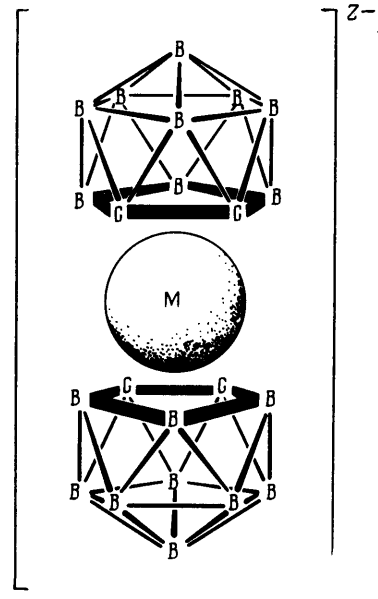


Figure 2.

Complexes based on *CC'*-dimethyl- and *C*-phenyl-1,2-dicarbollide ions have been obtained[16]. A method for the synthesis of dicarbollyliron complexes via the dithallium derivative of 1,2-dicarbollide was proposed recently[22]. The bis(dicarbollyl)iron(III) ion is resistant to the reaction of strong acids and alkalies and is thermally stable up to 300°C, but the corresponding *CC'*-dimethyl- and *C*-phenyl derivatives decompose in an aqueous alkaline solution on boiling via the mechanism

$$[(\pi\text{-}1,\ 2\text{-}B_9C_2H_9Me_2)_2Fe]^- + OH^- + 2H_2O \rightarrow 2\,[1,\ 2\text{-}B_9C_2H_{10}Me_2]^- + Fe(OH)_3.$$

Like ferrocene, the iron(II) complexes have the d^6 configuration and are diamagnetic, while the iron(III) complexes are paramagnetic. When a mixture of $C_5H_5^-$ and $1,2\text{-}B_9C_2H_{11}^{2-}$ ions was treated with iron(II) chloride in THF, low yields of π-cyclopentadienyl-π-dicarbollyliron complexes with the iron atom in the +2 or +3 formal oxidation state were obtained:

$$C_5H_5^- + 1,2\text{-}B_9C_2H_{11}^{2-} + FeCl_2 \rightarrow [(\pi\text{-}C_5H_5)\,Fe\,(1,2\text{-}B_9C_2H_{11})]^- \underset{Na/Hg}{\overset{[O]}{\rightleftarrows}} (\pi\text{-}C_5H_5)\,Fe\,(1,2\text{-}B_9C_2H_{11})\ .$$

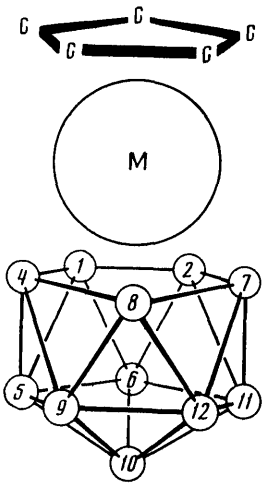


Figure 3.

A convenient method for the synthesis of the neutral complex $(\pi\text{-}C_5H_5)Fe(1,2\text{-}B_9C_2H_{11})$ in methanol with a yield in excess of 50% was proposed recently[23]. The structure of the π-cyclopentadienyl-π-dicarbollyliron(III) was determined[24] and the sandwich type of binding in this complex was confirmed (Fig. 3). It is interesting that the distances from the iron atom to the carbon atoms of the cyclopentadienyl ring and to the carbon and boron atoms in the pentagonal plane of the dicarbollyl ligand are the same, amounting to approximately 2.07 Å. The ESR spectra of all the dicarbollyliron(III) complexes showed the presence of an unpaired electron[25]. The experimental effective magnetic moments of the iron(III) complexes[26] were found to agree well with the values calculated theoretically[27]. Studies on the Mössbauer spectra of the complexes

$$[(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Fe^{III}]^-,\ (\pi\text{-}C_5H_5)\,Fe^{III}\pi\text{-}1,2\text{-}B_9C_2H_{11}]$$
$$[(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Fe^{II}]^{2-} \text{ and } [(\pi\text{-}C_5H_5)\,Fe^{II}\,(\pi\text{-}1,2\text{-}B_9C_2H_{11})]^-$$

showed[28,29] that their quadrupole splitting parameters are analogous to the values for the corresponding biscyclopentadienyl derivatives, although they are somewhat higher. The reason for this is the higher s-electron density at the iron atom in the dicarbollyl complexes than in the cyclopentadienyl complexes, which suggests a more effective withdrawal of d electrons through π-bonding from the metal in the former case.

In C-substituted derivatives the bis-(1,2-dicarbollyl)-iron(II)$^{2-}$ residue exhibits powerful electron-donating properties both via the inductive mechanism ($\sigma_I = -0.27 - -0.43$) and via the conjugative mechanism ($\sigma_R = -0.15 - -0.22$), the properties being more pronounced than those of the ferrocenyl group[30]. The ^1H and ^{11}B NMR spectra and the oxidation-reduction potentials of dicarbollyliron complexes have been published[16]. The latter are presented in Table 1.

The reduction potentials of π-(3)-1,2-dicarbollyliron(III) complexes in 50% aqueous acetone.

Compound	$E_{1/2}$ for $M^{III} + e^- \rightarrow M^{II}$, mV	Compound	$E_{1/2}$ for $M^{III} + e^- \rightarrow M^{II}$, mV
$Me_4N[(1,2\text{-}B_9C_2H_{11})_2Fe]$	−0.424	$Me_4N[(1,2\text{-}B_9C_2H_{10}Ph)_2Fe]$	−0.464
$Me_4N[(1,2\text{-}B_9C_2H_9Me_2)_2Fe]$	−0.538	$(C_5H_5)Fe(1,2\text{-}B_9C_2H_{11})$	−0.080

One should note the higher thermal stability and the higher resistance to the action of acids and bases of the dicarbollyliron complexes compared with their cyclopentadienyl analogues—ferrocene and the ferrocenium ion. In contrast to ferrocene, the dicarbollyliron(II) complexes are rapidly oxidised to iron(III) complexes, which are more stable in this case.

When the 1,2-dicarbollide ion was treated with an excess of iron pentacarbonyl, a dimeric carbonyl product with π-dicarbollyl ligands was obtained[31]:

$$1,2\text{-}B_9C_2H_{11}^{2-} + Fe(CO)_5 \xrightarrow[70^\circ]{THF} \{[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]_2Fe_2(CO)_4\}^{2-}\ .$$

In the solid state the complex in the form of the tetramethylammonium salt decomposes slowly in air, while in solution in acetone or acetonitrile the decomposition is rapid. The *trans*-structure proposed initially for the dimer[31] was not confirmed and it was shown that, like $[\pi\text{-}C_5H_5Fe(CO)_2]_2$, the μ-carbonylbis-[π(3)-1,2-dicarbollyl-iron] dianion has the *cis*-configuration[32].

The chemistry of dicarbollyliron complexes has been little investigated. It has been established that in a strongly acid medium (concentrated HCl, $HClO_4$–CH_3OH), the complex $[(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Fe^{II}]^{2-}$, which is an analogue of ferrocene, is protonated[33], but the ^1H NMR spectrum of $[(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Fe^{II}H]^{2-}$ in a high field does not show the hydrogen signal characteristic of the protonated form of ferrocene $(C_5H_5)_2FeH^+$. The appearance in the infrared spectrum of $[(1,2\text{-}B_9C_2H_{11})_2FeH]^-$ of a band at 1835 cm^{-1} can equally indicate both the presence of an Fe–H bond and of B–H–B bridging linkages. For this reason, the available data do not allow a choice between these two alternative schemes[33]. It has been shown that the protonated form of bis-(1,2-dicarbollyl)iron(II) reacts smoothly with dialkyl sulphides, the reaction being accompanied by the evolution of hydrogen and the formation of *B*-substituted products[33]:

$$R_2S + [HFe^{II}(1,2\text{-}B_9C_2H_{11})_2]^- \rightarrow H_2 + [Fe^{II}(1,2\text{-}B_9C_2H_{11})(1,2\text{-}B_9C_2H_{10}SR_2)]^-\ .$$

The latter are readily oxidised with formation of neutral stable paramagnetic iron(III) complexes. The reverse reduction process is also possible:

$$[Fe^{II}(1,2\text{-}B_9C_2H_{11})(1,2\text{-}B_9C_2H_{10}SR_2)]^- \underset{+e^-}{\overset{-e^-}{\rightleftarrows}} [Fe^{III}(1,2\text{-}B_9C_2H_{11})(1,2\text{-}B_9C_2H_{10}SR_2)]^0\ .$$

When hydrogen chloride was passed into a suspension of $[(1,2\text{-}B_9C_2H_{11})_2Fe^{III}]^-Cs^+$ in diethyl sulphide, a very low yield of the disubstituted complex $Fe^{II}(1,2\text{-}B_9C_2H_{10}SEt_2)_2$ was isolated together with the monosubstituted product. Chemical oxidation of the disubstituted complex led to the first example of cationic bis(dicarbollyl)metal complexes,

namely $[(1,2\text{-}B_9C_2H_{10}SEt_2)_2Fe^{III}]^+$.[33] The substitution mechanism at the boron atom of the dicarbollyl ligand is regarded as acid-catalysed nucleophilic substitution in which the proton removes the most hydridic hydrogen atom of the ligand with subsequent attack by the nucleophile at this position. The structure of the boron-substituted complexes, an example of which is presented in Fig. 4, was established on the basis of ^1H and ^{11}B NMR data.

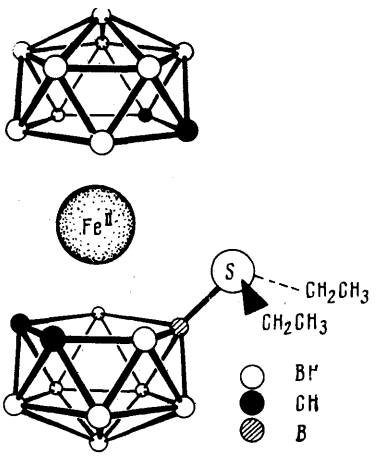


Figure 4.

When hydrogen chloride is passed into suspension of $[(1,2\text{-}B_9C_2H_{11})_2Fe^{III}]^-K^+$ in CS_2 in the presence of $AlCl_3$, a bridge-type dicarbollyl complex with an electron-deficient carbon atom is formed[34]:

$$[(1,2\text{-}B_9C_2H_{11})_2Fe]^- + CS_2 + H^+ \rightarrow \begin{matrix} 1,2\text{-}B_9C_2H_{10}S \\ Fe \\ 1,2\text{-}B_9C_2H_{10}S \end{matrix}\!\!>\!\!^{+}CH \ .$$

B. The Cobalt Group

In the cobalt group (Co, Rh, Ir) dicarbollyl complexes are known for cobalt only. The reaction of the 1,2-dicarbollide ion with cobalt chloride gives a high yield of the bis-(1,2-dicarbollyl)cobalt anion with the cobalt atom in the +3 formal oxidation state[16,35], the anion being an analogue of the cobalticinium ion:

$$2\,(3)\text{-}1,2\text{-}B_9C_2H_{11}^{2-} + 1,5\text{-}CoCl_3 \rightarrow \{[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]_2Co\}^- + 3Cl^- + 0.5Co^0 \ .$$

A complex with the ion (3)-1,7-$B_9C_2H_{11}^{2-}$ – $\{[\pi\text{-}(3)\text{-}1,7\text{-}B_9C_2H_{11}]_2CO\}^-$ was obtained analogously. When $CoCl_2$ interacts with a mixture of $C_5H_5^-$ and 1,2- or 1,7-$B_9C_2H_{11}^{2-}$ ions, neutral π-cyclopentadienyl-π-(3)-dicarbollylcobalt complexes are formed[16,35].

Improved methods for the synthesis of (π-C_5H_5)Co(π-1,2-$B_9C_2H_{11}$) complexes were proposed recently[23,36]. Dicarbollylcobalt complexes can be obtained via the dithallium dicarbollide[22]. X-Ray diffraction analysis of the caesium salt of bis-[(3)-1,7-dicarbollyl]cobalt(III)[37] confirmed that the structure presented in Fig. 2 is general. A series of π-cyclopentadienyl-π-C-substituted 1,2-dicarbollylcobalt complexes have been obtained[16,38], among which the greatest interest attaches to $(C_5H_5)Co^{III}[B_9C_2H_{10}\cdot(CH_2OH)]$. When CrO_3 was allowed to react with this complex, the *C*-formyl and *C*-carboxy-derivatives were synthesised[38]. The greater ease of the oxidation of the CH_2OH group to CHO compared with the oxidation of the latter to COOH is unusual in this case. The acid chloride was obtained from the acid; it enters into the Friedel–Crafts reaction with benzene in the presence of $AlCl_3$, giving a ketone:

$$(C_5H_5)Co[B_9C_2H_{10}(COCl)] + C_6H_6 \xrightarrow{AlCl_3} (C_5H_5)Co[B_9C_2H_{10}(COC_6H_5)] \ .$$

The pK_a for the acid $(C_5H_5)Co[B_9C_2H_{10}(COOH)]$ in 50% ethanol is 3.54.[38]

It is impossible to isolate dicarbollylcobalt(II) complexes. This suggests that the cobalt(II) complexes formed initially are rapidly oxidised by cobalt chloride with formation of very stable bis(dicarbollyl)cobalt(III) salts with the d^6 configuration. However, the existence of cobalt(II) complexes is supported by the oxidation-reduction potentials obtained by polarographic and cyclic volt-amperometric methods, which indicate the occurrence of one-electron reduction of bis(dicarbollyl)cobalt(III) and its *C*-substituted derivatives, i.e. the transition $d^6 \rightarrow d^7$ or $M^{III} + e^- \rightarrow M^{II}$.

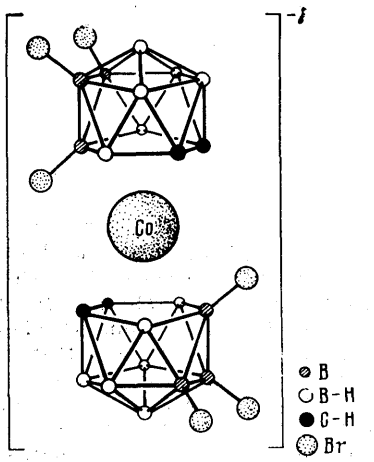


Figure 5.

In the case of an unsubstituted complex, the reversible one-electron M^{III} oxidation wave is observed at +1.57 mV, which led to the hypothesis that a dicarbollyl complex with a cobalt atom in the +4 formal oxidation state exists[16]. A careful electrochemical study of dicarbollylcobalt complexes led to the conclusion that the dicarbollyl ligand stabilises the metal in both the highest and the lowest oxidation states and for the complexes (π-C_5H_5)Co(π-1,2-$B_9C_2H_{11}$) and $[(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Co]^-$ the $M^{III} + e^- \rightarrow M^I$ transition is observed at –2.11 and –2.24 mV respectively together with $M^{III} + e^- \rightarrow M^{II}$.[39]

Bromination of the rubidium salt of $[(1,2\text{-}B_9C_2H_{11})_2Co]^-$ in acetic acid gave the hexabromo-derivative[16], where there are three halogen atoms in each π-ligand according to X-ray diffraction data[40] (Fig. 5). This compound is

interesting in the sense that its two one-electron reduction waves corresponding to the processes

$$Co^{III} + e^- \xrightarrow{-0.48\ mV} Co^{II} \text{ and } Co^{II} + e^- \xrightarrow{-1.48\ mV} Co^{I},$$

are displaced to the region of highly positive potentials and clearly confirm the possibility of the existence of π-bonded cobalt d^8-complexes[16].

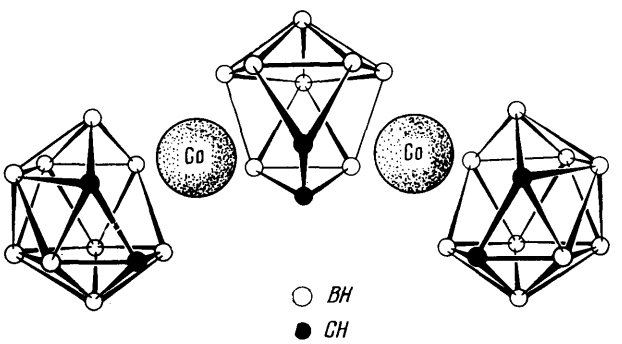
The 1,2-dicarbollide ion reacts with dicobalt octacarbonyl to form π-dicarbollyldicarbonylcobalt, which is readily oxidised[30]:

$$2(1,2\text{-}B_9C_2H_{11}^{2-}) + Co_2(CO)_8 \rightarrow 2\{[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]Co(CO)_3\}^- + 4CO.$$

In the synthesis of dicarbollyl complexes in a highly alkaline medium there is a possibility of further degradation of the dicarbollyl ligand in the complex with elimination of the BH unit. In this case the product is the bidentate π-bonding ligand $B_8C_2H_{10}^{4-}$, which has been called the (3,6)-1,2-dicarbanastide ion, whose interaction with an excess of the transition metal salt and the π-ligands leads to two- and three-metal derivatives. Thus in a highly alkaline medium $[(1,2\text{-}B_9C_2H_{11})_2Co]^-$ is converted by $CoCl_2$ and $1,2\text{-}B_9C_2H_{11}^{2-}$ ions into

$\{[(3)\text{-}1,2\text{-}B_9C_2H_{11}]Co[(3,6)\text{-}1,2\text{-}B_8C_2H_{10}]Co[(3)\text{-}1,2\text{-}B_9C_2H_{11}]\}^{2-}$ (Fig.6)

and $[\{[(3)\text{-}1,2\text{-}B_9C_2H_{11}]Co[(3,6)\text{-}1,2\text{-}B_8C_2H_{10}]\}_2Co]^{3-}$ (Fig.7) [41-44].



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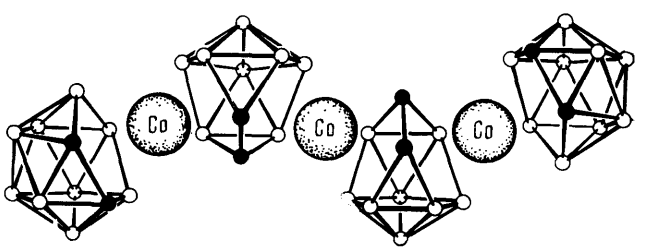

Figure 7.

$(C_5H_5)Co(1,2\text{-}B_9C_2H_{11})$ reacts with $CoCl_2$ and $C_5H_5^-$ in the presence of alcoholic alkali to form $[(C_5H_5)Co]_2[(3,6)\text{-}B_8C_2H_{10}]$ (Fig. 8) and $\{(C_5H_5)Co[(3,6)\text{-}1,2\text{-}B_8C_2H_{10}]\}_2Co$ (Fig. 9).[36] The ^{11}B NMR spectra of the $\eta[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]_2Co\}^-$ ion and of its *B*-deuteriated and *B*-halogenated derivatives have been recorded[45] at 70.6 MHz and the signals in the spectrum have been assigned to the corresponding boron atoms in the ligand. On the basis of the ^{59}Co NQR spectra of $Cs(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Co$, Harris[46] concluded that the π-dicarbollyl and π-cyclopentadienyl groups are almost indistinguishable as regards binding to Co^{III} and Fe^{II} and the boron atoms in the dicarbollyl ligand have an electron-donating capacity close to that of carbon atoms. However, subsequently this view was revised[28].

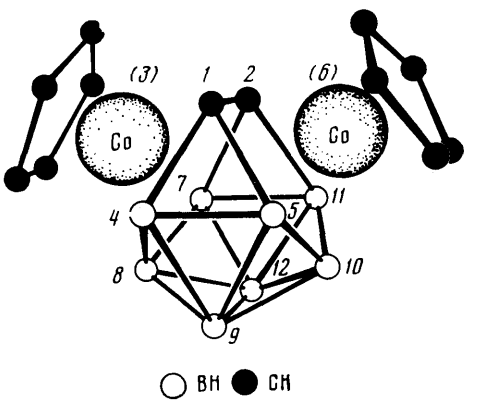

Figure 8.

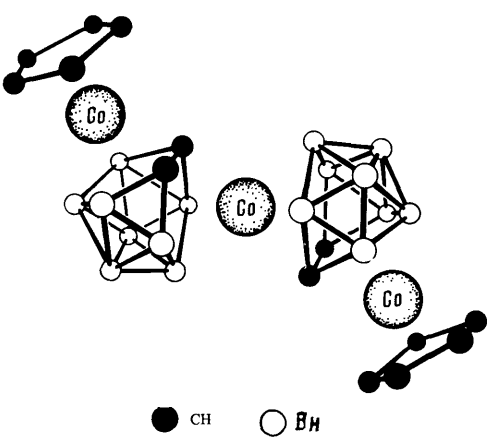

Figure 9.

As a substituent linked via the carbon atoms of the ligand, bis(dicarbollyl)cobalt is a weak electron acceptor via the inductive mechanism ($\sigma_i = -0.01 - 0.06$) and a moderately strong donor via the conjugative mechanism ($\sigma_R = -0.07 - -0.12$)[30]. The replacement of one dicarbollyl group by a cyclopentadienyl group increases the inductive electron-accepting capacity of the complex ($\sigma_i = 0.21$) but hardly alters the resonance electron-donating component ($\sigma_R - -0.10$). The ability of the bis(dicarbollyl) complex to enter into conjugation with π-substituents has been confirmed by the electronic spectra of bis-(*C*-alkenyldicarbollyl)cobalt[47].

In their attempts to alkylate bis(dicarbollyl)cobalt(III) under the conditions of the Friedel–Crafts reaction, Francis and Hawthorne[41,48] observed an interesting reaction involving the formation of a bridge-type derivative of the dicarbollyl complex with an electron-deficient carbon atom. When hydrogen chloride is passed into a suspension of bis(dicarbollyl)cobalt and $AlCl_3$ in CS_2, the –S–CH–S– bridge linked to the boron atoms of the ligands is formed between dicarbollyl ligands:

$$[(1,2\text{-}B_9C_2H_{11})_2Co]^- + CS_2 + H^+ \rightarrow \begin{matrix} 1,2\text{-}B_9C_2H_{10}S \\ Co^- \quad CH \\ 1,2\text{-}B_9C_2H_{10}S \end{matrix} \quad \text{(Fig. 10)}\ ^{49}$$

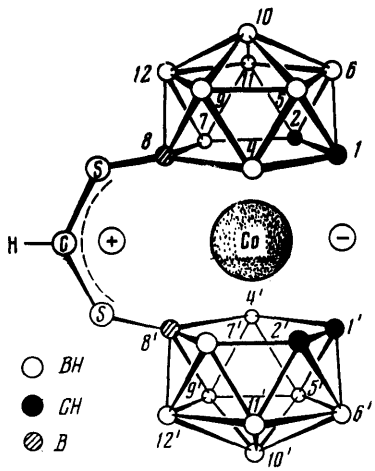

Figure 10.

The complex $(1,7\text{-}B_9C_2H_{10})_2CoS_2CH$ was obtained similarly from $\{[(3)\text{-}1,7\text{-}B_9C_2H_{11}]_2Co\}^-$. A bridge with an electron-deficient carbon atom is formed also in an acetic acid–acetic anhydride mixture in the presence of $HClO_4$ as a catalyst:

$$[(1,2\text{-}B_9C_2H_{11})_2Co]^- + MeCOOH \rightarrow (1,2\text{-}B_9C_2H_{11})Co(1,2\text{-}B_9C_2H_{10}OOCMe) \xrightarrow{H^+} \rightarrow (1,2\text{-}B_9C_2H_{10})_2CoO_2CMe\ .$$

The carbonium ionic centres in $(1,2\text{-}B_9C_2H_{10})_2CoS_2CH$ and $(1,2\text{-}B_9C_2H_{10})_2CoO_2CMe$ are relatively inactive with respect to protic solvents, probably owing to the proximity of the negative charges of the heteroatoms. A solution of $NaBH_4$ in ethanol reduces $(1,2\text{-}B_9C_2H_{10})CoS_2CH$ to $[(1,2\text{-}B_9C_2H_{10})_2CoS_2CH_2]^-$ in quantitative yield. Aqueous ethanol hydrolyses the bridge-type derivatives:

$$(1,2\text{-}B_9C_2H_{10})_2CoS_2CH \xrightarrow{EtOH,\ 70^\circ} \{[1,2\text{-}B_9C_2H_{10}(SH)]_2Co\}^-\ ,$$
$$(1,2\text{-}B_9C_2H_{10})_2CoO_2Me \xrightarrow{EtOH,\ 70^\circ} \{[1,2\text{-}B_9C_2H_{10}(OH)]_2Co\}^-\ .$$

Like bis(dicarbollyl)iron(II), bis(dicarbollyl)cobalt(III) enters into an acid-catalysed nucleophilic substitution reaction in diethyl sulphide, leading to a neutral product[33]:

$$[(1,2\text{-}B_9C_2H_{11})_2Co]^- + HCl + Et_2S \rightarrow Co(1,2\text{-}B_9C_2H_{11})[1,2\text{-}B_9C_2H_{10}SEt_2]\ .$$

When an aqueous solution of $K(1,2\text{-}B_9C_2H_{11})_2Co$ is treated with phenyldiazonium tetrafluoroborate, cation exchange and the formation of the phenyl diazonium salt of bis(dicarbollyl)cobalt$(PhN_2)^+[(1,2\text{-}B_9C_2H_{11})Co]^-$ are observed[50] instead of the expected formation of coupling or arylation products. At room temperature the salt is insoluble in benzene but on heating above 60°C it dissolves completely with liberation of a gas and the formation of biphenyl and a coupling product the structure of which is illustrated in Fig. 11. Decomposition of the phenyldiazonium salt in toluene and of the tolyldiazonium salt in benzene yielded coupling products containing the tolyl and phenyl groups respectively and methylbiphenyl, i.e. the aryl group from the diazonium cation does not enter into the composition of the complex. The reaction scheme in Fig. 12 was put forward on the basis of these products.

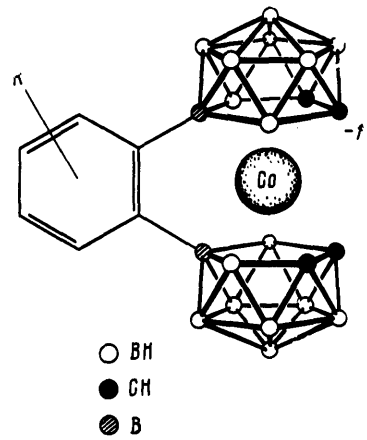

Figure 11.

The complexes $(\pi\text{-}C_5H_5)Co(\pi\text{-}1,2\text{-}B_9C_2H_{11})$ and $[(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Co]^-$ served as the starting materials for the synthesis of new metallocarboranes containing one and two boron atoms less than in the initial metallocarboranes[51,52]. The reaction has been called the "polyhedral contraction reaction". In general its equation is

$$[LCo(B_nC_2H_{n+3})]^z \xrightarrow[2.\ -2e^-]{1.\ -BH^{+}} [LCo(B_{n-1}C_2H_{n+1})]^g\ ,$$

where $z = 0$ for $L = C_5H_5^-$ and $z = -1$ for $L = (3)\text{-}1,2\text{-}B_9C_2H_{11}^{2-}$.

The base-catalysed degradation of the complexes with subsequent oxidation of the products by hydrogen peroxide gives rise to a new metallocarborane containing the π-(1)-2,4-$B_6C_2H_{10}^{2-}$ ion as one of the ligands (Fig. 13):

$$(\pi\text{-}C_5H_5)Co(\pi\text{-}1,2\text{-}B_9C_2H_{11}) \xrightarrow[2.\ H_2O_2]{1.\ OH^-} (\pi\text{-}C_5H_5)Co[\pi\text{-}(1)\text{-}2,4\text{-}B_6C_2H_{10}]\ ,$$
$$[(\pi\text{-}1,2\text{-}B_9C_2H_{11})_2Co]^- \xrightarrow[2.\ H_2O_2]{1.\ OH^-} \{[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]Co[\pi\text{-}(1)\text{-}2,4\text{-}B_6C_2H_{10}]\}^-\ .$$

The last complex forms with pyridine an inner salt having the composition $[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]Co[\pi\text{-}(1)\text{-}2,4\text{-}B_6C_2H_{10}\cdot C_5H_5N]$,[51] in which the 'onium nitrogen atom is linked to the boron atom of the π-(1)-2,4-$B_6C_2H_{10}$ ligand according to X-ray diffraction analysis[53,54]. Oxidation of complexes containing the (1)-2,4-$B_6C_2H_{10}$ ligand by iron(III) chloride in boiling ethanol results in their further degradation. In the case of the cyclopentadienyl-containing complex, a *nido*-metallocarborane is formed as the main product under these conditions. Like the neutral *nido*-carboranes $B_6C_2H_{12}$,[55–57] the *nido*-metallocarborane $(C_5H_5)Co(B_7C_2H_{11})$ slowly splits off hydrogen on heating to

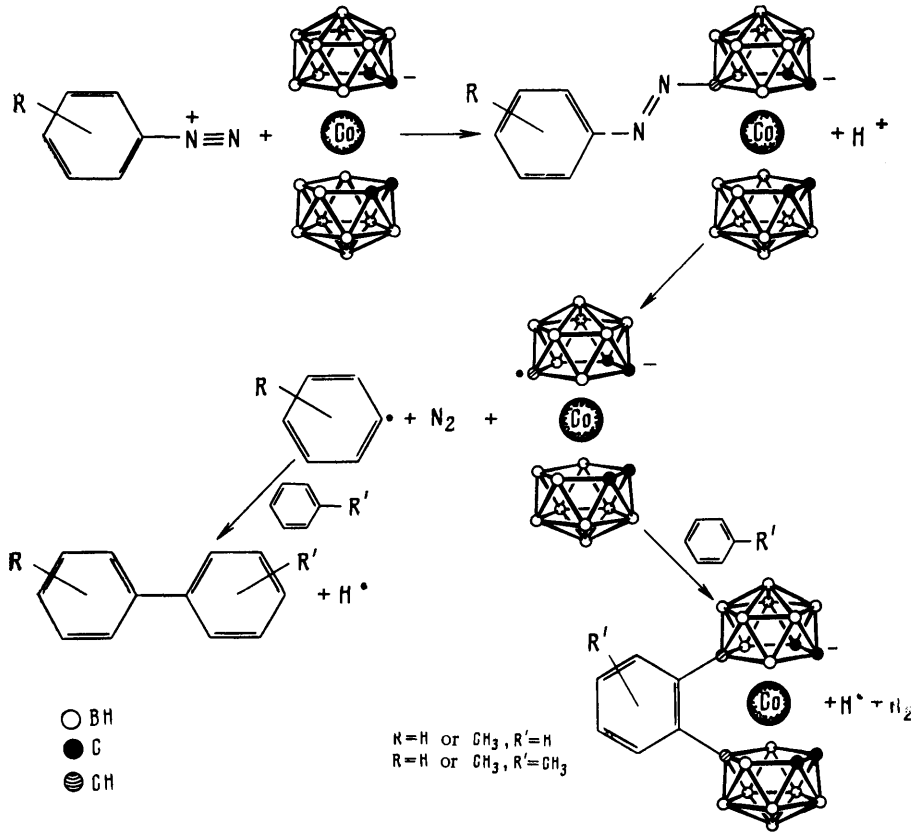

Figure 12.

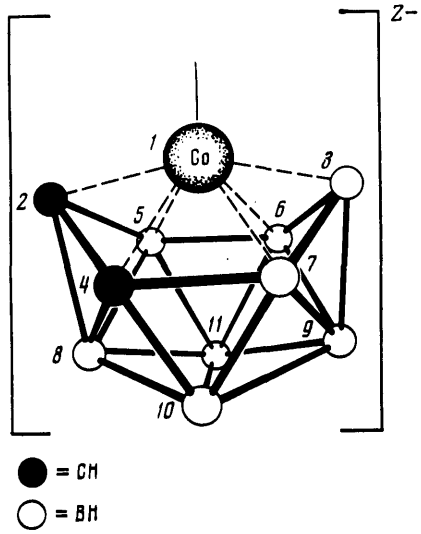

Figure 13.

70°C and is converted into a *closo*-metallocarborane with the π-(2)-6,7-$B_7C_2H_9$ ligand. However, at 70°C the π-(2)-6,7-$B_7C_2H_9$ ligand in the complex rearranges to π-(2)-1,6-$B_7C_2H_9$. Further rearrangement to the 1,10-isomer requires a temperature of 150°C.

The above sequence of reactions is illustrated schematically in Fig. 14. The complex $\{[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]Co.[\pi\text{-}(2)\text{-}1,6\text{-}B_7C_2H_9]\}^-$ was obtained similarly from $\{[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]Co[\pi\text{-}(1)\text{-}2,4\text{-}B_6C_2H_{10}]\}^-$ (Fig. 15).

An interesting property of π-cyclopentadienyl-π-(3)-1,2-dicarbollylcobalt and its *CC'*-dimethyl derivative is the ability to undergo a gas-phase rearrangement at 400–700°C with formation of isomeric complexes differing in the distribution of carbon atoms in the dicarbollyl ligand [58] (Fig. 16). In none of the isomers obtained do the carbon atoms in the ligand retain adjacent positions. Therefore the driving force of the rearrangement in the isomerisation of metallocarboranes as well as carboranes [4] is presumably the mutual repulsion of the carbon atoms, which are the most electropositive centres in the molecule.

C. The Nickel Group

In the nickel group (Ni, Pd, Pt) the dicarbollyl derivatives of all the metals are known. The paramagnetic complex $[(1,2\text{-}B_9C_2H_{11})_2Ni^{II}]^{2-}$ with the d^9 configuration, which is extremely readily oxidised to the nickel(III) complex with the d^7 configuration, was obtained by the reaction of the (3)-1,2-dicarbollide ion with nickel(II) salts in THF or in a highly alkaline medium [16,59]. Oxidation of the nickel(III) complex by iron(III) chloride leads to the neutral diamagnetic complex $(1,2\text{-}B_9C_2H_{11})_2Ni^{IV}$ with the d^6 configuration. Nickel complexes with the (3)-1,7-$B_9C_2H_{11}^{3-}$ ligand in which the nickel atom is in the +2, +3, and +4 formal oxidation states were obtained similarly [16].

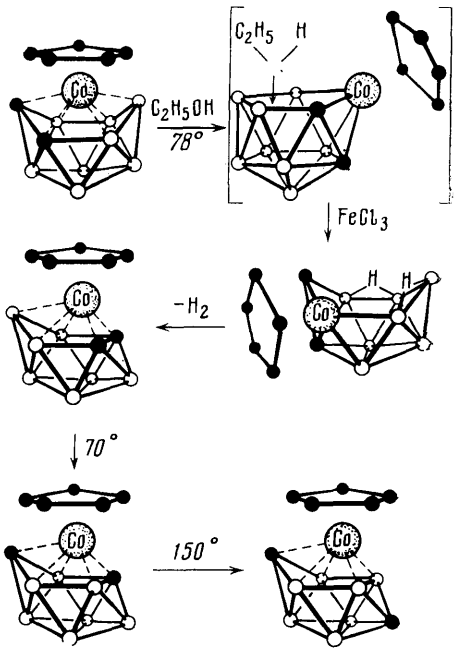

Figure 14.

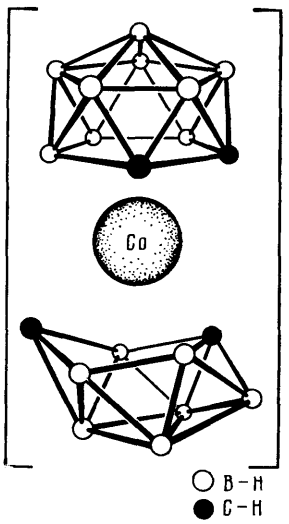

Figure 15.

Dicarbollylnickel complexes have characteristic structural features which depend on the formal oxidation state of the metal. The nickel(II) complexes have a distorted sandwich structure with the ligands displaced relative to one another in opposite directions (Fig. 17).[60] The nickel(III) complexes have the normal sandwich structure (Fig. 2), while a cisoid sandwich configuration, in which both carbon atoms of each ligand are located on the same side of the molecule, is characteristic of nickel(IV) (Fig. 18).[61] This gives rise to an appreciable dipole moment in $(1,2\text{-}B_9C_2H_{11})_2Ni^{IV}$, amounting, for example, to 6.16 D in cyclohexane. Owing to the high positive charge on the metal atom (+4), bis(dicarbollyl)nickel(IV) is a powerful-electron accepting substituent (σ_i = 0.50–0.65).[30] Complexes with *C*-methyl- and *C*-phenyl-1,2-dicarbollyl ligands have been obtained[62]. In this case enantiomers exist, so that three isomers are possible: the *meso*-isomer and the (±)-recemate. This was confirmed by the ^{19}F NMR spectra of *p*- and *m*-fluorophenyl-substituted nickel(IV) complexes, which contain two fluorine signals corresponding to the *meso*-form and the (±)-racemate.[30]

The complex $(1,2\text{-}B_9C_2H_{11})_2Ni^{IV}$ is readily reduced to $[(1,2\text{-}B_9C_2H_{11})_2Ni^{III}]^-$ by "hard" Lewis bases with some degradation of the complex[61]. An interesting property of

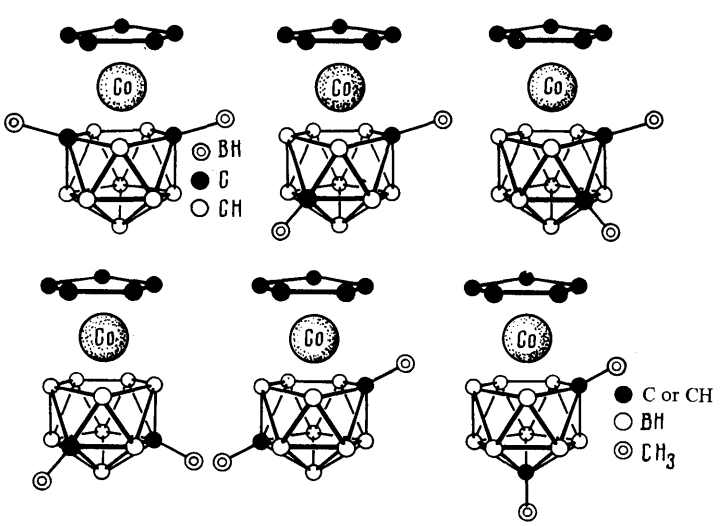

Figure 16.

$(1,2\text{-}B_9C_2H_{11})_2Ni^{IV}$ is the considerable acidity of the C–H bond in the dicarbollyl ligand, which was shown by the ease of deuterium exchange with D_2O in an alkaline medium, while in acid solutions (D_2SO_4 in DOAc) the deuterium exchange is slow and involves only the B–H bonds of the ligand. "Soft" Lewis bases, for example Cl^-, Br^-, and SCN^-, react with $(1,2\text{-}B_9C_2H_{11})_2Ni^{IV}$ to give 1 : 1 adducts, which can be isolated in a crystalline form. Similar adducts have been obtained with condensed aromatic hydrocarbons—pyrene naphthalene, and phenanthrene—and aromatic *n*-bases such as dimethylaniline [61].

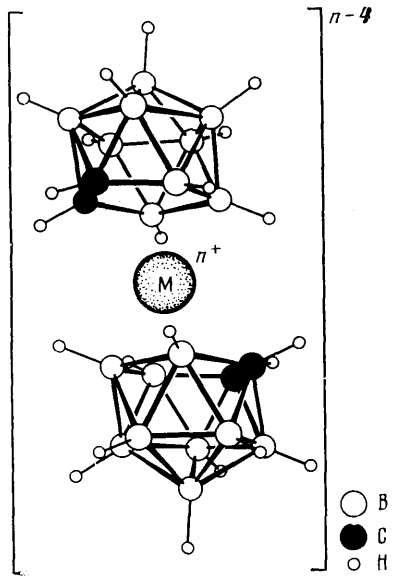

Figure 17.

Molecular rearrangements characteristic of metallocarboranes can be observed in *CC'*-disubstituted dicarbollylnickel complexes. There is a possibility of three isomeric series of compounds [62-64]: series A—compounds with adjacent carbon atoms on the binding surfaces of both ligands; series B—compounds with adjacent carbon atoms in both ligands but in one of the ligands one carbon atom is displaced to the interior of the ligand so that its binding plane contains four boron atoms and one carbon atom; series C—compounds with adjacent carbon atoms in both ligands and with (B_4C) binding surfaces. The conversions of series A compounds into series B and C compounds are irreversible. The reaction sequences and the electrochemical characteristics of the reactions of the bis-(*CC'*-dimethyldicarbollyl)nickel system are presented below:

$$Ni(acac)_2 + 2[(3)\text{-}1,2\text{-}B_9C_2H_9Me_2]^{2-}\dagger \rightarrow$$

Series A

$$\rightarrow [(Me_2Cb)_2Ni^{II}\text{—}A]^{2-} \underset{-0.55\,mV}{\rightleftharpoons} [(Me_2Cb)_2Ni^{III}\text{—}A]^- \xrightarrow[\downarrow 200^\circ]{[O]}$$

Series B

$$[(Me_2Cb)_2Ni^{II}\text{—}B]^{2-} \underset{-1.02\,mV}{\rightleftharpoons} [(Me_2Cb)_2Ni^{III}\text{—}B]^- \underset{+0.15\,mV}{\rightleftharpoons} [(Me_2Cb)_2Ni^{IV}\text{—}B]^0 \downarrow 100^\circ$$

Series C

$$[(Me_2Cb)_2Ni^{II}\text{—}C]^{2-} \underset{-1.19\,mV}{\rightleftharpoons} [(Me_2Cb)_2Ni^{III}\text{—}C]^- \underset{-0.10\,mV}{\rightleftharpoons} [(Me_2Cb)_2Ni^{IV}\text{—}C]^0 .$$

† $Me_2Cb \equiv [(3)\text{-}1,2\text{-}B_9C_2H_9Me_2]$.

Fig. 19 illustrates the structure of bis-*CC'*-dimethyl-1,2-dicarbollylnickel(IV) with one isomerised ligand.

Unsubstituted bis-(1,2-dicarbollyl)nickel(IV) is converted into the series B and C compounds in gas-phase isomerisation at 300–400°C. [62]

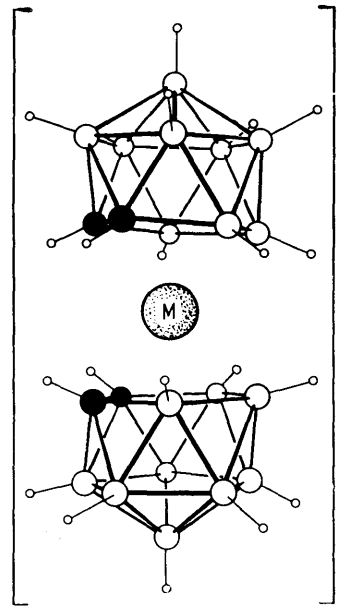

Figure 18.

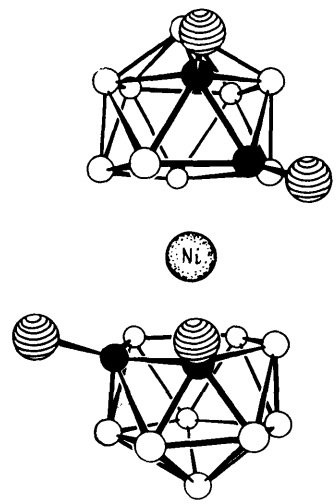

Figure 19.

A neutral mixed nickel(III) complex was obtained in a low yield by the reaction of $NiBr_2$ with $C_5H_5^-$ and $1,2\text{-}B_9C_2H_{11}^{2-}$ ions in THF [65]:

$$C_5H_5^- + 1,2\text{-}B_9C_2H_{11}^{2-} + NiBr_2 \rightarrow [(\pi\text{-}C_5H_5)Ni(\pi\text{-}1,2\text{-}B_9C_2H_{11})]^- \xrightarrow{[O]}$$

$$\rightarrow (\pi\text{-}C_5H_5)Ni(\pi\text{-}1,2\text{-}B_9C_2H_{11}) .$$

The cyclopentadienyl and dicarbollyl complexes of nickel exhibit many characteristic differences. Whereas the dicyclopentadienylnickel complex with the d^6 configuration, i.e. $(C_5H_5)_2Ni^{2+}$, has sometimes not been isolated, bis(dicarbollyl)nickel(IV) is an entirely stable crystalline compound. From this standpoint, the electrochemical reactions (the $E_{1/2}$ values) of the nickel complexes are of interest[65]:

$M^{IV} + e^- \rightarrow M^{III}$ and	$M^{III} + e^- \rightarrow M^{II}$.
$(C_5H_5)_2Ni$ + 0.77 mV	−0.09 mV
$(C_5H_5)Ni(B_9C_2H_{11})$ + 0.46 mV	−0.52 mV
$(B_9C_2H_{11})_2Ni$ + 0.18 mV	−0.56 mV

The wave corresponding to the oxidation of nickel to the quadrivalent state in the dicyclopentadienylnickel complex could be observed only at −40°C; above 0°C, this complex decomposes rapidly. In the d^6 state π-cyclopentadienyl-π-dicarbollylnickel(VI) is more stable and decomposes much more slowly than $(C_5H_5)_2Ni^{2+}$, but it could not be isolated. The higher stability of the dicarbollylnickel complexes has been explained by the higher negative charge of the dicarbollyl ligand (2- compared with 1- for the cyclopentadienyl ligand), which leads to a less effective positive charge of the nickel atom in the d^6 electronic state[65].

When palladium acetylacetonate is added to an excess of 1,2-dicarbollide ions, an unstable diamagnetic d^8-complex $[(1,2\text{-}B_9C_2H_{11})_2Pd^{II}]^{2+}$, extremely sensitive to air, is formed[66]. Its solutions decompose on standing in several hours, but, on rapid oxidation of the palladium(II) complex, an electrically neutral d^6-complex is formed in high yield:

$$[(1,2\text{-}B_9C_2H_{11})_2Pd]^{2-} \xrightarrow[CH_2Cl_2]{I_2} (1,2\text{-}B_9C_2H_{11})Pd \ .$$

When equimolar amounts of the palladium(II) and palladium(IV) complexes are mixed, $[(1,2\text{-}B_9C_2H_{11})_2Pd]^-$ is formed quantitatively[66]. It has been shown that palladium complexes have structures completely identical to those of the corresponding nickel complexes discussed above[62,66]. Chemically they also have much in common. For example, the neutral complex $(1,2\text{-}B_9C_2H_{11})_2Pd^{IV}$ is a strong Lewis acid and forms crystalline adducts with π- and n-bases[62]. Like the nickel complexes, the bis-(*CC'*-dimethyl-1,2-dicarbollyl)palladium system undergoes rearrangements leading to a change in the positions of the carbon atoms in the ligands[62]:

$$Pd(acac)_2 + 2[(3)\text{-}1,2\text{-}B_9C_2H_9Me_2]^{2-} \rightarrow$$

Series A

$$\rightarrow [(Me_2Cb)_2Pd^{II}\text{—}A]^{2-} \underset{-0.44\,mV}{\rightleftharpoons} [(Me_2Cb)_2Pd^{III}\text{—}A]^- \xrightarrow{[O]}$$

Series C

$$[(Me_2Cb)_2Pd^{II}\text{—}C]^{2-} \underset{-0.71\,mV}{\rightleftharpoons} [(MeCb)_2Pd^{III}\text{—}C]^- \underset{-0.47\,mV}{\rightleftharpoons} [(Me_2Cb)_2Pd^{IV}\text{—}C]^0 \ .$$

Mixed neutral complexes have been synthesised (yield 10%) by the reaction of the π-tetraphenylcyclobutadienylpalladium(II) dichloride dimer with the (3)-1,2-dicarbollide ion and its dimethyl derivative[16]:

$$(\pi\text{-}C_4Ph_4PdCl_2)_2 + 2[(3)\text{-}1,2\text{-}B_9C_2H_{11}]^{2-} \rightarrow 2(\pi\text{-}C_4Ph_4)Pd[\pi\text{-}1,2\text{-}B_9C_2H_{11}] \ .$$

A dicarbollide derivative of platinum was obtained by the reaction of cyclo-octa-1,5-dieneplatinum dichloride with the 1,2-dicarbollide ion[62]:

$$(1,5\text{-}C_8H_{12})PtCl_2 + (3)\text{—}1,2\text{-}B_9C_2H_{11}^{2-} \rightarrow (1,5\text{-}C_8H_{12})Pt[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}] \ .$$

A fundamentally new method of synthesising the dicarbollide complexes of nickel, palladium, and platinum was proposed by Stone and coworkers[22], who found that 1,8-$B_9C_2H_{11}$ (Tebbe et al.[67]) undergoes the polyhedral expansion reaction on treatment with $Ni(1,5\text{-}C_8H_{12})_2$, $(1,5\text{-}C_8H_{12})Ni(PEt_3)_2$, $Pd(t\text{-}BuNC)_2$, $Pt(PEt_3)_3$, or $Pt(PMe_2Ph)_3$, yielding respectively $(1,5\text{-}C_8H_{12})Ni(1,7\text{-}B_9C_2H_{11})$, $(Et_3P)_2Ni(1,7\text{-}B_9C_2H_{11})$, $(t\text{-}BuNC)_2Pd(1,7\text{-}B_9C_2H_{11})$, $(Et_3P)_2Pd(1,7\text{-}B_9C_2H_{11})$, and $(PhMe_2P)_2Pr(1,7\text{-}B_9C_2H_{11})$. The (3)-1,7-$B_9C_2H_{11}^{2-}$ ion then behaves as the dicarbollyl ligand. The reaction of 1,8-dicarba-*closo*-undecaborane(II) with bis(cyclo-octa-1,5-diene)nickel is illustrated schematically in Fig. 20.[22]

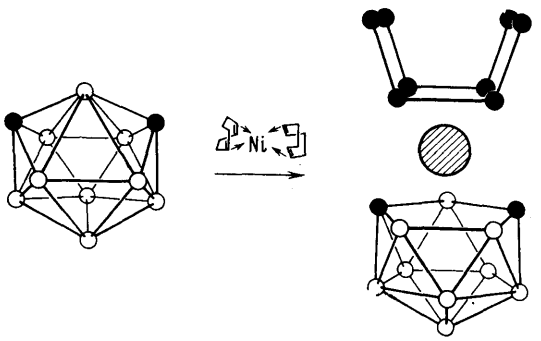

Figure 20.

D. The Copper Group

The dicarbollyl derivatives of all the metals of the copper group (Cu, Ag, Au) are known.

The addition of $CuSO_4$ in a highly alkaline medium to the 1,2-dicarbollide ion yields the paramagnetic d^9-complex $[(1,2\text{-}B_9C_2H_{11})_2Cu^{II}]^{2-}$, which is unstable in air and is readily converted into the diamagnetic d^8-complex $(1,2\text{-}B_9C_2H_{11})_2Cu^{III}$:[16,66]

$$CuSO_4 + 1,2\text{-}B_9C_2H_{11}^{2-} \rightarrow [(1,2\text{-}B_9C_2H_{11})_2Cu^{II}]^{2-} \underset{Na/Hg}{\overset{O_2}{\rightleftharpoons}} [(1,2\text{-}B_9C_2H_{11})_2Cu^{III}]^- \ .$$

The reaction of $AuCl_3$ with a large excess of 1,2-dicarbollide ions in dimethoxyethane with subsequent oxidation by aqueous hydrogen peroxide yields the stable complex $(1,2\text{-}B_9C_2H_9)_2Au^{III}$.[66] The salt is diamagnetic and can be reduced to the paramagnetic complex $[(1,2\text{-}B_9C_2H_9)_2Au^{II}]^{2-}$:

$$AuCl_3 + 1,2\text{-}B_9C_2H_{11}^{2-} \rightarrow [(1,2\text{-}B_9C_2H_{11})_2Au^{II}]^{2-} \underset{Na/Hg}{\overset{O_2}{\rightleftharpoons}} [(1,2\text{-}B_9C_2H_{11})_2Au^{III}]^- \ .$$

The attempts to obtain analogous bis(dicarbollyl) systems for silver were unsuccessful[66], but subsequently[68] the possibility of the existence of such complexes was briefly reported. It has been suggested that the (3)-1,2-dicarbollide ion be used for the qualitative detection of copper in aqueous solutions[69,70].

According to data for the polarographic reduction of the dicarbollyl complexes of copper and gold, the existence of the d^{10}-complexes is possible, since the polarograms show, together with the process $M^{III} + e^- \rightarrow M^{II}$, one-electron reduction waves corresponding to the process $M^{II} + e^- \rightarrow M^I$ (M = Cu or Au).

It is interesting that the most stable states of the copper and gold complexes are those in which the metal atom is in

the +3 formal oxidation state, i.e. the bivalent metal complexes are very powerful reducing agents[66].

An X-ray diffraction study of the bis(dicarbollyl) complexes of copper(II) and copper(III) showed[71,72] that they have a distorted sandwich structure analogous to those of the nickel(II) and palladium(II) complexes. Thus examination of the structures of complexes with electronic configurations ranging from d^5 to d^9 has shown that the d^5-, d^6-, and d^7-complexes have a symmetrical sandwich structure, while the d^8- and d^9-complexes have a distorted sandwich structure. Wing[66,71,72] explains the presence of such structures by π-allyl bonding in which six boron atoms enter into the first coordination sphere of the metal (three atoms from each dicarbollyl ligand).

E. The Chromium Group

The dicarbollyl complexes of all the metals in the chromium group (Cr, Mo, W) have been obtained. The reaction of $CrCl_3$ with the (3)-1,2- or (3)-1,7-$B_9C_2H_{11}^{2-}$ ions in THF leads to paramagnetic bis(dicarbollyl)chromium in which the metal atom is in the +3 formal oxidation state. In contrast to the isoelectronic chromocenium salts, which are readily hydrolysed in aqueous solutions[74], $[(\pi\text{-}B_9C_2H_{11})_2Cr]^-$ salts are stable in air and are not decomposed by hot concentrated H_2SO_4. However, these complexes decompose in a hot alkaline solution, regenerating the dicarbollide ion in a quantitative yield[73]. Neutral π-cyclopentadienyl-π-1,2-dicarbollylchromium has been obtained by the reaction of $CrCl_3$ with the $C_5H_5^-$ and 1,2-$B_9C_2H_{11}^{2-}$ ions. According to Clair et al.,[75] bis-(1,2-dicarbollyl)chromium has a regular sandwich structure.

Chromium, molybdenum and tungsten hexacarbonyls react with the 1,2-dicarbollide ion in THF on ultraviolet irradiation with displacement of three carbon monoxide molecules and the formation of π-dicarbollylmetal tricarbonyl complexes[16,31]:

$$(3)\text{-}1,2\text{-}B_9C_2H_{11}^{2-} + M(CO)_6 \xrightarrow[-3CO]{h\nu} \{[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]M(CO)_3\}^{2-} \quad (M = Cr, Mo, W)\ .$$

The complexes are isoelectronic with the complexes $(C_5H_5)M(CO)_3^-$ and enter into protonation and alkylation reactions[16]:

$$[(1,2\text{-}B_9C_2H_{11})Mo(CO)_3]^{2-} \xrightarrow{HCl} [(1,2\text{-}B_9C_2H_{11})Mo(CO)_3H]^-\ ,$$

$$[(1,2\text{-}B_9C_2H_{11})W(CO)_3]^{2-} \xrightarrow{MeI} [(1,2\text{-}B_9C_2H_{11})W(CO)_3Me]^-\ .$$

The reactions of the 1,2-dicarbollide ion with two moles of $M(CO)_6$ and the reactions of $M(CO)_6$ with $(1,2\text{-}B_9C_2H_{11})M(CO)_3^{2-}$ (M = W or Mo) lead to the same dinuclear products with the empirical formula $(B_9C_2H_{11})M_2(CO)_x^{2-}$ (x = 7 or 8).[16] Fig. 21 presents the structure of such a dinuclear complex obtained by the reaction

$$\{[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]Mo(CO)_3\}^{2-} + W(CO)_6 \rightarrow \{[\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}]Mo(CO)_3W(CO)_5\}^{2-}\ .$$

F. The Manganese Group

Bromomanganese pentacarbonyl and bromorhenium pentacarbonyl react rapidly with the 1,2-dicarbollide ion at room temperature with liberation of one mole of carbon monoxide. On heating, a further two moles of carbon monoxide are evolved and a π-dicarbollylmetal tricarbonyl anion is formed[16,76]:

$$1,2\text{-}B_9C_2H_{11}^{2-} + BrM(CO)_5 \xrightarrow[-CO]{80^\circ} [(\sigma\text{-}1,2\text{-}B_9C_2H_{11})M(CO)_5]^- \xrightarrow[-2CO]{70^\circ}$$

$$\rightarrow [(\pi\text{-}1,2\text{-}B_9C_2H_{11})M(CO)_3]^- \quad (M = Mn, Re)\ .$$

An X-ray diffraction analysis of the rhenium derivative has been carried out[77]. The closeness of the C–Re and B–Re distances (Fig. 22), which are 2.31 and 2.35 A respectively, is noteworthy.

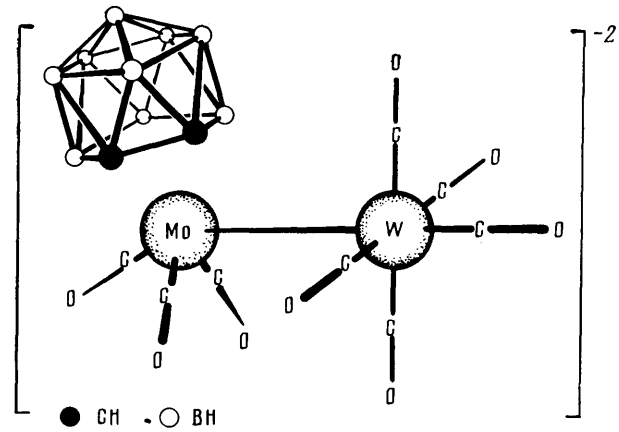

Figure 21.

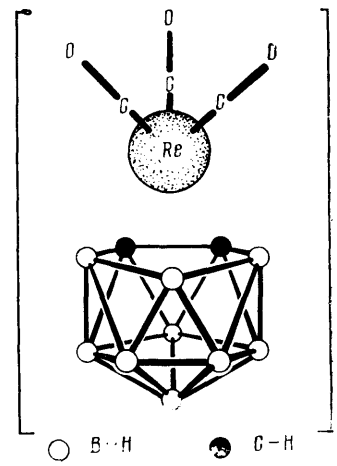

Figure 22.

When $[(\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11}(Mn)(CO)_3]^-$ is acted upon by triphenylphosphine under ultraviolet irradiation in THF for 12 h at 60°C, one carbonyl group is substituted by the triphenylphosphine group[78]:

$$[(\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11})Mn(CO)_3]^- + PPh_3 \xrightarrow{h\nu} [(\pi\text{-}(3)\text{-}1,2\text{-}B_9C_2H_{11})Mn(CO)_2PPh_3]^-\ .$$

2. Mono- and Hetero-Carbollyl Complexes of Transition Metals

The monocarbollide ion $B_{10}CH_{11}^{3-}$ is readily formed *in situ* on deamination and deprotonation of the carborane $B_{10}H_{12}CNMe_3$ by metallic sodium in THF[79]. This reaction proceeds more readily and with a higher yield in the

presence of naphthalene[80]. Two general methods have been proposed for the synthesis of π-complexes[81-83].

1. By adding butyl-lithium or sodium hydride to a mixture of $B_{10}H_{12}CNH_2R$ or a salt of $B_{10}H_{12}CH^-$ and the metal halide in THF or by adding the metal halide to the trisodium salt $Na_3B_{10}CH_{11}$ obtained directly.

2. By the interaction in a highly alkaline medium between $B_{10}H_{12}CNH_2R$ or a salt of $B_{10}H_{12}CH^-$ and the metal halide. This method gives high yields for nickel and cobalt.

Both methods have been used to synthesise the bis-(π-carbollyl) complexes of iron, cobalt, nickel, chromium, and manganese. Fig. 23 presents the general type of the structure of the λ-complexes obtained from the $B_{10}CH_{11}^{3-}$ and $B_{10}CH_{10}NH_2R^{2-}$ ions.

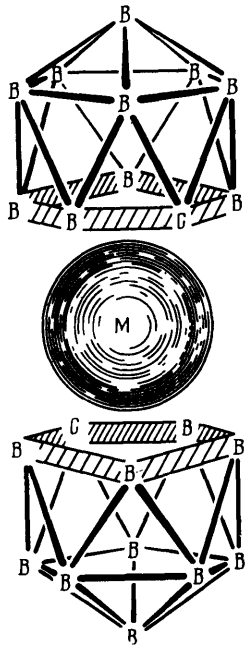

Figure 23.

The π-monocarbollyl ligand stabilises a high oxidation state of the metal to an even greater extent than the π-dicarbollyl ligand. Whereas the synthesis of $(1,2\text{-}B_9C_2H_{11})_2Ni^{IV}$ requires the oxidation of the nickel(III) complex by iodine or iron(III) chloride, $[(B_{10}CH_{11})_2Ni^{IV}]^{2-}$ and $(B_{10}CH_{10}NH_2R)_2Ni^{IV}$ are formed directly during isolation in air. Moreover, the diamagnetic complex $[(B_{10}CH_{11})_2Co]^{3-}$, which contains cobalt in the +3 formal oxidation state, is oxidised by cerium(IV) ions to the paramagnetic complex $[(B_{10}CH_{11})_2Co]^{2-}$ in which the cobalt atom is in the +4 formal oxidation state.

In the monocarbollyl complexes isolated directly from the reaction mixture, manganese is in the +4 formal oxidation state and iron, cobalt, and chromium are in the +3 formal oxidation state. All the complexes obtained, with the exception of that of manganese, are stable in air and do not decompose in acid media.

The complexes obtained from $B_{10}H_{12}CNH_3$ are of interest from the standpoint of reactions involving the amino-group. For example, $(B_{10}H_{10}CNH_3)_3Ni$ reacts with nitric acid and dimethyl sulphate to form $[(B_{10}H_{10}COH)_2Ni]^{2-}$ and $(B_{10}H_{10}CNHMe_2)_2Ni$ respectively[82,83].

Muetterties and coworkers[84] synthesised metallocarboranes with a monocarbollyl ligand starting with the $B_{10}H_{13}^-$ ion and Group VI metal carbonyls (ultraviolet irradiation). The $[(B_{10}H_{10}COH)M(CO)_4]^-$ anions formed initially react with sodium hydride to form the dianions $[(B_{10}H_{10}COH)NCO(CO)_3]^{2-}$, whose structure is illustrated in Fig. 24 for the molybdenum derivative as an example. Both types of compounds are decomposed quantitatively by bases with the removal of a carbon atom from the icosahedral skeleton and the formation of complexes belonging to the class of *nido*-metalloboranes.

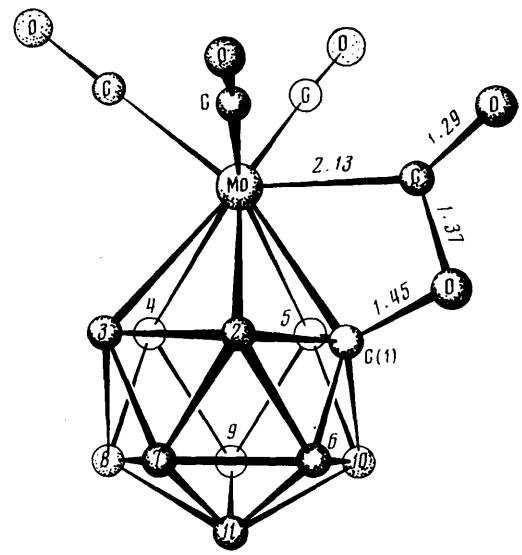

Figure 24.

Like carboranes(10) ($B_{10}H_{10}C_2H_2$), when acted upon by piperidine, 1,2- and 1,7-phosphacarboranes and 1,2- and 1,7-arsacarboranes give rise to the phospha- and arsa-carbaundecaborate anions, whose deprotonation generates heterocarbollide ions[85] isoelectronic with the dicarbollide ion and capable of behaving as π-ligands in transition metal complexes:

$$B_{10}H_{10}CHE \xrightarrow{C_5H_{10}NH} B_9H_{10}CHE^- \xrightarrow{NaH} B_9H_9CHE^{2-} \quad (E = P, As)\ .$$

A characteristic feature of the heterocarbaundecaborate anions is the presence of phosphorus or arsenic atoms which can be alkylated; the compounds then become neutral. Their deprotonation leads to heterocarbollide ions with a single negative charge[85,86]:

$$B_9H_{10}CHE^- + MeI \rightarrow B_9H_{10}CHEMe \xrightarrow{NaH} B_9H_9CHEMe^-\ (E = P, As)\ .$$

When the 1,2- and 1,7-$B_9H_9CHP^{2-}$ ions are acted upon by iron(II) chloride in THF solution, salts of $[(1,2\text{-}B_9H_9CHP)_2Fe^{II}]^{2-}$ and $[(1,7\text{-}B_9H_9CHP)_2Fe^{II}]^{2-}$ are formed

respectively[85,86]. Treatment of $[(1,7\text{-}B_9H_9CHP)_2Fe]^{2-}$ with methyl iodide leads to the neutral compound $(1,7\text{-}B_9H_9CHPMe)_2Fe$, which is identical with the complex obtained from $1,7\text{-}B_9H_9CHPMe^-$ and $FeCl_2$ (Little et al.[86]):

$$[(1,7\text{-}B_9H_9CHP)_2Fe]^{2-} + MeI \rightarrow (1,7\text{-}B_9H_9CHPMe)_2Fe \leftarrow 1,7\text{-}B_9H_9CHPMe^- + FeCl_2 \ .$$

This complex exists as a mixture of isomers (the shaded circles in Fig. 25 indicate the possible positions of the carbon atoms).

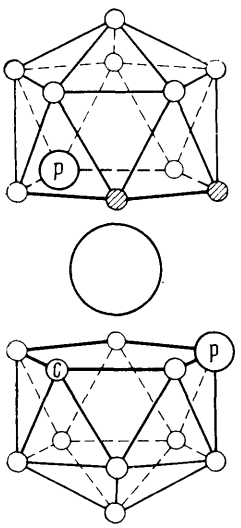

Figure 25.

In contrast to the bis(dicarbollyl) and bis(monocarbollyl) complexes of iron, bis(phosphacarbollyl)iron(II) is not oxidised by air in aqueous solution, although oxidation with cerium(IV) ions gives a small yield of the paramagnetic complex $[(1,7\text{-}B_9H_9CHP)_2Fe^{III}]^-$.[86]

The neutral complex $(\pi\text{-}C_5H_5)Fe(\pi\text{-}1,7\text{-}B_9H_9CHPMe)$ has been obtained by the interaction of the $C_5H_5^-$ and $1,7\text{-}B_9H_9CHPMe^-$ ions and $FeCl_2$. The reactions of 1,2- and $1,7\text{-}B_9H_9CHPMe^-$ ions with $CoCl_2$ give rise to bis(phosphacarbollyl) complexes in which the metal atom is in the +2 formal oxidation state and does not exhibit a tendency towards oxidation. In contrast, the reactions of the 1,2- and $1,7\text{-}B_9H_9CHP^{2-}$ ions with $CoCl_2$ lead to complexes in which the cobalt atom is in the +3 formal oxidation state.

The dianion $1,7\text{-}B_9H_9CHP^{2-}$ reacts with $NiCl_2$ to form bis-(1,7-phosphacarbollyl)nickel in which the nickel is in the +2 formal oxidation state.[85] The mixed complexes $(1,7\text{-}B_9H_9CHPMe)Mn(SO)_3$ and $[(1,7\text{-}B_9H_9CHP)Mn(CO)_3]^-$ have been obtained[86]. The substitution of one carbonyl group by a triphenylphosphine group in $[(1,7\text{-}B_9H_9CHP)Mn.(CO)_3]^-$ takes place readily on ultraviolet irradiation[78].

The reaction of triphenylcyclopropenylnickel carbonyl bromide with $1,7\text{-}B_9H_9CHPMe^-$ in THF gave a mixed nickel complex in 40% yield[87]:

$$[C_3Ph_3NiBr(CO)]_2 + 1,7\text{-}B_9H_9CHPMe^- \rightarrow C_3Ph_3Ni(1,7\text{-}B_9H_9CHPMe) \ .$$

The interaction of allylmagnesium chloride and $1,7\text{-}B_9H_9CHPMe^-$ with $NiCl_2$ results in the formation of a π-allyl complex[87]:

$$CH_2\text{-}CHCH_2MgCl + 1,7\text{-}B_9H_9CHPMe^- + NiCl_2 \rightarrow (C_3H_5)Ni(1,7\text{-}B_9H_9CHPMe) \ .$$

π-Methylallyl-π-phosphacarbollylnickel has been obtained similarly. When nitric oxide was passed through a solution of $1,7\text{-}B_9H_9CHPMe^-$ and $NiCl_2$ in THF, a nitrosyl complex was isolated in a low yield:

$$NO + 1,7\text{-}B_9H_9CHPMe^- + NiCl_2 \rightarrow (NO)Ni(1,7\text{-}B_9H_9CHPMe) \ .$$

The arsacarbollide ion reacts with transition metals like the phosphacarbollide ion. This is illustrated by the synthesis of π-cyclopentadienyl-π-1,2-arsacarbollylcobalt with the metal atom in the +3 formal oxidation state[88]:

$$C_5H_5^- + 1,2\text{-}B_9H_9CHAs^{2-} + CoCl_2 \rightarrow (C_5H_5)Co(1,2\text{-}B_9H_9CHAs) \ .$$

Arsacarbollyl complexes of manganese and iron have been obtained[88]. Under the conditions of the photochemical reaction, bis-(1,7-heterocarbollyl)iron(II) reacts with Group VI metal hexacarbonyls to form complicated complexes[89]:

$$[(1,7\text{-}B_9H_9CHE)_2Fe]^{2-} + M(CO)_6 \xrightarrow{h\nu} \{[1,7\text{-}B_9H_9CHEM(CO)_5]_2Fe\}^{2-} \quad (M = Cr, Mo, W) \ .$$

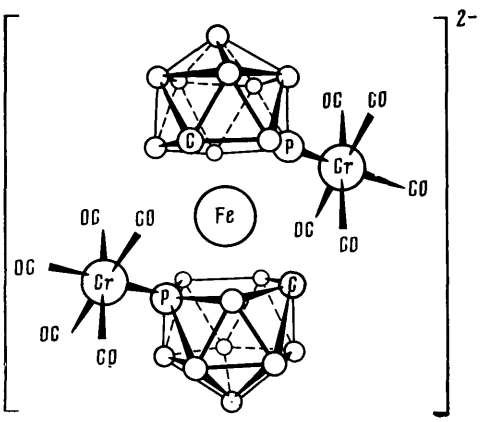

Figure 26.

In these complexes the heterocarbollyl ligand is π-bonded to the iron atom and σ-bonded via the phosphorus or arsenic atom to the Group VI metal atom. The structure of the $\{[1,7\text{-}B_9H_9CHP.Cr(CO)_5]_2Fe\}^{2-}$ ion is illustrated in Fig. 26.

3. Complexes Based on the $\pi\text{-}B_7C_2H_9$ Ligands

The axial hydrogen atoms of the methine groups in 1,3-dicarba-*nido*-nonaborane(13) ($1,3\text{-}B_7C_2H_{13}$) are acidic and when the carborane is treated with sodium hydride one mole of H_2 is evolved with formation of the dianion $B_7C_2H_{11}^{2-}$.[90,91] The reaction of anhydrous $CoCl_2$ with $B_7C_2H_{11}^{2-}$ leads to additional liberation of H_2 and the formation of a complex with the metal atom in the +3 formal oxidation state. It is suggested that five atomic orbitals, in which six electrons are located, originate from the five atoms of the ligand (they are predominantly sp^3-hybridised). The ligand is illustrated schematically in Fig. 27.

The name dicarbazapide given to the $B_7C_2H_9^{2-}$ ligand originates from the Greek work "zapato" (nine)‡. In the synthesis of bis(dicarbazapyl)cobalt products with different positions of the carbon atoms in the ligand are obtained depending on the reaction conditions[91]:

$$2\,(1,3\text{-}B_7C_2H_{11})^{2-} + 1.5\,Co^{2+} \xrightarrow{70^\circ} \{[\pi\text{-}(2)\text{-}1,6\text{-}B_7C_2H_9]_2\,Co\}^- + 0.5\,Co^0 + 2H_2\,,$$

$$2\,(1,3\text{-}B_7C_2H_{11})^{2-} + 1.5Co^{2+} \xrightarrow{25^\circ} \{[\pi\text{-}(2)\text{-}6,7\text{-}B_7C_2H_9]_2Co\}^- + 0.5Co^0 + 2H_2\,.$$

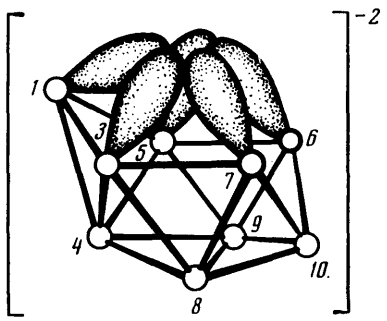

Figure 27.

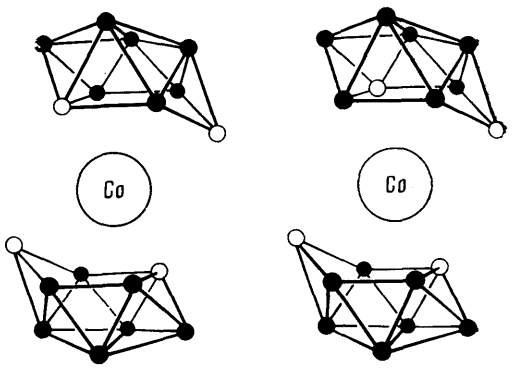

Figure 28.

At 70°C the product is a complex in which the carbon atoms are located in the 1- and 6- or 7-positions according to X-ray diffraction[92]. There is a possibility of the existence of *syn*- and *anti*-isomers (Fig. 28), but there is no information about the formation of more than one isomer. An isomer with the carbon atoms in the 6- and 7-positions is formed at room temperature (Fig. 29). A third isomer in which the carbon atoms are in the 1- and 10-positions has been obtained by heating $Cs(1,6\text{-}B_7C_2H_9)_2Co$ at 315°C for 24 h.[91,93]

‡ "Zapato" is a Spanish noun describing a shoe which resembles the shape of the $B_7C_2H_9^{2-}$ dianion[91] (Ed. of Translation).

The reaction of the $B_7C_2H_{11}^{2-}$ and $C_5H_5^-$ ions with $CoCl_2$ leads to $(\pi\text{-}C_5H_5)Co(\pi\text{-}1,6\text{-}B_7C_2H_9)$. No data have been obtained concerning the formation of the 6,7-isomer. Like the symmetrical complex, π-cyclopentadienyl-π-1,6-dicarbazapylcobalt isomerises on prolonged heating at 315°C with formation of the 1,10-isomer (Fig. 30).

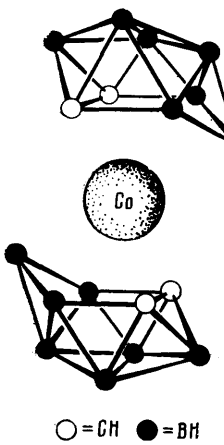

Figure 29.

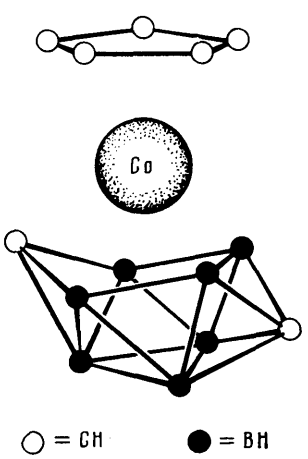

Figure 30.

Acetylation of π-cyclopentadienyl-π-1,6-dicarbazapylcobalt under the conditions of the Friedel–Crafts reaction yielded an acetyl derivative substituted at the boron atom[94]. An attempt to rearrange the compound with the 1,6-carborane structure to the 1,10-structure was unsuccessful. When the acetyl derivative is treated with $LiAlH_4$, the corresponding carbinol is not formed but the carbonyl group disappears. When $(C_5H_5)Co(1,6\text{-}B_7C_2H_9)$ is brominated in CCl_4 at room temperature, the *b*-dibromo-derivative is formed together with an insignificant amount of the *b*-tribromo-product. The bromine atoms are probably bonded to the boron atoms in the 8- and 10-positions in the ligand[94].

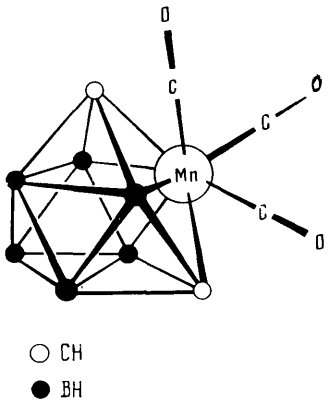

Figure 31.

An attempt was made to synthesise carbonyl derivatives of manganese with the π-$B_7C_2H_9$ ligand by treating $B_7C_2H_{11}^{2-}$ in boiling THF with bromomanganese pentacarbonyl[95,96]. However, the product was a complex with the π-$B_6C_2H_8$ ligand for which the structure presented in Fig. 31 was proposed.

4. π-Complexes Based on the Lowest Carboranes

Certain *nido*-carboranes or their deprotonation products react with transition metal derivatives to form π-complexes in which the π-carborane ligand is regarded as isoelectronic with the π-cyclopentadienyl ligand.

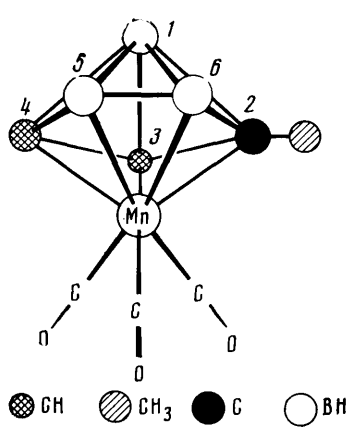

Figure 32.

2-Methyltricarbahexaborane(7) reacts with manganese carbonyl at 175–200°C in a sealed tube and gives rise to a quantitative yield of the isoelectronic analogue (π-2-$MeC_3B_3H_5$)$Mn(CO)_3$ (whose structure is illustrated in Fig. 32) of the known metallocene (π-C_5H_5)$Mn(CO)_3$:[97]

$$MeC_3B_3H_6 + \frac{1}{2}\,Mn_2(CO)_{10} \rightarrow (\pi\text{-}MeC_3B_3H_5)\,Mn(CO)_3 + \frac{1}{2}\,H_2\ .$$

Another method of synthesising this complex uses the reaction of sodium tricarbahexaborate with bromomanganese pentacarbonyl[98]. A σ-derivative is then formed as an intermediate and on heating is converted into a π-complex:

$$NaMeC_3B_3H_5 + BrMn(CO)_5 \xrightarrow[\text{fast}]{25^\circ} (\sigma\text{-}MeC_3B_3H_5)\,Mn(CO)_5 \xrightarrow[\text{slow}]{100^\circ} (\pi\text{-}MeC_3B_3H_5)\,Mn(CO)_3\ .$$

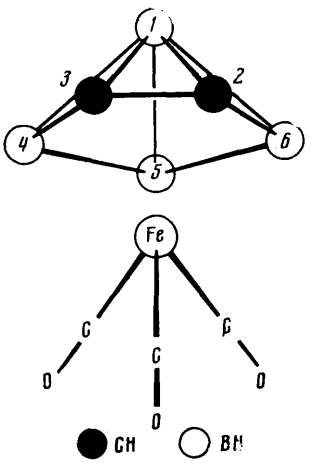

Figure 33.

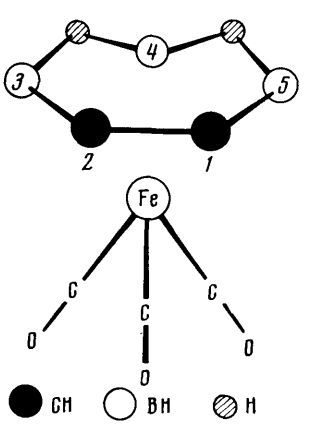

Figure 34.

The interaction of 2,3-dicarbahexaborane(8) ($C_2B_4H_8$) with iron pentacarbonyl at 240°C results in the formation of two π-complexes[99]: (π-$B_4C_2H_6$)$Fe(CO)_3$ (Fig. 33) and (π-$B_3C_2H_7$)$Fe(CO)_3$ (Fig. 34). The second complex is also formed in the reaction between dicarba-*nido*-pentaborane(7) with iron pentacarbonyl under ultraviolet irradiation[100]. The iron complexes obtained are isoelectronic with the (π-C_5H_5)$Fe(CO)_3^+$ cation and the π-$B_4C_2H_6$ and π-$B_3C_2H_7$ ligands have two negative charges.

Another pathway to the synthesis of π-carborane complexes of iron consists of the reaction of sodium dicarbahexaborate with cyclopentadienyliron dicarbonyl iodide and

subsequent photochemical decomposition of the μ-iron complex[101]:

$$NaC_2B_4H_7 + (\pi\text{-}C_5H_5)\,Fe(CO)_2I \xrightarrow{25^\circ} \mu\text{-}[(\pi\text{-}C_5H_5)\,Fe(CO)_2]_2C_2B_4H_7 \xrightarrow{h\nu} (\pi\text{-}C_5H_5)\,Fe^{II}(\pi\text{-}B_4C_2H_7) + (\pi\text{-}C_5H_5)\,Fe^{III}(\pi\text{-}B_4C_2H_6)\,.$$

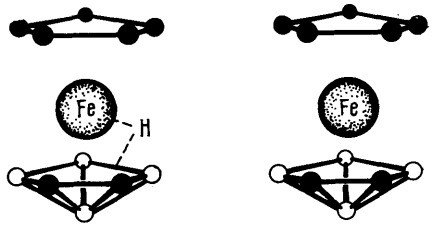

Figure 35.

The structures of both complexes have been deduced on the basis of ^{11}B NMR spectra and are presented in Fig. 35.

IV. METALLOCARBORANES OBTAINED BY THE POLYHEDRAL EXPANSION REACTION

The method of synthesis of metallocarboranes by the reduction of *closo*-carboranes has been called the polyhedral expansion reaction, since the resulting metallocarboranes have the structure of a polyhedron in which the number of vertices is greater by unity than in the initial carborane. The polyhedral expansion reaction has been largely applied to carboranes of the general type $B_nH_nC_2H_2$.

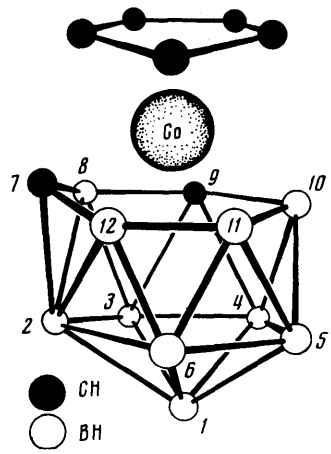

Figure 36.

The carborane 1,2-$B_{10}H_{10}C_2H_2$ is reduced by two moles of naphthalenesodium in THF to the dianion $B_{10}H_{10}C_2H_2^{2-}$,[102-103] which reacts with sodium cyclopentadienide and with $FeCl_2$ or $CoCl_2$ to form π-cyclopentadienyl-π-dodecahydrocarba-*nido*-dodecaboratoiron(III) or the corresponding cobalt(III) complex respectively[104,105]:

$$C_5H_5^- + B_{10}H_{10}C_2H_2^{2-} + MCl_2 \rightarrow [(\pi\text{-}C_5H_5)\,M^{II}(\pi\text{-}B_{10}C_2H_{12})]^- \xrightarrow{-e^-} \rightarrow (\pi\text{-}C_5H_5)\,M^{III}(\pi\text{-}B_{10}C_2H_{12}) \quad (M = Fe, Co)\,.$$

The iron(III) complex is paramagnetic (the effective magnetic moment is 2.12 Bohr magnetons) and is readily reduced by $NaBH_4$ to the iron(II) complex[105].

The red cobalt(III) complex, obtained directly from the reaction mixture, rearranges on boiling in hexane into an orange cobalt(III) complex, which is in turn converted on boiling in benzene into a red-orange cobalt(III) complex. X-Ray diffraction analysis[106] of the red complex (π-C_5H_5)Co^{III} (π-$B_{10}H_{10}C_2H_2$) showed that it exists in the form of a pair of enantiomers with the carbon atoms in the 7- and 9-positions or 7- and 11-positions (Fig. 36).

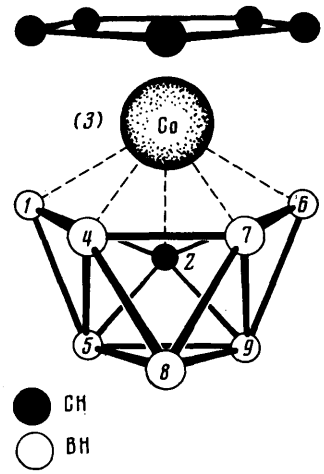

Figure 37.

In the orange isomer the carbon atoms occupy the 6- and 7-positions and in the red-orange isomer the 5- and 7-positions[107]. Alkaline degradation of the orange complex (π-C_5H_5)Co^{III} (π-$B_{10}C_2H_{12}$) leads to a new metallocarborane—π-cyclopentadienyl-π-octahydro-2-carba-*nido*-octaboratocobalt [(π-C_5H_5)Co^{III} (π-2-B_7CH_8)]$^-$,[107,108] for which the structure illustrated in Fig. 37 was proposed.

The reaction of the dianion $B_{10}C_2H_{12}^{2-}$ with cobalt(II), iron(II), and nickel(II) salts proceeds in accordance with the equation

$$2\,B_{10}C_2H_{12}^{2-} + M^{n+} \rightarrow [(\pi\text{-}B_{10}C_2H_{12})_2\,M]^{n-4} \quad (n = 2,3)\,.$$

and leads to bis-(π-dodecahydrodicarba-*nido*-dodecaborate) complexes (Fig. 38)[105,109].

The reaction of the dianion $B_{10}C_2H_{12}^{2-}$ with molybdenum and tungsten hexacarbonyls under ultraviolet irradiation leads to carboranylmetal tricarbonyl units[105]:

$$B_{10}C_2H_{12}^{2-} + M(CO)_6 \xrightarrow[-CO]{h\nu} [(\pi\text{-}B_{10}C_2H_{12})\,M(CO)_3]^{2-} \quad (M = Mo, W)$$

Zakharkin and Kalinin[109,110] found that the iron(III), cobalt(III) and nickel(II) complexes obtained from the dianions of carborane(10) and its *C*-substituted derivatives are readily oxidised by $CuCl_2$ with formation of carboranes. A characteristic feature of these complexes is the

ease of their rearrangements associated with a change in the relative positions of the carbon atoms in the π-carborane ligand. While oxidation of the complexes obtained directly by the reaction leads to the initial carborane 1,2-$B_{10}C_2H_{12}$ and its derivatives, oxidation of the rearranged complexes yields the 1,7- and 1,12-$B_{10}C_2H_{12}$ carboranes and their derivatives. This method has been recommended by the authors for the low-temperature isomerisation of 1,2-$B_{10}C_2H_{12}$ carboranes to 1,7-$B_{10}C_2H_{12}$ carboranes. In the $(B_{10}C_2H_{12})_2M^{n-4}$ complexes reversible transitions from the *closo*- to the *nido*-structure are observed in the ligands:

$$closo\text{-}B_{10}C_2H_{12} \underset{CuCl_2(-4e^-)}{\overset{+2e^-+MX_n}{\rightleftharpoons}} nido\text{-}(B_{10}C_2H_{12})_2\ M^{n-4}\ .$$

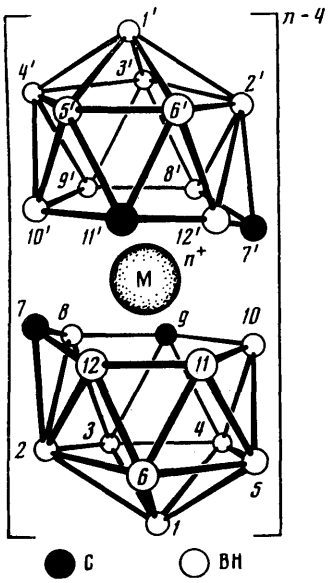

Figure 38.

The oxidation of the complexes $(B_{10}C_2H_{12})_2M^{n-4}$ has also been investigated by Brattsev and Stanko[111], but their results require additional confirmation.

The polyhedral expansion reaction applied to the carborane 1,8-$B_9C_2H_{11}$ leads to a metallocarborane containing the π-(3)-1,7-dicarbollyl ligand (see Section III, 1).

Polyhedral expansion of the carborane 1,6-$B_8C_2H_{10}$ using naphthalenesodium, sodium cyclopentadienide, and $CoCl_2$ leads to two main products[112]: $(\pi\text{-}B_8C_2H_{10})Co^{III}(\pi\text{-}C_5H_5)$ (Fig. 39) and $[(\pi\text{-}B_8C_2H_{10})_2Co^{III}]^-$. Next, on treatment of π-cyclopentadienyl-π-decahydrodicarba-*nido*-decaboratocobalt with naphthalenesodium and subsequent addition of sodium cyclopentadienide and $CoCl_2$, a two-metal carborane complex was obtained[113]:

$$C_5H_5CoB_8C_2H_{10} \xrightarrow[\text{THF, } 50^\circ]{\substack{1.\ 3(Na^+C_{10}H_8^-),\\ 2.\ Na^+C_5H_5^-\\ 3.\ CoCl_2}} C_5H_5CoB_8C_2H_{10}CoC_5H_5\ .$$

A structure with a bidentate π-linked $B_8C_2H_{10}$ ligand (dicarbacanastide), which, in contrast to the ligand considered previously (Fig. 7), contains carbon atoms in the 8- and 10-positions (Fig. 40), was proposed for the complex[113].

Treatment of the carborane 1,7-$B_6C_2H_8$ with two equivalents of naphthalenesodium in THF and subsequent addition of sodium cyclopentadienide and $CoCl_2$ lead to the formation, together with the normal product $(\pi\text{-}C_5H_5)Co^{III}(\pi\text{-}B_6C_2H_8)$ (Fig. 41), of the two-metal complex[114]

$(C_5H_5)_2Co_2B_6C_2H_8$[114].

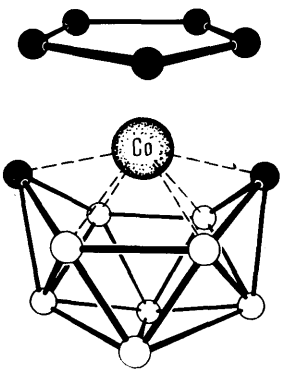

Figure 39.

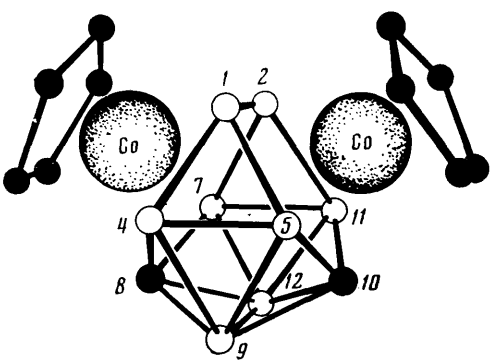

Figure 40.

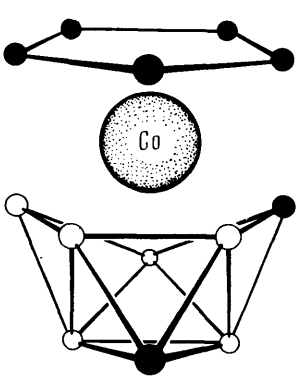

Figure 41.

The complex was shown to have an unusual structure with the two cobalt atoms occupying adjoining vertices of the polyhedron (Fig. 42).[7,8] The structure quoted by Dunks and Hawthorne[114] is incorrect.

Interesting results were obtained by Miller and Grimes when they applied the polyhedral expansion reaction to the carborane 2,4-$B_5C_2H_7$.[115] Its treatment with two moles of naphthalenesodium gave the dianion $B_5C_2H_7^{2-}$ whose interaction with sodium cyclopentadienide and $CoCl_2$ and subsequent oxidation by atmospheric oxygen leads to the formation of more than twenty neutral metallocarboranes, eight of which have been isolated and characterised. The structures proposed for these complexes are illustrated in Fig. 43. All the complexes are formally derivatives of the ligands $B_4C_2H_6^{2-}$, $B_4C_2H_6^{4-}$, $B_5C_2H_7^{2-}$, $B_5C_2H_7^{4-}$, $B_6C_2H_8^{2-}$, and $B_6C_2H_8^{4-}$.

The authors considered the possible mechanism of the formation of the metallocarboranes and proposed the following reaction sequence[115]: (1) the formation of the $B_5C_2H_7^{2-}$ dianion from $B_5C_2H_7$ and naphthalenesodium; (2) the formation of the $(\pi\text{-}B_5C_2H_7)Co^{II}(\pi\text{-}C_5H_5)^-$ anion from $CoCl_2$, NaC_5H_5, and $B_5C_2H_7^{2-}$; (3) the reaction of the $(\pi\text{-}B_5C_2H_7)Co^{II}(C_5H_5)^-$ ion with $B_5C_2H_7^{2-}$ via electron transfer (a) and alkaline degradation (b) mechanisms leading to the formation of the open-chain metallocarborane anions $(\pi\text{-}B_5C_2H_7)Co^{II}(\pi\text{-}C_5H_5)^{3-}$ and $(\pi\text{-}B_4C_2H_6)Co^{II}(\pi\text{-}C_5H_5)^{3-}$ respectively; (4) the insertion of the Co^{2+} ion in

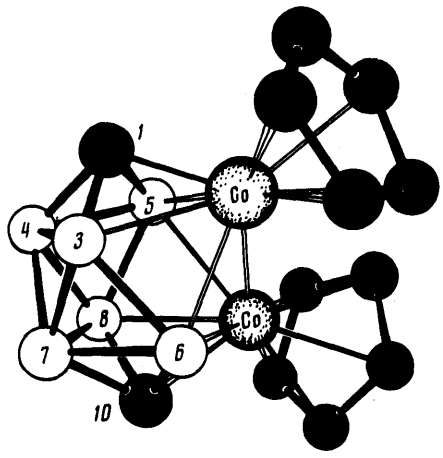

Figure 42.

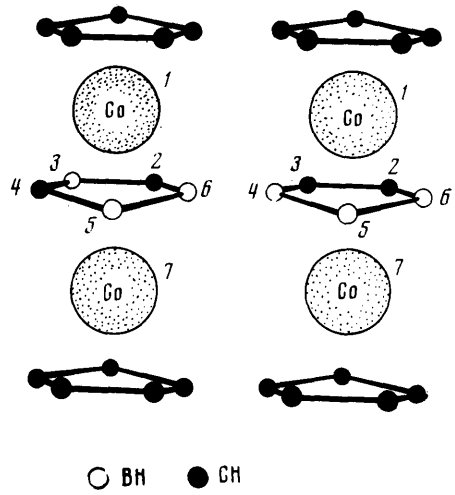

Figure 44.

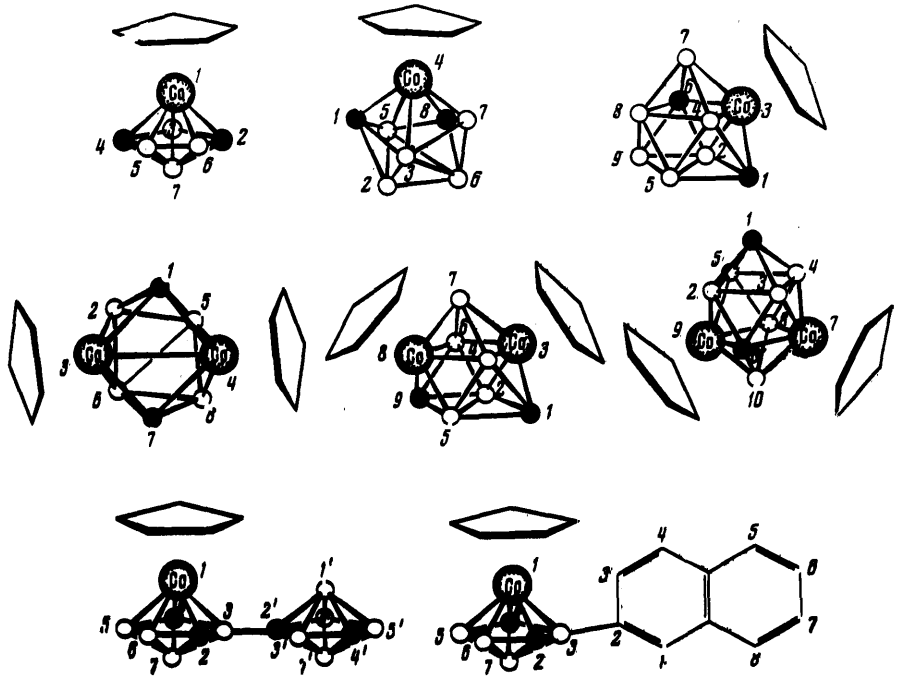

Figure 43.

certain open-chain metallocarborane ions with formation of two-metal units; (5) oxidation by air of the cobalt(II) ions formed in stages (2), (3), and (4) to the neutral cobalt(III) metallocarboranes $(\pi\text{-}B_{n-2}C_2H_n)Co^{III}(\pi\text{-}C_5H_5)$ and $(\pi\text{-}B_{n-2}C_2H_n)Co_2(\pi\text{-}C_2H_5)$; (6) side reactions associated with the deprotonation of the carborane units and the formation of their σ-bonded derivatives.

Nor can one rule out the possibility of the disproportionation of the $B_5C_2H_7^{2-}$ anion to $B_4C_2H_6^{2-}$, $B_6C_2H_8^{2-}$, and other units before the stage in which the metal is inserted into the *nido*-carborane system[115]. All the π-carborane ligands discussed above had a three-dimensional structure. Grimes and coworkers[116] were the first to obtain π-complexes with planar π-ligands. By treating the carborane 1,6-$B_4C_2H_6$ with naphthalenesodium and the subsequent reaction of the dianion $B_4C_2H_6^{2-}$ with $C_5H_5^-Na^+$ and $CoCl_2$, the dinuclear complex $[(\pi\text{-}1,7)\text{-}2,4\text{-}B_3C_2H_5]Co_2(\pi\text{-}C_5H_5)_2$ was obtained; its structure is shown in Fig. 44.

The isomeric complex $[(\pi\text{-}1,7\text{-})\text{-}2,3\text{-}B_3C_2H_5]Co_2(\pi\text{-}C_5H_5)_2$ was synthesised by the reaction of sodium dicarba-*nido*-hexaborate $NaB_4C_2H_7$ with C_5H_5Na and $CoCl_2$ (Fig. 44).[116] Both complexes obtained are formally derivatives of the $B_3C_2H_5^{4-}$ ligand. The π-carborane complexes are structurally similar to the complex $[Ni(C_5H_5)_3]^+$.[117] However, in contrast to the $[Ni_2(C_5H_5)_3]^+$ system, which is readily converted into nickelocene under the influence of moisture, the $(B_3C_2H_5)Co_2(C_5H_5)_2$ systems are resistant to the action of water, atmospheric oxygen, and solvents.

V. CARBORANE DERIVATIVES OF NON-TRANSITION METALS

The possibility of the formal substitution of the BH vertices in the polyhedral carborane structures by isoelectronic units is clearly illustrated, for example, by the isoelectronic series of compounds $B_{12}H_{12}^{2-}$, $B_{11}CH_{12}^-$, and $B_{10}C_2H_{12}$, from which it follows that the BH unit is isoelectronic with the CH^+ unit.[4] By analogy, Be is isoelectronic with the BH unit and therefore one might expect the existence of the neutral compound $BeB_9C_2H_{11}$.

Using the familiar reaction whereby the dicarbollide ion is built up with the aid of phenylboron dichloride to the icosahedral carborane structure[118], Popp and Hawthorne[119,120] attempted to build up the dicarbollide ion with beryllium chloride:

$$(3)\text{-}1,2\text{-}B_9C_2H_{11}^{3-} + BeCl_2 \rightarrow (3)\text{-}BeCl - 1,2\text{-}B_9C_2H_{11}^-.$$

but they were unable to obtain a berylcarborane by this reaction.

The $B_9C_2H_{13}$ carborane, which may be regarded as a diprotonated dicarbollide ion, was used to synthesise a berylcarborane. Its reaction with metal alkyls should result in the formation of an alkane on protolysis of the metal–carbon bond and the metal should be inserted in the open face of the icosahedral fragment. For dialkylberyllium, the presence of electron-donating solvents is necessary to stabilise the product. Accordingly, dimethylberylliumdiether and diethylberyllium-diether were used for the synthesis[119,120]:

$$(3)\text{-}1,2\text{-}B_9C_2H_{13} + BeR_2 \cdot 2(OEt_2) \xrightarrow{\text{benzene/ether}} 2RH + (3)\text{-}Be\text{-}1,2\text{-}B_9C_2H_{11} \cdot OEt_2.$$

The product is very sensitive to moisture and on hydrolysis yields the (3)-1,2-$B_9C_2H_{12}^-$ ion.

When the reaction was carried out with diethylberyllium containing only one-third of the required amount of ether, an insoluble polymeric product consisting of [(3)-Be-1,2-$B_9C_2H_{11}$]n units with icosahedral geometry, linked by Be–H–B bridges, was obtained. When the ether adduct of the berylcarborane is treated with trimethylamine, the complex (3)-[BeNMe$_3$]-1,2-$B_9C_2H_{11}$, whose structure is illustrated in Fig. 45, is formed.

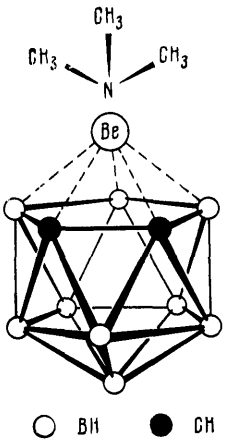

Figure 45.

Mikhailov and Potapova obtained an aluminacarborane in the form of an adduct with two THF molecules by the reaction of the 1,2-dicarbollide ion with ethylaluminium dichloride in THF[121]:

$$1,2\text{-}B_9C_2H_{11}^{3-} + EtAlCl_2 \xrightarrow{THF} (3)\text{-}EtAl - 1,2\text{-}B_9C_2H_{11} \cdot 2THF.$$

This compound was the first example of metallocarboranes containing a non-transition metal in the polyhedron. Subsequently the ability of the carborane $B_9C_2H_{13}$ to undergo protolysis at the metal–carbon bond was used to synthesise alumina- and galla-carboranes[122,123]. When equimolar amounts of trialkylaluminium and $B_9C_2H_{13}$ were mixed and heated at 50°C for 1 h, 7,8-μ-dialkylalumina-1,2-dicarba-*nido*-undecaborane(13) was formed:

$$(3)\text{-}1,2\text{-}B_9C_2H_{13} + R_3Al \rightarrow (3)\text{-}AlR_2\text{-}1,2\text{-}B_9C_2H_{13} + RH.$$

According to X-ray diffraction[124,125], the aluminium atom in $B_9C_2H_{12}AlR_2$ deviates from the open face of the icosahedral fragment and the angle between the $B_{(7)}$–Al–$B_{(8)}$ and $B_{(7)}$–$B_{(8)}$–$B_{(4)}$–$C_{(1)}$–$C_{(2)}$ planes is 130° (Fig. 46). It is suggested that the aluminium atom is linked to the $B_{(7)}$ and $B_{(8)}$ atoms by two bridging hydrogen bonds. A low-temperature study of the ^{11}B NMR spectra established[123] the occurrence of a tautomeric process involving the exchange of the bridge positions between the dialkylaluminium fragment and the proton H_b, as shown in Fig. 46. At low temperatures the ^1H NMR spectra reveal the splitting of the signal corresponding to the Me_2Al group, which indicates the *endo*- and *exo*-locations of the methyl groups relative to the open face[123]. The gallium derivative was obtained similarly:

$$(3)\text{-}1,2\text{-}B_9C_2H_{13} + Et_3Ga \rightarrow (3)\text{-}GaEt_2\text{-}1,2\text{-}B_9C_2H_{13} + C_2H_6.$$

When 7,8-μ-dialkylalumina-1,2-dicarba-*nido*-undecaborane(13) is heated in benzene, 3-alkyl-3-alumina-1,2-dicarba-*closo*-dodecaborane(12) is formed:

$$(3)\text{-}AlR_2\text{—}1,2\text{-}B_9C_2H_{12} \xrightarrow[25\ h]{77^\circ} (3)\text{-}RAl - 1,2\text{-}B_9C_2H_{11} + RH\ .$$

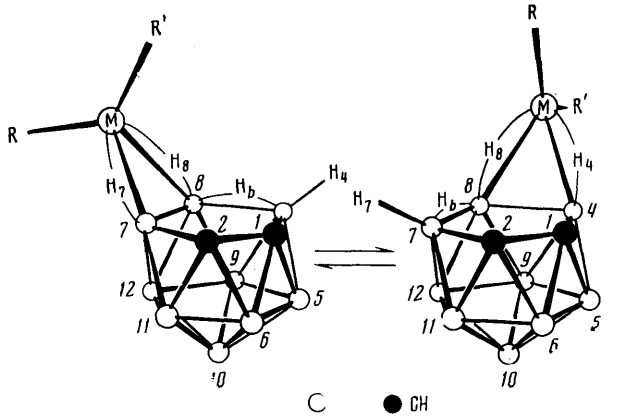

Figure 46.

It has been established that the monoethylaluminium derivative has the closed icosahedral structure with an EtAl unit [122,126]. This compound forms with THF the adduct obtained previously by Mikhailov and Potapova.

Heating the diethylgallium derivative also leads to the formation of a closed structure:

$$(3)\text{-}1,2\text{-}B_9C_2H_{12}GaEt_2 \xrightarrow{77^\circ} (3)\text{-}GaEt - 1,2\text{-}B_9C_2H_{11} + C_2H_6\ .$$

At 410°C 3-ethyl-3-alumina-1,2-carborane undergoes thermal isomerisation in the gas phase forming 3-ethyl-3-alumina-1,7-carborane [123]:

$$(3)\text{-}AlEt - 1,2\text{-}B_9C_2H_{11} \xrightarrow{410^\circ} (3)\text{-}AlEt - 1,7\text{-}B_9C_2H_{11}\ .$$

The selective formation of the 1,7-isomer in the isomerisation process resembles the behaviour of the carborane $1,2\text{-}B_{10}C_2H_{12}$, which rearranges to $1,7\text{-}B_{10}C_2H_{12}$ at 400–500°C, [4] but its behaviour differs from that of other metallocarboranes, particularly $Ni[(3)\text{-}1,2\text{-}B_9C_2H_9Me_2]_2$ and $Pd[(3)\text{-}1,2\text{-}B_9C_2H_9Me_2]_2$, [62,63] for which rearrangements leading to a 1,6- disposition of the carbon atoms are characteristic.

Alumina- and galla-carboranes are sensitive to the action of moisture and are readily hydrolysed with formation of the $(3)\text{-}1,2\text{-}B_9C_2H_{12}$ ion. Their reaction in benzene with anhydrous HCl gives a quantitative yield of $(3)\text{-}1,2\text{-}B_9C_2H_{13}$. An interesting property of the compounds $B_9C_2H_{12}AlEt_2$ and $B_9C_2H_{11}AlEt_2$ is their ability to form with $TiCl_4$ complexes whose solutions polymerise ethylene like the Ziegler–Nata catalysts [123].

The dicarbollide ion interacts with bivalent Group IVB metal salts, forming a product resulting from the insertion of the metal in the open face of the dicarbollide [127,132]:

$$(3)\text{-}1,2\text{-}B_9C_2H_{11}^{2-} + MX_2 \rightarrow (3)\text{-}M\text{-}1,2\text{-}B_9C_2H_{11} \quad (Me{=}Ge, Sn, Pb)\ .$$

The metallocarboranes obtained are stable in air, but are hydrolysed in acid and alkaline media to the anions $B_9C_2H_{12}^-$.

A similar reaction involving the building up of 1,2- and 1,7-phosphacarbollide and 1,2- and 1,7-arsacarbollide ions with the aid of GeI_2 leads to phospha- and arsa-germacarboranes containing three heteroatoms in the icosahedral structure [129]:

$$1,2\text{-}B_9H_9CHE^{2-} + GeI_2 \rightarrow 1,2,3\text{-}GeB_9H_9CHE,$$
$$1,7\text{-}B_9H_9CHE^{2-} + GeI_2 \rightarrow 1,2,7\text{-}GeB_9H_9CHE. \qquad (E = P, As)$$

When the monocarbollide ion was built up with trichloromethylgermane, a germacarborane was obtained [130]:

$$Na_3B_{10}H_{10}CH + MeGeCl_3 \rightarrow B_{10}H_{10}CHGeMe - 1.2\ .$$

The gas-phase reaction of trimethylgallium or trimethylindium with 1,3-dicarba-*nido*-hexaborane(8) yields 1-methyl-1-galla- or 1-methyl-1-inda-2,4-dicarba-*closo*-heptaborane(7): [131,132]

$$B_4C_2H_8 + GaMe_3 \xrightarrow{215^\circ} MeGaB_4C_2H_6;\ B_4C_2H_8 + InMe_3 \xrightarrow{95-110^\circ} MeInB_4C_2H_6\ .$$

The structure of the gallacarborane is illustrated in Fig. 47. The indacarborane probably has a similar structure.

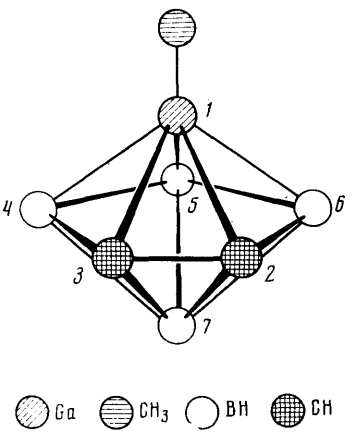

Figure 47.

After the manuscript had been sent to the editors, a number of papers on metallocarboranes were published. Certain early investigations have been summarised in Snaith and Wade's review [133]. The polyhedral expansion reaction has been developed further. Hawthorne and coworkers [134] described in detail the application of this reaction to the $1,7\text{-}C_2B_6H_8$, $4,5\text{-}C_2B_7H_9$, $1,6\text{-}C_2B_8H_{10}$, $1,10\text{-}C_2B_8H_{10}$, and $1,8\text{-}C_2B_9H_{11}$ systems. Using $CoCl_2$ and NaC_5H_5, metallocarboranes of the following types were obtained: $C_5H_5CoC_2B_nH_{n+2}$, $(C_5H_5Co)_2C_2B_nH_{n+2}$, and $C_5H_5CoC_2B_nH_{n+1}(C_2B_nH_{n+1})$. The formation of the mixed ferracarboranes from the $1,7\text{-}C_2B_6H_8^{2-}$ and $1,6\text{-}C_2B_8H_{10}^{2-}$ dianions, NaC_5H_5, and $FeCl_2$ has been described [134].

The application of the polyhedral expansion reaction to metallocarboranes yielded interesting results. The reduction of the complex $(\pi\text{-}C_5H_5)Co^{III}(\pi\text{-}1,6\text{-}C_6B_7H_9)$ by naphthalenesodium in THF and its subsequent reaction with NaC_5H_5 and $FeCl_2$ led to the formation of the bimetallocarborane $(\pi\text{-}C_5H_5)Co(\pi\text{-}C_2B_7H_9)Fe(\pi\text{-}C_5H_5)$ in which there is one paramagnetic and one diamagnetic centre [135].

The cobaltaferracarborane $(\pi\text{-}C_5H_5)Co^{III}(\pi\text{-}C_2B_9H_{11})Fe^{III}(\pi\text{-}C_5H_5)$ was obtained by the alkaline degradation of the complex $(\pi\text{-}C_5H_5)Co^{III}(\pi\text{-}C_2B_{10}H_{12})$ in the presence of $FeCl_2$ and C_5H_6.[135]

The reaction of the reduced form of $(\pi\text{-}C_5H_5)Co^{III}(\pi\text{-}1,6\text{-}C_2B_7H_9)$ with NaC_5H_5 and $CoCl_2$ leads to the formation of $(C_5H_5Co)_2C_2B_7H_9$ and $(C_5H_5CO)_3C_2B_7H_9$.[136] It is suggested that the last complex has an icosahedral structure with the cobalt atoms at three vertices. The reaction of the reduced complex $[Me_4N](\pi\text{-}C_5H_5)Co^{III}(\pi\text{-}CB_7H_8)$ with NaC_5H_5 and $NiBr_2$ yielded the two-metal monocarbon metallocarborane $(\pi\text{-}C_5H_5)Co^{III}(\pi\text{-}CB_7H_8)Ni^{IV}(\pi\text{-}C_5H_5)$.[137]

Salentine and Hawthorne[137] quote tentative structures for metallocarboranes. The study of the chemical properties of certain metallocarboranes has been continued[138]. Hawthorne and coworkers[139] attempted to classify metallocarboranes in terms of the total number of electrons involved in the formation of the polyhedra. The $2n + 14$, $2n + 16$, and $2n + 26$ electron rules are valid for *closo*-polyhedral heteroboranes containing one transition metal at the vertex, for *nido*-polyhedra of this type, and for *closo*-polyhedra with two transition metals at the vertices respectively. A series of X-ray diffraction studies have been made on metallocarboranes, confirming the structures proposed previously: $(B_6C_2H_8)Mn(CO)_3$,[140] $(B_3C_2H_7)Fe(CO)_3$,[141] and $(B_9C_2H_{11})_2Ni$.[142]

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Modern Methods for the Chromatographic Analysis of Nucleic Acids and Their Components

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The literature data for the chromatographic separation of nucleic acids and their components are considered in the review. Particular attention has been devoted to the commonest types of column chromatography, thin layer chromatography using different adsorbents, and electrophoresis. The applicability of each type of chromatography in the study of the primary nucleic acid structure and the formation of complexes by nucleic acids with natural products of other classes is demonstrated. The bibliography includes 597 references.

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I. INTRODUCTION

The development of modern biology, which has led to many important discoveries, would have been impossible without the development of microanalytical methods. Paper chromatography and electrophoresis and ion exchange column chromatography have played an outstanding role in the establishment of this science, permitting the elucidation of the most general characteristics of the structures of nucleic acids and proteins. However, further improvement in the extent of our knowledge and the acquisition of more detailed information in this field required the solution of specific problems in the isolation and determination of the structures of specific individual nucleic acid and protein molecules, only a few of which are sometimes present in the cell. The previous micromethods were relatively unsuitable for the solution of these new problems and, although the old procedures were still used in the determination of the structures of the first individual nucleic acids, the necessity for the development and utilisation of new, much more sensitive analytical methods became quite evident.

Nowadays the employment of thin-layer chromatography in combination with labelled compounds permits the analysis of amounts of compounds not less than 10^{-12} g. So far column chromatography has a lower sensitivity (10^{-7}—10^{-9} g) but it often permits the necessary spectroscopic analysis of the substance. The contribution of ultramicromethods to modern research is continuously increasing.

This review gives a general account of the advances in the field of analytical methods for nucleic acids in the last 10 years. Readers interested in work carried out prior to this can become acquainted with it in reviews published previously[1-5].

In the present review attention has been concentrated on ultramicromethods. Since the principles and chromatographic systems employed in ultramicroanalysis are general, the review includes also less sensitive methods which can be employed in ultramicroanalytical procedures.

The analytical methods for nucleic acids are general and can be used also in other fields of research. The authors hope that the review will be useful not only to chemists, physicists, and biologists working in the field of molecular biology but also to organic chemists employing micromethods in their work.

To facilitate the practical employment of the review, the data are divided into sections combining identical types of compounds to be analysed. The abbreviations and symbols for nucleic acids and their components employed in the review are those recommended by the IUPAC Commission and IUB.[6]

Large numbers of adsorbents of different types are used to analyse nucleic acids and their components. The detailed characteristics of these adsorbents and the names of the firms manufacturing them are given in Lur'e's handbook[7].

II. NUCLEIC ACIDS

The number of different types of nucleic acids in the cell is fairly large and it is therefore extremely difficult to isolate the individual components. Moreover, their limited solubility in aqueous solutions and their capacity for aggregation and non-specific interaction with sorbents greatly reduce the number of methods available for the fractionation of nucleic acids. However, fairly numerous systems are described in the literature for the chromatographic resolution of nucleic acids into individual components. Experience gained in their application shows that, for a successful isolation of a homogeneous substance, it is insufficient to employ a single chromatographic procedure. Stepwise fractionation of nucleic acids is most useful. The nucleic acid mixtures are initially divided into fractions with identical specific features—transfer RNA (tRNA), ribosomal RNA (rRNA), messenger RNA (mRNA), DNA, etc. Selective extraction, a combination of different precipitation methods, centrifugation[8], and chromatographic methods are frequently employed for this purpose. The nucleic acid fractions are then subjected to a more detailed resolution. Among chromatographic methods separation on ion-exchange resins, partition and affinity chromatography, and other procedures are most widely used.

1. ION-EXCHANGE CHROMATOGRAPHY

A. Adsorbents Containing Proteins

One of the types of such chromatography—fractionation on columns with methylated albumin sorbed on Kieselguhr (MAK-chromatography)—has become very common in the separation of all types of nucleic acids. Their mobility on MAK-columns is determined largely by three factors: (1) the length of the polynucleotide chain (the overall molecular charge), (2) the conformation of the nucleic acid in solution, and (3) its nucleotide composition. The first factor determines the strength of ionic binding of the substance chromatographed to the adsorbent. The second and third factors determine the degree of hydrophobic interaction and the interaction via hydrogen bonding. The chromatographic behaviour of nucleic acids on MAK columns shows that the second and third factors play a more significant role in the separation of nucleic acids.

During elution in an NaCl concentration gradient from 0.2 to 1.2 M, nucleic acids are separated into fractions corresponding to their functions in the cell: tRNA, DNA, etc.[9,10]. The separation is carried out at 15—25°C and sometimes at 35°C. An increase of temperature is undesirable, since part of the nucleotide material is then retained by the adsorbent. A decrease of temperature is likewise undesirable in view of the less clear-cut separation. One should recall that the NaCl concentration at which the given type of nucleic acid is eluted can vary for different batches of Kieselguhr and methylated albumin, which can be accounted for by the different degrees of methylation of the albumin. However, the elution sequence [tRNA—DNA—(rRNA, mRNA)] does not as a rule change[9-12].

The elution profile depends on the source of nucleic acid. Thus, in the separation of bacterial nucleic acids on MAK columns, tRNA and both types of rRNA (16S and 23S) are satisfactorily separated from one another and the rapidly labelled RNA are separated into several fractions. In nucleic acids from animal tissues the rRNAs are separated somewhat less satisfactorily and mRNAs are eluted as a mixed fraction[10-11]. If the nucleic acid is denatured, it is eluted from the column at higher salt concentrations than the native form. This is true of both DNA [13-15] and RNA.[16-18] The yield of substance from the column is usually 90—100% for native preparations, but is much lower for denatured nucleic acids (50—70%),[13,14] and when the column is overloaded the deoxynucleotides for example, may not be eluted at all.[19]

The optimal separation conditions on an MAK-column are 0.5—2 mg of the nucleic acid mixture per 10 ml of the MAK suspension with an overall volume of the gradient solution of 800 ml. The methods of preparation of the adsorbents and the chromatographic techniques have been described[9,10,20-25]. In the preparation of the columns one can employ both bovine albumin[10,20,23-25] and human albumin[26,27]. Kieselguhr can be replaced by silica gel[17,28-31] (MASA-chromatography); the adsorbent capacity with respect to the amount of nucleotide material is then significantly increased[30,32].

Chromatography on MAK and MASA columns is also used to separate the nucleic acid fractions into individual components. In the separation of DNA the position of the DNA being eluted depends on the length of the molecule, its conformation, and nucleotide composition. DNA with long molecules and containing more guanine—cytosine pairs (GC pairs) are eluted at higher salt concentrations[24,32]. Certain types of DNA, for example those of *B. subtilis* and calf and mouse thymus are eluted at the same salt concentrations[33]. The *E. coli* and T2 and T4 phage DNA are satisfactorily separated from one another. The T5 phage DNA can be resolved into two components[8,34]. Glycosylation of the DNA bases leads to firmer binding to the sorbent[35].

Chromatography on MAK and MASA columns has been widely used for the separation of the native and denatured forms of DNA.[13,15,36-43]. With the aid of this method, it is possible to isolate DNA-RNA hybrids, the replicated forms of phage DNA and complementary DNA strands[44-47]. MAK chromatography has been proposed by Japanese investigators for the separation of tRNAs [48] and has been successfully used for the fractionation of tRNAs [49-58] from a wide variety of sources[16,22,25,26,49-58] and of its chemically modified derivatives[30,31,59].

Basic proteins and polypeptides adsorbed on Kieselguhr are also used as supports for the chromatography of nucleic acids[60-67]. The chromatographic profile and the characteristics noted previously (the effect of the molecular weight, nucleotide composition, etc.) in fractionation on these adsorbents are the same as in chromatography on MAK and MASA columns[68-71]. An interesting modification of the method is the separation on Celite of a ribonucleoprotein complex (RNP complex)[72]. The RNP proteins are then adsorbed on Celite and are not eluted from the column, while the RNA is fractionated as in the separation on MAK. The chromatography of DNA on protein powders from wool has been described[73]. The behaviour of DNA on such columns resembles its chromatography on MAK.

It is noteworthy that the principle of the chromatography of nucleic acids on proteins sorbed on carriers of the type of Kieselguhr or silica gel is extremely promising, since in this case separation is determined primarily by specific adsorption and hydrogen bonding forces. We believe that the employment for these purposes of other proteins, for example, immunoglobulins, etc. might significantly extend the scope of the fractionation of nucleic acids.

B. Adsorbents Based on Cellulose and Sephadex

In the separation of nucleic acids on ion-exchange polysaccharides the binding of nucleic acids to the resin via ionic interactions is stronger than for adsorbents containing methylated and basic proteins. For this reason, the effect of other factors (conformation and composition of the nucleic acid and non-ionic interactions with sorbent) on the separation is significant only for nucleic acids with a low molecular weight. High-polymer nucleic acids are adsorbed by anion exchangers so strongly that their elution requires high salt concentrations. For this reason, the separation of DNA and high-polymer RNA on ion-exchange celluloses and different types of Sephadex is comparatively rare[8,74,75]. These adsorbents have found extensive applications only in the fractionation of tRNA.[76-78] The chromatography of tRNA on diethylaminoethylcellulose (DEAE-cellulose)[76-85], triethylaminoethylcellulose (TEAE-cellulose)[86], and DEAE-Sephadex[76-78,87-99] has been used in numerous modifications (Table 1).

The behaviour of tRNA from *E. coli* and yeast on ion exchangers has been most thoroughly investigated. tRNA from *E. coli* is eluted from the column at higher salt concentrations, but the elution sequence of the tRNAs in terms

of their specificity with respect to a particular aminoacid is retained. Chromatography on polysaccharide anion exchangers is nowadays used in the first stage of the purification of tRNA. The method permits the separation in a single step of up to 100 g of the total tRNA.[100]

Table 1. Conditions in the separation of tRNA on ion-exchange resins.

Adsorbent	Separation conditions	Concn. of eluent for tRNA		Refs.
		from *E.coli*	from yeast	
DEAE-cellulose	pH 5.0; salt gradient	0.4-0.7 M NaCl	0.4-0.65 M NaCl	76
	pH 7.5; urea, salt gradient	0.33-0.40 M NaCl	0.28-0.35 M NaCl	76
	pH 7.5; 0.36 M NaCl, urea gradient	2-5 M urea	2-6 M urea	76
	pH 4.2; 7 M urea	0.35-0.45 M NaCl	0.30-0.40 M NaCl	76
	pH 4.2; 0.40 M NaCl urea gradient	1-6 M urea	1-6M urea	76
	pH 4.2; 4 M urea, salt gradient	0.42-0.53 M NaCl	0.38-0.50 M NaCl	76
	pH 6.0; 65°, salt gradient	0.8-1.6 M NaCl	0.8-1.3 M NaCl	77
TEAE-cellulose	pH 3.6; 38-40°, 7 M urea, salt gradient	–	0.35-0.55 M NaCl	86
DEAE-Sephadex	pH 6.0; 0.9 M NaCl, temperature gradient	65-20°	65-20°	77
	pH 7.5; 7 M urea, salt gradient	0.45-0.65 M NaCl	0.40-0.60 M NaCl	76
	pH 4.2; 7 M urea, salt gradient	0.55-0.75 M NaCl	0.49-0.65 M NaCl	76
	pH 4.5; salt gradient	0.5-0.80 M NaCl	0.5-0.85 M NaCl	76
	pH 5.3; 1% dimethylformamide, salt gradient	0.75-1.6 M $(NH_4)_2SO_4$*	–	94
	pH 6.2; 5% dimethyl formamide, 1 M phosphate 33°, salt gradient	0.45-0.4 M KCl*	–	94
	pH 7.5; salt gradient		0.37-0.52 M NaCl	95
	pH 7.2; salt gradient	0.375-0.525 M NaCl**	0.008-0.016 M $HgCl_2$	97

* tRNA from *I. utilis*.
** tRNA from rat liver.

The most effective separation of tRNA takes place in chromatography of benzoylated DEAE-cellulose (BD-cellulose). The use of this hydrophobic adsorbent increases the contribution of adsorption forces to the chromatographic separation process. BD-cellulose was first proposed for the separation of tRNA by Tener's group[101,102]. Effective fractionation of tRNA is observed (Fig. 1) for elution by salt solutions at low temperatures. The method has been widely used to isolate the individual tRNAs.[95,97,103-109]. The chromatographic profiles for tRNAs from different sources mainly give rise to similar patterns. Phe-, Cys-, Tyr-, Ser-, and Leu-specific tRNAs are retained on BD-cellulose more strongly than other tRNAs. Phenylalanine tRNA from yeast and rat liver is eluted at higher salt concentrations than the analogous tRNAs from *E. coli*[102,107] and halophilic bacteria[109]. The lower degree of adsorption can probably be accounted for by the absence from these tRNAs of the hydrophobic base Y, which has been found in the $tRNA^{Phe}$ from yeast and rat liver.

The employment of additional procedures—gradient elution by alcohol[110,111] and ether[112,113] solutions—in many instances improves the separation and increases the elution from the column. BD-cellulose proved to be extremely effective in the chromatography of DNA and other types of RNA.[8,114-117] A sorbent analogous to BD-cellulose was proposed recently by Osterman for the fractionation of tRNA.[118]

C. Hydroxyapatite

Hydroxyapatite (HA) is a weak anion exchanger, which permits its employment for the chromatography of anions. The range of applications of HA chromatography is fairly considerable: the behaviour of low- and high-molecular-weight and RNA and DNA from different sources on HA columns has been thoroughly investigated[119-144]. In the elution of nucleic acids from HA columns one usually employs a phosphate buffer at pH 6.8 (Table 2). However, more acid solutions have also been used for elution.

Table 2. The concentration of phosphate buffer and the recovery of nucleotide material from the column in chromatography on HA.

Substance	Concn. of phosphate buffer at pH 6.8, M	Recovery from column, %
Mononucleotides	0.001	100
Oligonucleotides	0.01—0.02	100
Polynucleotides		
polypyrimidine	0.1—0.12	100
polypurine	0.22—0.25	60—80
Polynucleotides in 1% formaldehyde	0.05—0.17	100
RNA	0.11—0.18	100
Denatured DNA	0.11—0.18	50—100
Native DNA		
from higher organisms	0.11—0.18	50—100
from bacteria	0.20—0.22	90
from phages	0.25—0.27	90

A significant factor in chromatography on HA is that the adsorption of nucleic acids is almost independent of the concentration of anions other than phosphate. For this reason, this method is very convenient in rechromatography after other procedures involving the separation and concentration of nucleic acids in salt solutions. One must make certain that the solutions do not contain substances forming complexes with Ca^{2+}. If a phosphate buffer containing other anions (for example Cl^-) is used in the elution of the test substance from HA columns, the concentration of phosphate at which nucleic acids are eluted from the column increases.[138,144] The separation is usually carried out at +4°C or at about 20°C.

In most cases the separation is independent of temperature. However, for certain polynucleotides, for example polyuridylic and polycytidylic, which have an ordered structure at low temperatures, the eluting concentration is higher at low temperatures than at 20°C.[138] An impression has been created that a polynucleotide with an ordered structure is eluted after the same polynucleotide whose secondary and tertiary structures have been disrupted[128,138,139,144]. The method permits the separation of denatured and native DNA,[128,135,139,144-154] of different isoacceptor tRNA,[123,129,130,131,133,140,143,155,156] and different

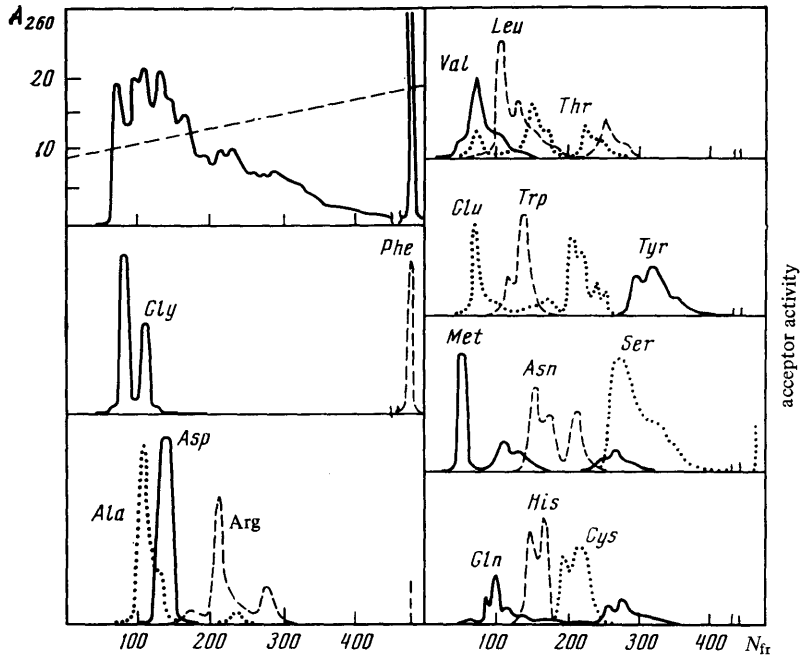

Figure 1. Fractionation of tRNA from *E. coli* on BD-cellulose[102].

forms of cyclic DNA.[157,158] Glycosylated DNA from T-even phages are retained more firmly on HA than the DNA from *E. coli* or from T-odd phages[138,159].

The behaviour of DNA on HA columns depends also on the nucleotide composition. The greater the number of GC pairs in the molecule the more firmly is it bound to HA.[128,139,144]

Both gradient and stepwise elution from HA has been used for the fractionation of nucleotide material. In connection with the stepwise fractionation of nucleic acids on HA, one should bear in mind the presence of "false fractions", i.e. fractions of the substance which on rechromatography are eluted at a lower molarity of the phosphate buffer[128,144]. To avoid this, it is useful to employ gradient elution.

A satisfactory separation requires 10 ml of HA per milligram of the nucleotide material for an overall volume of the gradient eluent of 200–300 ml. The optimal rate of elution is 0.1–0.2 ml min^{-1} cm^{-2}. The preparation of the sorbent and the chromatographic technique have been described[138,144,160-162].

D. Cation Exchangers with Charges Balanced by Polyvalent Metal Cations

Ion exchangers with charges balanced by the cations of polyvalent metals should have properties resembling those of weak anion exchangers of the type of HA. It has been noted that DNA is adsorbed from solutions by Amberlite IRC-50 electrically neutralised by Mg^{2+}. On elution, it was possible to isolate several DNA fractions differing in composition and sedimentation coefficient[163,164]. Chromatography of DNA on Amberlite IR-120 columns electrically neutralised by Al^{3+} leads to the isolation of seven DNA fractions differing sharply in their chromatographic properties[165-167]. The separation profile is independent of the protein impurities[168], RNA,[169] and the pH,[170] but does vary markedly as a function of the method of isolation of DNA,[171] which is probably due to the degradation of DNA during its isolation.

Chromatography on cation exchangers electrically neutralised by Al^{3+} appears to be very promising, since it permits the separation under mild conditions and does not entail the degradation of DNA. The elution of the nucleotide material from the resin is complete.

2. COUNTERCURRENT DISTRIBUTION AND REVERSED-PHASE CHROMATOGRAPHY

The separation of nucleic acids by countercurrent distribution has been proposed at the beginning of the 1960's and immediately proved useful as a qualitative method for the fractionation of DNA and different types of RNA.[172-179] This chromatographic technique has been most widely used for tRNA.[180-182] However, the complexity of the equipment, the small amounts of substances separated, and the fairly low resolving power greatly limited the scope of the method. The principle of countercurrent distribution has been used in chromatography in aqueous organic systems on different adsorbents. The adsorbent is saturated by the organic phase and is then transferred to a column and equilibrated with the aqueous phase. Systems for this type of chromatography were initially taken from studies on the countercurrent distribution of nucleic acids[183-190]. Partition chromatography on columns (reversed-phase chromatography) eliminated the above disadvantages of countercurrent distribution.

The introduction into the organic phase of ammonium salts containing aliphatic hydrocarbon residues significantly improved the resolving power of the method[191-194]. Chromatography on Chromosorb impregnated with tricaprylmethylammonium bromide in tetrafluoropropane (Freon) has been most widely used[192,195-198]. The application of a special type of PTFE impregnated with trioctylpropylammonium bromide[199,200], which was proposed recently, permits a satisfactory separation of tRNA (Fig. 2). The separation curves clearly show that the resolution of tRNA in the "reversed phase" is very promising.

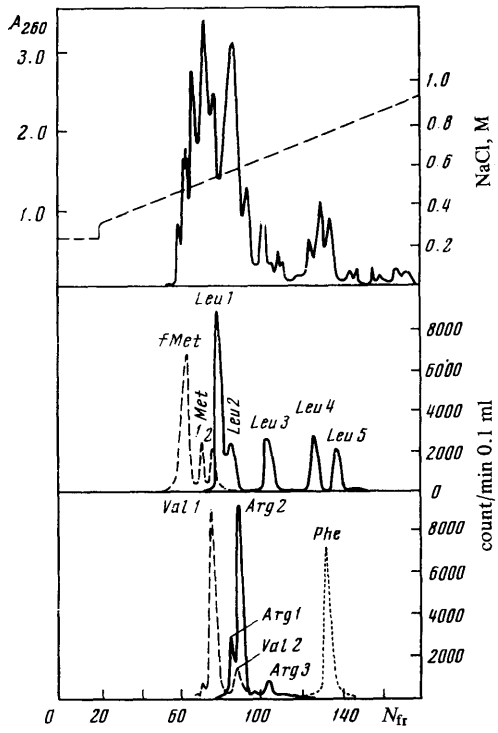

Figure 2. Chromatography of tRNA from *E. coli* on PTFE.[199]

It is noteworthy that reversed-phase chromatography can probably be used also for the fractionation of other types of nucleic acids, since it is well known that aliphatic amine salts of different types of nucleic acids are soluble in aqueous solutions at different NaCl concentrations[201].

3. AFFINITY CHROMATOGRAPHY

The name of this method comes from the English word "affinity", since this type of chromatography employs the interaction between two substances exhibiting affinity with respect to one another. One of these is in solution and the other is on an insoluble matrix (adsorbent). The test mixture is passed through a column containing the adsorbent under optimal conditions for the interaction of the fixed substance and one of the mixture components. In this interaction the adsorbent retains only the component which exhibits affinity with respect to the substance on the adsorbent. The remaining mixture components are not retained. Thus the substance exhibiting affinity with respect to that fixed on the adsorbent is separated from the remaining components of the mixture.

The application of affinity chromatography for the separation of polynucleotides and nucleic acids dates back to 1962 when two types of adsorbents were proposed at the same time. The first of these comprised gels containing nucleic acids (mechanical adsorption)[202] and the second consisted of cellulose with mono- and poly-nucleotides bound by covalent bonds (chemical binding)[203,204]. Mechanical adsorption in agar–agar[202,205-208], acetylated phosphocellulose[202], and polyacrylamide[209] gels permits the preparation of sorbents with a high content of nucleotide material. Nucleic acids and polynucleotides are within the grains.

The gels exhibit a high selectivity with respect to mRNA and adsorb from solutions only their "own" mRNA, while "foreign" mRNA is not retained[202-208]. The retained mRNA can be removed from the gels by a temperature gradient elution or by reducing the ionic strength. The mRNA fractions with a high GC content are then eluted from the column at a higher temperature[207]. Polyuridylic acid in polyacrylamide gel forms complexes with oligo- and poly-adenylic acids[209].

The simplicity of the preparation of the gels containing polynucleotides and the fairly mild conditions in their preparation, which tend to preserve the native form of nucleic acids, constitute undoubted advantages of the mechanical method of preparation of affinity adsorbents. It is noteworthy that in this case adsorption from solutions can be observed only for substances with a lower molecular weight than that of the nucleotide in the gel. This disadvantage can be eliminated by employing gels whose grains are coated on the outside by polynucleotide molecules and are then "cross-linked" to one another under the influence of ultraviolet irradiation[210-212]. It is noteworthy that the gels frequently have a low mechanical strength. These disadvantages must be borne in mind in experiments with these materials.

Nitrocellulose is also used as an adsorbent for the affinity chromatography of nucleic acids. Under certain conditions, nitrocellulose is known to bind irreversibly denatured DNA. The nature of the binding is unknown, but neither native DNA nor RNA are retained by nitrocellulose. Low-molecular-weight fragments of denatured DNA are not sorbed by nitrocellulose[213]. Denatured DNA immobilised by nitrocellulose binds selectivity polynucleotides with affinity for DNA. This method can be used to investigate the formation of complexes with DNA.[214-223]

Proteins immobilised by nitrocellulose, particularly the aminoacids of tRNA ligase, permit the investigation of the complexes of these enzymes with tRNA and the isolation of enriched tRNA preparations[224,225].

Mention should also be made of DNA immobilised by cellulose as a mechanical affinity sorbent[225,226]. However, this sorbent is so far used widely only for the purification of proteins forming specific complexes with nucleic acids[226-229].

The affinity chromatography of nucleic acids and polynucleotides has been widely used on sorbents containing covalently bound polynucleotides. Such sorbents are synthesised by the condensation of cellulose or phosphocellulose with mono-[203,230-232], oligo-, and poly-nucleotides[204,230,232-235], RNA,[204,230,232] and DNA [236-238] in the presence of dicyclohexylcarbodiimide or Sepharose treated

with cyanogen bromide[239]. RNA—DNA complexes[236-238], the purification of tRNA,[235] and the separation of poly- and oligo-nucleotides[231,233-235] can be investigated by chromatography on such adsorbents.

The employment of enzymes covalently bound to Sephadex[240], and of mercury-containing adsorbents which are capable of specific binding of DNP complexes containing SH groups[241,242], for the chromatography of nucleic acids has also been described. To isolate polynucleotides with a free *cis*-glycol group at the 3′-end of the molecule, one can use borate-containing cellulose[243,244].

Thus it is evident that affinity chromatography can be used successfully to fractionate various nucleic acids and polynucleotides. In contrast to the methods described previously, this type of chromatography makes it possible to employ more refined mechanisms for separation—the affinity of the substance to be isolated for a specially prepared adsorbent. In the application of this affinity, one can use a specific reactive group (the affinity of the SH groups of DNA for the terminal ribose residue), the complementary interaction forces (RNA—DNA complexes, polynucleotide interactions), and the formation of complexes with proteins.

4. GEL FILTRATION AND OTHER SEPARATION METHODS

The separation of nucleic acids on Sephadex and polyacrylamide gels is used only for the partial elimination of other types of nucleic acids and low-molecular-weight compounds. Gel chromatography has been most widely used for the purification of tRNA [245-255] and even partial fractionation of tRNA is then observed[256,257]. The method is likewise suitable for the isolation of large tRNA fragments and for the investigation of their interaction with one another[258,259]. Gel filtration is of limited applicability to nucleic acids with large molecular weights, since their aqueous solutions are very viscous, which greatly hinders chromatographic separation by this procedure.

Nucleic acid fractionation methods, such as paper and thin-layer chromatography, have found only limited applications[260-262].

III. OLIGONUCLEOTIDES

Recently the development of methods for the fractionation of oligonucleotides has been determined by trends associated with the elucidation of the structures of nucleic acids and their fragments responsible for important biochemical functions and by studies on the synthesis of oligonucleotides and nucleic acids. The advances in this field (the determination of the structures of more than 50 tRNAs, of several 5S RNAs, and of large fragments of ribosomal and viral RNA, the synthesis of the DNA copy of alanine tRNA, etc.) can be accounted for in many respects by the achievements in the development of micromethods for the fractionation of oligonucleotides, Column, paper, and thin-layer ion-exchange chromatography, partition paper and thin-layer chromatography, and combinations of these methods with electrophoresis have found extensive applications in the separation of nucleotides.

1. ION-EXCHANGE CHROMATOGRAPHY

The method has a high resolving power and can be used on both preparative and analytical scales. The main factor determining separation is the overall charge of the nucleotide. This quantity can be readily calculated[263,264] at different pH using the pK of the ionic groups of the nucleotides. Since the force of binding to the adsorbent is determined primarily by the charge of the oligonucleotide (the higher the charge the stronger the binding), it follows that, having determined this quantity, it is possible to predice the mobility of the oligonucleotides relative to one another under the conditions of the separation. The sequence of the elution of the oligonucleotides from the column based on the calculation of the charges will undoubtedly be approximate, since, apart from the ionic interaction with the adsorbent, hydrophobic and hydrogen bonding interactions are also observed. However, calculation of the charges of the nucleotides is in many cases undoubtedly useful, since it permits the selection of the optimal pH for the separation.

The literature data for oligonucleotide chromatographic fractionation systems lead to the conclusion that single-stage ion-exchange column chromatography yields satisfactory results only for simple mixtures of oligonucleotides and is insufficiently effective for complex mixtures. In such cases repeated fractionation is necessary.

The principles of the selection of the binary systems (two-dimensional column chromatography), put forward in 1963,[263] proved to be justified in the separation of complex oligonucleotide mixtures[265-270].

In the selection of the binary systems it is desirable to employ different types of adsorbents and to carry out the separation at significantly different pH values. Satisfactory results have been obtained in the successive separation at initially neutral pH values in aqueous solutions of salts in 7 M urea (chromatography by Tener's method)[271-273] on DEAE-cellulose or TEAE-Sephadex and then either in an acid or in an alkaline medium for adsorbents of any type. In 7 M urea solution in the pH range 5.4—8.0 mixtures of oligonucleotides are resolved into fractions, each of which contains an identical number of nucleotide residues (mono-, di-, and tri-nucleotides, etc.). This system can be used to separate both ribo- and dioxyribo-oligonucleotides[271-276] and gives a satisfactory resolution of the fractions down to decanucleotides. Other conditions being equal, best results are achieved on DEAE-Sephadex[266,270]. The use of urea is not obligatory for homo-oligonucleotides[277,278].

The separation in an acid medium is usually carried out at pH 2—5. Among the adsorbents which give rise to the best results mention may be made of Dowex-1,[263,268,279] DEAE-cellulose[275,280,281], DEAE-Sephadex[263,264,270], and TEAE-cellulose[282]. DEAE-Sephadex and DEAE-cellulose are as a rule employed in fractionation in an alkaline medium. A satisfactory separation is observed at pH 8.5—9.0.[263,283,284] As an example of the two-dimensional fractionation of oligonucleotides, one may quote the separation of the oligonucleotides in the pyrimidyl-ribonuclease (pyridyl-ribonuclease) hydrolysate of tRNA^{Val} from yeast[285] (Fig. 3).

It is noteworthy that in both acid and alkaline media the individual isomeric oligonucleotides are separated[263,286].

A few words should be said about chromatography on hydroxyapatite. This sorbent was proposed recently for oligonucleotides[144,287,288]. The efficiency of the separation of oligonucleotides on HA in 7 M urea in a phosphate buffer concentration gradient (0.001—0.2 M) at pH 6.8 is higher than in chromatography by Tener's method on DEAE-Sephadex.

In order to achieve a satisfactory resolution in the fractionation of oligonucleotides on ion-exchange resins,

the separation is usually carried out on columns with a diameter : height ratio in the range from 1 : 10 to 1 : 50, an amount of the gradient eluent equivalent to 100—200 column volumes, and a rate of elution of 0.2—0.6 ml min^{-1} cm^{-2}. It is then desirable to employ an adsorbent whose particles have the same dimensions. The accounts of methods of fractionation of ion exchangers with respect to dimensions published by Hamilton[289] and Koprda and Fojtik[290] may be recommended. The homogeneity of the dimensions of the adsorbent particles (a scatter of 5—10 μm) is particularly necessary in experiments on columns and on the ultramicroscale.

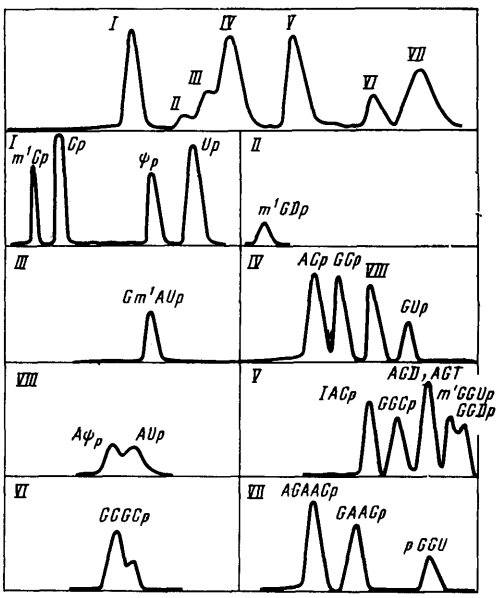

Figure 3. Separation of the oligonucleotides in the pyrimidyl-ribonuclease hydrolysate of $tRNA_1^{Val}$ from yeast on an ultramicroscale[285].

The sensitivity of the chromatographic column methods may be increased in two ways—by increasing the sensitivity of the detector[291] and by reducing the scale of the chromatographic process. The decrease of the chromatographic scale permits the reduction of the amount of the substances to be separated by 2—3 powers of 10 for the same detector sensitivity[285,291]. Thus, in experiments on 0.6 × 100 mm columns and with 300 μl of the gradient eluent, it is possible to separate 10^{-7}—10^{-9} mole of nucleic acids and oligonucleotides[285,292-294]. A significant factor in experiments on the ultramicroscale is that published chromatographic systems, tested on large amounts of substances[285,292-294], can be used.

The fractionation of oligonucleotides on ion-exchange papers[295-298] is less common than column chromatography, since it does not allow the application of gradient elution and has a lower resolving power. Moreoever, the low mechanical strength of ion-exchange paper makes this method relatively unpromising. As a result, chromatography on ion-exchange papers is hardly used nowadays as an independent method.

The disadvantages of fractionation on ion-exchange papers were eliminated by the fractionation of oligonucleotides in thin layers of ion-exchange cellulose. The application of this method to the components of nucleic acids is due to Randerath[299-302]. The ease of preparation of the sorbents and the simplicity of the preparation of the plates make this method extremely attractive. The thin-layer chromatography of oligonucleotides is usually carried out on polyethyleneimine cellulose (PEI-cellulose) in two-dimensions. The sensitivity of the method with the detection of fractions based on ultraviolet absorption is extremely high, amounting to 0.5—1 μg of the substance in the spot and can be significantly improved by using radioactive preparations *in vivo* or by the artificial introduction of a radioactive label, as suggested for oligonucleotides[303,304]. Thin-layer chromatography on PEI-cellulose is distinguished by a high resolving power[305-307] (Fig. 4).and does not require either complicated equipment or long separation times. Moreover, mixtures of PEI-cellulose with other adsorbents, for example with cellulose[308], can be used to prepare the plates, which gives rise to great possibilities for varying the separation conditions.

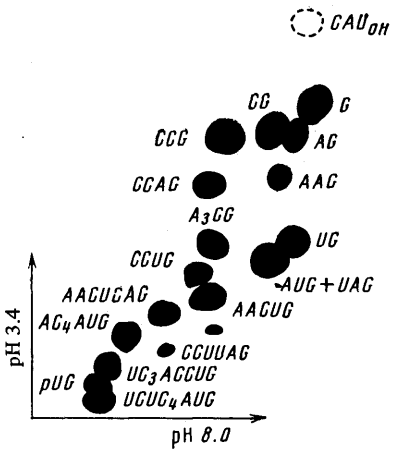

Figure 4. Separation of the pyrimidyl-ribonuclease hydrolysate of 5S RNA from *E. coli* on PEI-cellulose plates[307].

Various salt systems are used to develop the chromatograms[305,306,309,310]. To facilitate the experiment, one frequently employs volatile buffer solutions based on pyridine, or based on lithium salts, since these are effectively extracted by methanol. This makes it easy to desalinate the oligonucleotides directly on the plates. Unfortunately, thin-layer chromatography on PEI-cellulose is still not used on a sufficiently large scale for the fractionation of oligonucleotides. However, advances in the separation of various mixtures of oligonucleotides[305-310], studies on the formation of complexes by polynucleotides with oligonucleotides[311], and also the excellent results obtained in the separation of complex mixtures of long oligonucleotides in combination with electrophoresis (see below) make it possible to state confidently that the fractionation of oligonucleotides in

thin layers of PEI-cellulose is one of the most promising separation procedures. The preparation of adsorbents for thin-layer chromatography and the technique of the separation have been described[305,312-314].

2. PARTITION CHROMATOGRAPHY

The chromatography of oligonucleotides on various adsorbents in aqueous organic media is not a new method. It was discovered at the beginning of the 1950's but it still has not lost its importance in the study of nucleic acids and their components. The classical version of this chromatography—two dimensional paper chromatography—has played a significant role in the study of the structure of tRNA [315-319] and in the analysis of the cleavage products of DNA.[320,321] The commonest solvent system is isobutyric acid—0.5 M NH_3 at pH 3.7 for chromatography in one direction and either a 1:1 butanol—formic acid mixture at pH 3.8 [315,317-319,321] or a mixture of butanol with volatile buffers[316,320,322] for chromatography in the other direction. Apart from the above systems, solvents containing acetonitrile[323] and ethanol[324] can be recommended for the separation of simple mixtures of oligonucleotides. The knowledge or the R_f values in different systems for synthetic oligonucleotides and their derivatives may be of great assistance to chemists engaged in synthesis[325-336].

The solvent systems used in paper chromatography have proved extremely effective also in the separation of oligonucleotides in thin layers of cellulose[337-339] and silica gel[336,340]. Nevertheless partition chromatography is nowadays rarely used, since, in view of the availability of other methods of separation, the difficulties associated with the desalination of the oligonucleotides before and after separation make the experiments on the separation of oligonucleotides by this procedure extremely laborious.

3. ELECTROPHORESIS AND VARIOUS COMBINATIONS OF CHROMATOGRAPHIC METHODS

The presence of a negative charge on oligonucleotides permits their separation by electrophoresis. At a potential gradient E the oligonucleotide molecule migrates to the anode. The rate of migration V is described fairly satisfactorily by the equation $V = EQ/K$, where E is the potential gradient, Q the overall charge of the oligonucleotides, and K a constant which depends on the dimensions and shape of the molecule and on the medium in which the separation takes place (adsorbent, composition of the ions, etc.). K increases with the ionic strength of the buffer solution in which the separation takes place and decreases with increase of temperature[341,342]. If the electrophoresis is carried out on a neutral carrier, for example on paper or in a thin layer of cellulose, the rate of migration is higher the higher the overall charge of the substance. A different picture arises when the electrophoresis is carried out on ion-exchange columns. In this case the rate of migration of the substance is higher the smaller its charge. The decrease of the rate of migration of substances with a large charge is due to the fact that they are more firmly retained by the ionic groups of the carrier. Both types of carriers are used to fractionate oligonucleotides.

Best results are obtained when the electrophoresis is carried out in an acid medium in two perpendicular directions on acetylated cellulose and DEAE-paper. In this version the method was proposed for the first time by Sanger et al.[343] for [^{32}P]-oligonucleotides. The separation on acetylated cellulose is carried out in a pyridine—acetate buffer at pH 3.5 or in the same buffer in 7 M urea[343-348]. The technique of the electrophoresis has been described[342-354].

DEAE-paper[349] at pH 9.7 is also used instead of cellulose acetate. The replacement of the acetylated cellulose by Whatman 3 MM paper leads to somewhat worse separation[350].

The solvents employed for separation in the second direction are a mixture of 2.5% formic acid and 8.7% acetic acid (by volume) at pH 1.9, 7% formic acid[344-347], or a buffer solvent at pH 3.5 and 6.5.[346,349] The electrophoresis is carried out on DEAE-cellulose[343-349], aminoethylcellulose (AE-cellulose) and ECTEOLA-cellulose[349].

Sanger's method gives a satisfactory separation with a resolution of up to 200 fractions of oligonucleotides (Fig. 5) and has been widely used to analyse the structures of nucleic acids.

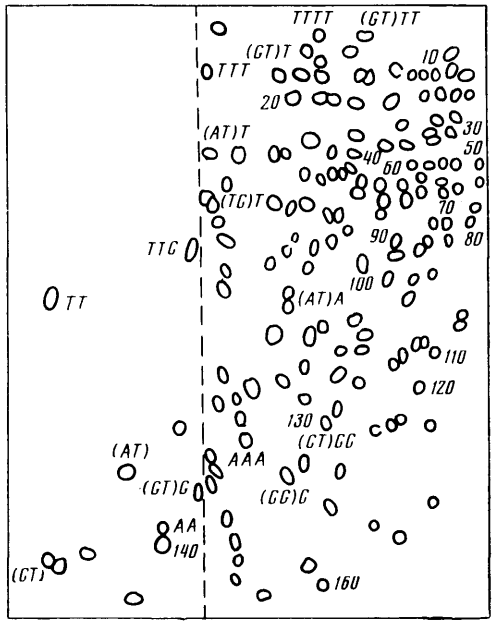

Figure 5. Separation of [^{32}P]-deoxyribo-oligonucleotides by two-dimensional high-voltage electrophoresis[349].

Interesting modifications of this method involve the employment of the electrophoresis in combination with ion-exchange chromatography on thin layers of PEI-cellulose[306,308] and the "homochromatographic" method[351-356]. The essential feature of "homochromatography" is as follows. When a plate with a thin layer of ion-exchange cellulose is placed with one end dipping in a solution of a mixture of oligonucleotides and the solution is allowed to rise a certain distance, the oligonucleotides are separated in the following way along the plate. At the top of the plate are the mononucleotides with the dinucleotides below, etc. i.e. the oligonucleotides are distributed in bands of equal chain length.

Hence the name of the method—"homochromatography". It is noteworthy that this distribution in bands of substances of equal chain length is possible only if the amount of oligonucleotide is greater than the capacity of the ion exchanger bands, since only then would longer oligonucleotides displace shorter oligonucleotides in consequence of their less strong binding to the ion exchanger.

In the chromatography of [^{32}P]-oligonucleotides in "homomixtures" of non-radioactive oligonucleotides an effective separation of long oligonucleotides (down to 40–50 nucleotide residues and less) is achieved. The fractionation is carried out at elevated temperatures (50–60°C), which gives rise to better equilibration and rules out the possibility of the formation of complexes by complementary oligonucleotides. The compositions of the "homomixtures" have been published[294,345,351,352].

The two-dimensional method for the fractionation of oligonucleotides permitted the determination of the structures of a number of tRNA,[354,357-367] low-molecular-weight RNA,[317,351,368-370] large fragments of 16S and 23S ribosomal RNA,[346,371,372,379] and phage RNA.[353,373-378] The possibility of the employment of this method for the analysis of the DNA structure has also been demonstrated[349,355,356]. One disadvantage, associated with the impossibility of identifying the substance by ultraviolet spectroscopy, which is particularly important for minor components, is not of fundamental importance. For nucleic acids which are difficult to obtain in a radioactive form, a radioactive label may be introduced into the terminal nucleotide[303,304,379], which greatly extends the scope of the method. The method is undoubtedly one of the best for the fractionation of oligonucleotides.

IV. NUCLEOTIDES

1. THIN-LAYER CHROMATOGRAPHY

A. Cellulose

This method is apparently most widely used at present for the analysis of mixtures of nucleotides, nucleosides, and nucleic acid bases. The preparation of cellulose layers has been described in fair detail in reviews[305,380-383] and other publications[384-387].

Randerath carried out a comparative separation of nucleotides in a thin layer of cellulose and on paper in four different solvents under identical conditions[384,388]. He established that the solvent systems developed for paper can be used for separation on a thin layer.

A multiplicity of systems have been used for the fractionation of nucleotides in a thin cellulose layer[380,382,385-390]. The corresponding R_f values for certain solvents are listed in Table 3. In most cases, the nucleotides are separated both with respect to the bases and with respect to the carbohydrate residue. To achieve a satisfactory reproducibility of the results, the specimen to be chromatographed must be neutralised and freed from salts and proteins[385]. In the separation of nucleotides with similar R_f values one can re-run the solvent in the same direction.

Nucleotides are satisfactorily separated by two-dimensional chromatography[385,390-395] or by a combination of thin-layer chromatography and thin-layer electrophoresis[337,396-398]. For example, Bergquist[337] separated the enzymatic tRNA hydrolysate by electrophoresis in one direction (phosphate buffer, pH 2.45), then by chromatography in another direction using the 50 : 50 : 2 t-butyl alcohol–0.08 M formic acid–isopentyl alcohol solvent system, and finally by chromatography again in the same direction using the 86 : 14 n-butyl alcohol–water solvent system. All four ribonucleotides and the isomeric 5'- and 3'-phosphates of adenylic and guanylic acids were separated by thin-layer electrophoresis and subsequent chromatography on cellulose using the 80 : 18 : 2 saturated ammonium sulphate–1 M sodium acetate–isopropyl alcohol solvent system[396]. This method was also used for determining the nucleotides composition of RNA. The R_f values for each nucleotide have been published[396].

Table 3. The R_f values in the chromatography of ribonucleotides and deoxyribonucleotides in a thin layer of cellulose[385,395].

Nucleotide	Solvent I	II	III	IV	Nucleotide	Solvent I	II	III	IV
AMP	0.34	0.34	—	0.38	dAMP	0.25	0.27	0.07	0.54
CMP	0.39	0.73	—	0.34	dCMP	0.53	0.63	0.09	0.49
GMP	0.26	0.53	—	—	dGMP	0.15	0.47	0.05	0.33
UMP	0.62	0.71	—	0.37	dTMP	0.89	0.54	0.18	0.58

Solvent composition: I) Isopropyl alcohol–HCl–water (65 : 16.7 : 18.3); II) n-butyl alcohol–water (86 : 14); III) n-butyl alcohol–water–90% formic acid (60 : 30 : 10); IV) n-butyl alcohol–acetone–acetic acid–5% aqueous ammonia–water (3.5 : 2.5 : 1.5 : 1.5 : 1.0 for deoxyribonucleotides and 4.5 : 1.5 : 1 : 1 : 2 for ribonucleotides).

Two-dimensional chromatography in various solvent systems permits a successful separation of the alkaline hydrolysates of RNA [396-400] or enzymatic hydrolysates of DNA.[401]

B. Silica Gel

Among inorganic sorbents, silica gel is frequently used in the chromatographic analysis of nucleic acid components, usually without a binder[402-420], although in some cases binders are also employed[421-428]. The separation on silica gel is as a rule poorer than on cellulose[300,381,384,426,427] and therefore it is rarely employed for analytical purposes and for the separation of unprotected derivatives. However, since the capacity of silica gel layers greatly exceeds that of cellulose, separation on silica gel is frequently used for preparative purposes, particularly in the case of synthetic derivatives of nucleic acids[402,415,418,419,426]. Various silica gels are employed for the separation[426-432]. The R_f values for nucleotides have been published[426]. Nucleoside 2'(3')-monophosphates can be separated from the 5'-phosphates but neither can be separated with respect to the bases. When the solvent is rerun in the same direction, the separation is improved. Silica gel treated with 5% tetraborate has been suggested for the fractionation of a mixture of adenosine, 3'- and 5'-adenylic acid, and cyclic AMP.[411]

The separation of the nucleotides in an alkaline hydrolysate of RNA was achieved by employing a 9 : 1 mixture of cellulose and silica gel[433]. Under these conditions, the presence of salts in the hydrolysate had hardly any influence on the separation of the nucleotides.

C. Ion-Exchange Resins

Methods for the chromatography of nucleotides and their derivatives in a thin layer of ion-exchange cellulose have been rapidly developed and adopted in the last 10 years. Ion-exchange celluloses can be prepared by treating unmodified or modified cellulose with high-molecular-weight basic or acid derivatives[391,434].

A comparative study of the fractionation of nucleotides and oligonucleotides on various kinds of ion-exchange cellulose[434-437] showed that cellulose treated with PEI is superior to other ion-exchange celluloses as regards the clear-cut separation of compounds. Evidently the results of the separation depend on the PEI-content, which determines the capacity of the layer[438]. A satisfactory separation has been achieved on layers containing 0.5—1% PEI,[380,388,435,438]. Cellulose plates prepared as described by Randerath are usually employed[309,311,380,388,391,435,436,438].

In contrast to layers of unmodified cellulose, a large volume of solution may be deposited on a PEI-cellulose plate without partial drying, since nucleotides are fairly firmly bound to the ion exchanger and are therefore concentrated in the centre of the spot. It was noted that, for optimal separation of nucleotides, the pH of the specimen deposited should be approximately equal to that of the first solvent[439]. The solutions analysed must be very dilute. For analytical purposes, it is best to employ concentrations ranging from 0.0005 to 0.005 M and in micropreparative studies (with several milligrams of the test substance) from 0.005 to 0.02 M.[305]

Nucleotides are separated on PEI-cellulose plates with development by aqueous electrolyte solutions[305,438,440-449]. In certain cases organic solvents are added to electrolyte solutions[305]. Both stepwise and continuous gradient elution is usually carried out in the fractionation of nucleotides. The mobility of each substance is largely determined by the negative charge, which depends on the pH. Best and most clear-cut results in the separation of nucleotides are obtained at acid pH (1—3 M formic acid with added LiCl).[305,438,439,443]. Table 4 lists the R_f values for various mononucleotides.

Mixtures of nucleotides can be successfully separated by the stepwise elution with a solvent at an increasing electrolyte concentration[438]. The first solvent is allowed to rise to a certain height after which the plate is transferred, without drying, to a chamber with another solvent, etc. Alkaline RNA hydrolysates and mixtures of nucleoside 5′-monophosphates are separated with the aid of one-dimensional chromatography on PEI-cellulose layers using stepwise elution with acetic acid and LiCl solutions[309,444]. The rate of migration of the components of the alkaline RNA hydrolysate decreases in the following sequence: nucleosides > 2′- + 3′-CMP, 2′-AMP > 3′-AMP > 2′- + 3′-UMP > 2′- + 3′-GMP. The same elution sequence holds for the 5′-isomers and the corresponding derivatives containing deoxyribose[380,444]. Sometimes elution using a salt concentration gradient is employed[440-445].

In the stepwise chromatography of a mixture of nucleoside mono-, di-, and tri-phosphates in 0.6, 0.8, and 1.25 M NaCl without intervening drying of the plates, a clear-cut separation of these derivatives is achieved[310,436,446,447].

The components of alkaline RNA hydrolysates are usually satisfactorily separated by continuous ascending chromatography[380,440]. The technique employing a continuous linear salt gradient has been described in fair detail[448].

Deoxyribonucleotides can be separated from ribonucleotides in solvents containing borate[437,438,450-452]. The borate complexes of ribonucleotides have an additional negative charge and move more slowly than deoxyribonucleotides[438]. The following solvent systems are usually employed in the separation of ribonucleotides and deoxyribonucleotides: 2 : 1 2% H_3BO_3—2 M LiCl for nucleoside monophosphates and 4 : 3 4% H_3BO_3—4 M LiCl for nucleoside triphosphates[438,453]. Since satisfactory fractionation of deoxyribonucleotides is achieved in the reverse system, it is sometimes used to separate enzymatic DNA hydrolysates[442,453,454].

Table 4. The R_f values (×100) for nucleotides and their derivatives in thin-layer chromatography on PEI-cellulose[380,438].

Substance	Solvent*												
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII
AMP	11	52	65	68	80	80	80	80	80	80	61	69	74
IMP	13	59	74	40	60	73	80	19	53	78	04	52	72
GMP	06	40	51	28	45	57	65	41	50	72	07	45	62
CMP	15	64	75	70	80	80	80	80	80	80	76	79	80
UMP	20	74	80	51	72	80	80	20	64	80	06	62	77
ADP	00	26	54	03	10	32	75	03	29	70	00	19	52
IDP	00	30	63	00	04	14	49	00	03	55	00	05	30
GDP	00	17	45	00	02	09	34	00	13	61	00	05	27
CDP	00	33	64	03	20	45	80	04	35	73	00	26	56
UDP	00	41	71	02	07	24	60	00	11	60	00	08	40
ATP	00	00	34	00	00	04	24	00	04	33	00	01	12
ITP	00	09	39	00	00	02	11	00	02	17	00	00	05
GTP	00	05	25	00	00	00	07	00	02	24	00	00	05
CTP	00	11	41	00	02	05	29	00	04	37	00	02	16
UTP	00	14	49	00	00	02	17	00	02	20	00	01	07

*Solvent composition: I) 0.25 M LiCl; II) 1.0 M LiCl; III) 1.6 M LiCl; IV) 0.5 M sodium formate—formic acid buffer, pH 3.4; V) 1.0 M sodium formate—formic acid buffer, pH 3.4; VI) 2.0 M sodium formate—formic acid buffer, pH 3.4; VII) 4.0 M sodium formate—formic acid buffer, pH 3.4; VIII) 1.0 *N* HCOOH; IX) 2.0 *N* HCOOH—0.5 M LiCl; X) 2.0 *N* HCOOH—2.0 M LiCl (1 : 1); XI) 1.0 *N* CH_3COOH; XII) 1.0 *N* CH_3COOH—3 M LiCl (9 : 1); XIII) 1.0 *N* CH_3COOH—4 M LiCl (8 : 2).

Mixtures of nucleotides or RNA hydrolysates can also be fractionated by two-dimensional chromatography on PEI-cellulose layers[439,449]. Before passing the second solvent, it is important to remove the first from the plate. Randerath[380,438] proposed previously that, after drying, the plate be washed with methanol for this purpose. However, when a volatile solvent is used in the first direction, for example formic acid, it is sufficient to simply dry the plate before the second chromatographic step[439]. A mixture of ribonucleotides containing various nucleoside mono-, di-, and tri-phosphates was fractionated by ascending two-dimensional chromatography and PEI-cellulose[455] (Fig. 6). Stepwise elution by LiCl solutions was used in the first direction and stepwise elution by a sodium formate buffer (pH 3.4) in the second direction. The entire separation of the nucleotide mixture lasts about 3 h. The fractionation of a complex mixture of ribonucleosides and deoxyribonucleoside triphosphates by two-dimensional chromatography has been described[450]. In later studies[452,456-458] analogous chromatography was used to separate biological materials. For best separation,

extracts from the biological material are sometimes subjected to preliminary purification before chromatography, but in most cases chromatography is carried out without such purification. The chromatography of specimens containing large amounts of salts has been described by Foster et al.[441]

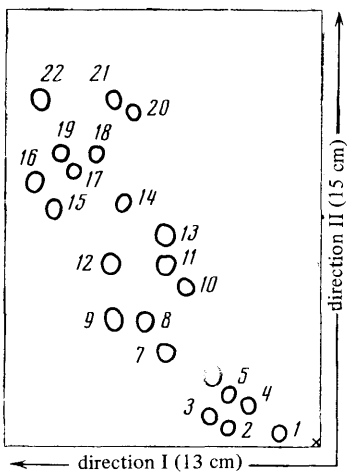

Figure 6. Two-dimensional chromatography of nucleotides on a PEI-cellulose layer. First direction: 0.2 M LiCl for 2 min, 1 M LiCl for 6 min, and 1.6 M LiCl up to 13 cm. Second direction: 0.5 M buffer for 30 s, 2 M buffer for 2 min, and 4 M buffer up to 15 cm (sodium formate buffer, pH 3.4)[455]: 1) GTP; 2) ITP; 3) UTP; 4) ATP; 5) CTP; 6) GDP; 7) IDP; 8) UDP; 9) UDPGA; 10) ADP; 11) CDP; 12) GDPM; 13) GMP; 14) IMP + TPN; 15) UDPG; 16) UDPAG; 17) ADPG; 18) UMP; 19) CDPG; 20) AMP; 21) CMP; 22) DPN.

Since PEI-cellulose has a high capacity, it can be used also in micropreparative separations. Layers 1–1.5 mm thick, which permit the fractionation of milligram amounts, are used for this purepose[305,438]. In thin-layer chromatography the fractions are desalinated by washing the entire plate with methanol and subsequent elution (usually with volatile buffers or with dilute HCl solutions) of the individual spots[380,438,439]. For the standard method of preparation of the plates, the average deviations of the R_f values do not exceed those for the usual thin-layer chromatography, amounting to ±0.005–0.025 on the basis of 10 determinations[459]. However, the reproducibility of the R_f depends on the amount of cellulose. When the plates are stored for about 100 days (in the dark at room temperature), the R_f values hardly change[459].

Quantitative extraction of nucleotides from a PEI-cellulose layer has been described in fair detail[380,382,442,443,458,460]. The optimal amounts of substances for a quantitative determination are 5–50 nanomoles[380,442]. The sensitivity of the method can be greatly improved and substances in amounts down to 1 nanomole and less can be determined by reducing the volume of the eluent and by measuring the absorption in microcuvettes or by employing a radioactive label[443,458].

Together with cellulose, DEAE- and ECTEOLA-cellulose layers have been used for the analysis of ribonucleotides and deoxyribonucleotides phosphorylated to different extents[385,392,440,461-481]. The principal advantage of these celluloses is the rapidity of separation. For example, a mixture of 10^{-2} mole of ADP and ATP is separated in 4–5 min on ECTEOLA-cellulose[461,464,467]. The preparation of DEAE-cellulose[302,385,440,463] and ECTEOLA-cellulose[462,475] plates has been described. Dilute solutions of hydrochloric or formic acids are usually employed as eluents[302,385,392,461,463,464,467]. The use of dilute sodium chloride solutions gives a less clear-cut separation[461]. Randerath[461,464] claims that DEAE- and ECTEOLA-cellulose layers give approximately identical results, the fractionation on an ECTEOLA-cellulose layer being the faster.

The rate of migration of different nucleotides decreases in the sequence C > A > G > U. Adenine and cytidine nucleotides with the same content of phosphate groups are poorly separated in a dilute acid, but can be separated in 0.1 M NaCl.[461,464] The R_f values for mono-, di-, and tri-nucleotides on DEAE-cellulose in dilute formic or hydrochloric acid solutions are listed in Table 5.

Table 5. The R_f values for nucleoside mono-, di-, and tri-phosphates in thin-layer chromatography on DEAE-cellulose[461,463,467].

Substance	In hydrochloric acid				In formic acid		
	0.01 *N*	0.02 *N*	0.03 *N*	0.04 *N*	1%	4%	10%
AMP	0.45	0.65	—	—	0.87	0.96	0.97
ADP	0.24	0.48	0.68	—	0.19	0.49	0.68
ATP	0.06	0.11	0.20	0.56	0.01	0.03	0.11
GMP	0.36	0.60	0.75	—	0.55	0.73	0.87
GDP	0.09	0.27	0.51	—	0.04	0.18	0.56
GTP	0.05	0.07	0.14	0.41	0.01	0.01	0.06
CMP	0.46	0.65	—	—	0.90	0.96	0.97
CDP	0.31	0.53	—	—	0.35	0.55	0.71
CTP	0.09	0.13	0.31	0.64	0.10	0.05	0.16
UMP	0.31	0.49	—	—	0.33	0.51	0.68
UDP	0.07	0.15	0.25	—	0.02	0.06	0.14
UTP	0.04	0.04	0.08	0.18	0.01	0.01	0.02
IMP	—	—	—	—	0.33	0.54	0.76
IDP	—	—	—	—	0.03	0.07	0.23
ITP	—	—	—	—	0.01	0.01	0.04
Inorganic phosphate	—	—	—	—	0.44	0.67	0.81

Satisfactory results are obtained in the analysis of a mixture of ribonucleotide and deoxyribonucleotide mono-, di-, and tri-phosphates with identical heterocyclic bases by two-dimensional chromatography on DEAE-cellulose. A clear-cut separation with respect to the number of phosphate groups takes place in the first direction and with respect to the sugar residue in the second[385,465].

The employment of two-dimensional gradient elution (1.0 M NH_4HCO_3–0.15 M NH_4HCO_3 for the first direction and 2.0 M NH_4HCO_3 at pH 4.2–0.2 M NH_4HCO_3 at pH 2.8 for the second) permits the separation of a mixture of the mono-, di-, and tri-phosphates of the four principal nucleotides with the exception of CTP and UTP.[440] This method can be used to analyse biological materials[462,463,466,476]. The authors suggest gel filtration in a thin layer on G-25 Sephadex before chromatography in order to separate them from polysaccharides and

fluorescent materials which are always present[440]. The nucleotide material is eluted from Sephadex by water and lyophilised.

A DEAE-cellulose layer can be used also to separate ribonucleoside and deoxyribonucleoside 2′- amd 3′-phosphates in alkaline or enzymatic RNA and DNA hydrolysates[385,477,478]. Nucleotide 2′- and 3′-phosphates are chromatographed in 0.05 *N* HCl for both ribonucleoside and deoxyribonucleoside derivatives in the first direction and in 0.035 *N* HCl for ribonucleoside derivatives and 0.02 *N* HCl for deoxyribonucleotide derivatives in the second[385,464,477]. 2′ and 3′-Adenylic acids are fractionated under these conditions[385,464]. The separation of the 2′- and 3′-isomers of all nucleotides is achieved on DEAE-cellulose containing 10% of $CaSO_4$.[478]

2. PAPER ELECTROPHORESIS AND ELECTROPHORESIS IN A THIN LAYER OF CELLULOSE

Nucleotides and their derivatives contain different ionisable groups so that electrophoresis on paper and in a thin layer of cellulose is a valuable method for their analytical and preparative separation. The relative mobilities of nucleotides can be calculated at any pH from their charges using the pK_a of the ionisable groups, which are known[265].

The four principal ribonucleotides and deoxyribonucleotides are separated at pH 3.5. At this pH the 2′- and 3′-isomers of guanylic acid have different mobilities[265,343,482,483].

Certain minor nucleotides can also be separated from other nucleotides by paper electrophoresis, but for a complete analysis, for example of a tRNA hydrolysate, additional separation and by thin-layer or column chromatography (see the relevant Sections) is necessary[343,482,483]. The mobilities of ribonucleotides are listed in Table 6.

Table 6. The relative mobilities of ribonucleotides* in paper electrophoresis[265].

Nucleotide	pH 3.5**	pH 2.1***
4,5-Dihydrouridylic acid	1	–
Ribothymidylic acid	0.98	–
Pseudouridylic acid	0.98	–
Inosinic acid	0.90	–
Guanylic acid	0.73	0.38
7-Methylguanylic acid	0.98	–
1-Methylguanylic acid	–	0.30
N^2-Methylguanylic acid	–	0.30
N^2N^2-Dimethylguanylic acid	0.76	0.25
Adenylic acid	0.50	0
N^6-Methyladenylic acid	0.46	–
N^6N^6-Dimethyladenylic acid	0.42	–
2-Methyladenylic acid	0.25	–
Cytidylic acid	0.41	0

* The mobility of uridylic acid was adopted as unity.
** 0.05 M ammonium formate at pH 3.5.[343,348]
*** 0.05 M phosphate buffer at pH 2.1.[482]

Mono-, di-, and tri-phosphates are separated best in a citrate buffer at pH 5.0 or 7.0 depending on the number of dissociable phosphate groups. In the presence of bivalent cations the mobility of nucleoside triphosphates decreases[265].

2′- and 3′-Ribonucleotides can be separated from 5′-ribonucleotides in a borate buffer at pH 9.2.

Electrophoretic separation of nucleotides after hydrolysis can be used to determine the incorporation of various nucleotide analogues in nucleic acids. For example, the p*K* of 5-fluoro-, 5-bromo-, 5-chloro-, and 5-iodouridylic acids, 2-thiouridylic acid, and 8-azaguanylic acid are lower than those of uridylic, guanylic, and thymidylic acids and therefore at pH 9.0 these nucleotides migrate faster than all others[265].

The components of the RNA or DNA hydrolysates can also be separated by electrophoresis on cellulose layers[397,461,483-486]. Best separation is then achieved on carefully degassed cellulose washed with a solution of the sodium salt of EDTA[485].

Fractionation of 2′, 3′-ribonucleotides and deoxyribonucleotides is achieved at pH 3.4–3.5.[397,484,486] Adenine and inosine nucleotides are separated at pH 5.1.[486] Deoxyribonucleoside mono-, di-, and tri-phosphates can be easily separated from one another with respect to each base at pH 5.5.[484]

The employment of thin-layer electrophoresis permits the improvement of the separation of certain nucleotide mixtures which are difficult to fractionate by partition or ion-exchange chromatography. For this purpose, the electrophoresis is usually carried out in one direction in two-dimensional chromatography[337,396-398]. A microversion of electrophoresis was employed by Edström to analyse the nucleotides obtained fron the nucleic acids in a single cell [487,488].

3. ION-EXCHANGE COLUMN CHROMATOGRAPHY

Ion-exchange column chromatography on polystyrene resins, introduced by Cohn[1], has been used successfully for the fractionation of various natural nucleic acids on analytical and preparative scales. The general principles of separation by ion exchange column chromatography were examined by Cohn as early as 1955. Ion-exchange column chromatographic methods have been described in fair detail in three articles in the "Methods in Enzymology" series[489].

A mixture of ribo- or deoxyribo-nucleotides[490,491] can be very conveniently separated on a strong anion exchanger of the type of Dowex-1 in acid[492] or alkaline[493-496] systems. In acid systems the elution sequence of the nucleotides is as follows: cytidylic, adenylic, uridylic, and guanylic acids. In columns with a large height : diameter ratio guanylic acid sometimes overtakes uridylic acid[497]. Isomeric nucleotides can be separated into the 5′-, 2′-, and 3′-phosphates and are eluted from the column in this sequence[497].

In alkaline systems the elution sequence of nucleotides changes as follows: cytidylic, uridylic, adenylic, and guanylic acids[495].

In the simplest cases the relative dimensions of the column are unimportant, but in the separation of complex multicomponent mixtures tall columns (height : diameter = 50 : 1) give a satisfactory separation[497].

In the majority of systems used to separate a known mixture of nucleic acid derivatives on columns, the concentration or the pH of the eluent are increased in steps. However, in selecting the separation conditions or in the separation of a complex mixture, gradient elution is employed in which the eluent composition varies smoothly in accordance with the specified gradient. A linear gradient is usually employed.

Chromatographic separation of nucleotides on ion-exchange columns has been described in greater detail in other reviews[1,5,491,497].

The ability of purine and pyrimidine derivatives to absorb radiation intensely in the region 260—290 nm has been used to develop micromethods for the chromatography of nucleotides permitting the determination of small amounts of the latter and greatly reducing the duration of the fractionation[498-501]. Thus Anderson and coworkers[498,499] and somewhat later Hori et al.[500] described a method for the automatic analysis of nucleic acids whereby it is possible to separate and analyse the nitrogenous bases, nucleosides, and nucleotides in 24 h on a single column with Dowex-1 × 8 (200—400 mesh) resin using a linear acetate buffer concentration gradient at pH 4.4. For qualitative analysis, 0.02 μmole of substance is sufficient. Specimens containing large amounts of salts (for example, RNA and DNA hydrolysates) are subjected to preliminary desalination by gel filtration and then dissolved in a buffer solution. Pyrimidine and purine bases and nucleosides are eluted first and then nucleotides. Under these conditions, 2′-UMP is not completely separated from 3′-UMP; with the exception of 5′-CMP, 5′-nucleotides are not separated from 2′- and 3′-nucleotides and 5′-IMP and 5′-AMP are not separated at all. However, this hardly reduces the practical value of the method. It can be used to separate the 5′-nucleotides obtained from RNA by nuclease hydrolysis and 2′- and 3′-nucleotides formed in the alkaline hydrolysis of RNA. Deoxyribonucleotides are separated under analogous conditions[498].

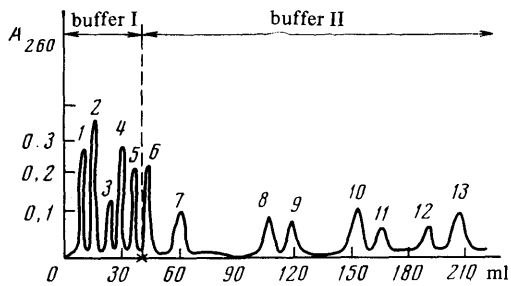

Figure 7. Chromatography of nucleotides, nucleosides and bases on Aminex A-4 cation-exchange resin (0.9 × 50 cm column); citrate (I) and acetate (II) buffers used for separation; rate of elution 60 ml h^{-1};[503] 1) UMP-5′ + IMP-5′ + UMP-2′ and UMP-3′ + ATP; 2) GMP-5′ + ADP + GMP-2′ + GMP-3′; 3) CMP-5′; 4) uridine + AMP-2′; 5) AMP-5′ + CMP-2′ + CMP-3′ + AMP-3′; 6) uracil; 7) inosine + thymine; 8) hypoxanthine; 9) guanosine; 10) adenosine; 11) cytosine; 12) guanine; 13) adenine.

The employment of AG-50W × 4 cation-exchange resin for the fractionation of ribo- and deoxy-ribonucleotides was described in 1967 by Blattner and Erikson[502], who achieved a clear-cut separation of the four principal 5′-deoxyribonucleotides after the enzymatic hydrolysis of DNA and of 2′- and 3′-ribonucleotides after the alkaline hydrolysis of RNA. They employed 0.1 M ammonium formate at pH 3.2 as the eluting solution in the first case and 0.25 M ammonium formate at pH 4.1 in the second. The sequence in which the nucleotides are eluted from the column is the same for deoxyribonucleotides and ribonucleotides: T(U) > G > C > A. The presence of Ca^{2+} and Mg^{2+} ions, snake venom phosphodiesterase, and pancreatic deoxyribonuclease in the specimen does not interfere with the separation. A change in pH or in the molarity of the buffer impairs the separation. The employment of a volatile buffer for elution makes it possible to obtain the nucleotides in a pure form after the evaporation of the solutions.

A clear-cut separation of four 5′-mononucleotides was achieved also on another cation-exchange resin Aminex A-4 (Fig. 7)[503].

Nucleotides phosphorylated to different extents can be readily separated quantitatively with the aid of DEAE-Sephadex A-25 in an ammonium bicarbonate or triethylammonium acetate gradient at pH 7.0.[504,505] Nucleotides are eluted from the column in order of increasing acidities[504].

The efficiency of column chromatography and the speed of analysis were subsequently significantly improved by employing very fine anion- and cation-exchange resins and high pressures[506-509]. New types of resin such as Zipax[507-510], AA-15,[506] and a surface-layer cation-exchange resin[511] were developed for this purpose. The application of highly sensitive detector systems permits nowadays the quantitative analysis of nucleic acid hydrolysates at the level of 10^{-12} mole without the use of a radioactive label[511].

V. NUCLEIC ACID BASES AND NUCLEOSIDES

1. THIN-LAYER CHROMATOGRAPHY

Partition chromatography in a thin layer of cellulose is widely used for the analytical determination and identification of the nucleic acid bases and nucleosides[380,382,385-401]. As in paper chromatography, the usual solvent systems for the separation of the bases and nucleosides are mixtures of water or aqueous solutions of salts, acids, or bases with organic solvents (alcohols, acids, etc.). Table 7 lists the R_f values for various nucleic acid bases, their derivatives, and nucleosides in a series of solvents[385]. These systems are fairly simple and give reliably reproducible results. Comparison of the R_f values in the above systems provides an idea about the influence of the pH of the solution and the salt concentration in the systems on the chromatographic mobilities of the substances being separated. The amphoteric properties of nucleic acid bases, as a result of which the pH of the system can alter the polarity of the bases and nucleosides and hence the partition coefficient, plays an important role in this process. The introduction of substituents alters significantly the polarity and the dissociation constants, so that, knowing the position and nature of the substituent, it is possible to predict, at least by analogy, the R_f value.

A satisfactory separation of the bases by thin-layer chromatography has been achieved with the aid of different versions of Kirby's system[380,401], widely used in the paper chromatography of the bases. Thus the separation of all four bases after the acid hydrolysis of DNA was achieved by one-dimensional chromatography in a 65 : 17 : 18 MeOH—HCl—H_2O mixture[380,401]. The standard system for paper chromatography isopropyl alcohol—HCl—water has also been used successfully[385,512].

The bases and the corresponding nucleosides can be readily separated on cellulose with elution by water[386]. A number of other less common systems have been described for the separation of bases and nucleosides[386,390,392,393,513-523].

Table 7. The R_f values for bases and nucleosides in thin-layer chromatography on cellulose[38].

Substance	Solvent*					
	I	II	III	IV	V	VI
Adenine	0.31	0.38	0.88	0.35	0.40	0.10
2-Methyladenine	0.38	0.43	0.91	0.45	0.49	0.08
6-Dimethyladenine	0.50	0.68	0.88	0.65	0.55	0.08
6-Methyladenine	0.45	0.52	0.91	0.52	0.52	0.08
Cytosine	0.41	0.24	0.59	0.31	0.39	0.59
5-Methylcytosine	0.51	0.27	0.64	0.35	0.44	0.51
5-Hydroxymethylcytosine	0.39	0.10	0.64	0.25	0.33	0.66
Uracil	0.70	0.31	0.57	0.35	0.47	0.54
6-Methyluracil	0.72	0.36	0.63	0.44	0.55	0.44
1,3-Dimethyluracil	0.98	0.70	0.82	0.80	0.73	0.56
Thymine	0.80	0.45	0.65	0.57	0.57	0.44
Guanine	0.26	0.33	0.87	0.39	0.41	0.10
1-Methylguanine	0.16	0.06	0.50	0.13	0.25	0.15
2-Methylguanine	0.53	—	0.74	—	—	0.11
2,2-Dimethylguanine	0.32	—	0.75	0.32	—	0.10
Adenosine	0.23	—	—	—	0.41	—
Deoxyadenosine	0.27		0.82	0.37	0.42	0.09
Cytidine	0.36	—	0.65	0.27	—	0.52
Deoxycytidine	0.50	—	0.65	0.35	—	0.47
Methyldeoxycytidine	0.59	—	0.73	0.40	0.42	0.39
Guanosine	0.22	—	0.50	0.09	0.26	0.27
Deoxyguanosine	0.14	—	0.59	0.17	0.36	0.23
Uridine	0.62	—	—	—	—	—
Deoxyuridine	0.77	—	0.61	0.33	0.47	0.45
Thymidine	0.88	—	0.66	0.52	0.55	0.37
Pseudouridine	0.42	—	0.42	0.08	0.24	0.57

*Solvent composition: I) isopropyl alcohol—HCl—H_2O (65 : 16.7 : 18.3); II) n-Butyl—alcohol—water (86 : 14); III) isobutyric acid—water—25% NH_4OH (400 : 208 : 0.4); IV) isopropyl alcohol—water—conc. (28%) NH_4OH (85 : 15 : 1.3); V) n-butyl alcohol—water—formic acid (77 : 13 : 10); VI) sat. $(NH_4)_2SO_4$—1 M sodium acetate—isopropyl alcohol (80 : 18 : 2).

The R_f values for methylated purines and purine nucleosides have been quoted by Broom and coworkers[517,520]. Data for the separation of deoxyribonucleosides and their R_f values have also been published[395,402,524]. Ribonucleosides can be readily separated from deoxyribonucleosides or ribonucleosides with substituted *cis*-glycol hydroxy-groups in alkaline systems containing borate[382]. The formation of borate complexes with the *cis*-glycol group of the ribose residue has a marked influence on chromatographic mobility.

In this case, when the mixture of bases is too complex for a satisfactory separation by one-dimensional chromatography, two-dimensional chromatography can be employed. An example of a successful application of this method is probided by the separation of a mixture of bases using the 70 : 20 : 10 MeOH—HCl—H_2O system in the first direction and the 60 : 20 : 20 : 2 BuOH—MeOH—H_2O—conc.NH_4OH in the second system[380,525]. A mixture of 6-methyladenine, adenine, cytosine, and 5-methylcytosine can be readily separated into individual compounds by two-dimensional chromatography using the solvent system I in the first direction and the solvent system II in the second (for solvent systems I and II, see Table 7), while the employment of only one system does not lead to a clear-cut separation of the mixture[385].

In the two-dimensional fractionation of the enzymatic hydrolysate of tRNA from *E. coli* and yeast there is a clear-cut separation of 8 nucleosides including minor nucleosides: dehydrouridine, inosine, pseudouridine, and ribothymidine[521]. Electrophoresis is sometimes employed in one direction in two-dimensional thin-layer chromatography[401,484]. For example, a mixture of the five principal and eight methylated bases found in DNA and RNA was separated by this method and it was shown that it yields better results than one-dimensional chromatography[385]. The application of high-voltage electrophoresis and two-dimensional chromatography helps the separation of the majority of bases and deoxyribonucelosides present in DNA hydrolysates[401].

Thus the fractionation of nucleic acid derivatives in a thin layer of cellulose is used nowadays in all cases where paper chromatography was employed previously, but separation in a thin cellulose layer is of shorter duration than paper chromatography, more clear-cut, and the sensitivity is higher by a factor of approximately 10.

The employment of labelled nucleic acid preparation and also of chemical methods for the introduction of radioactive isotopes into nucleic acid components increases the sensitivity of the method to 10^{-12} mole[343,526-528]. In particular, Randerath oxidised the *cis*-glycol group of the ribose residue by periodate with subsequent reduction by sodium borotritide in order to introduce the isotope label into ribonucleosides in the analysis of RNA hydrolysates. The resulting mixture of tritium-labelled compounds was resolved into components by two-dimensional chromatography in thin layers of cellulose or silica gel[304,529-533]. The positions of the individual compounds on the chromatograms were determined by radioautography. The quantitative analysis was carried out by measuring the radioactivity of the eluted substances. The method has a high resolving power and sensitivity[304,529-531]. It was developed and applied to determine the nucleotide composition of RNA in those cases where a minimal amount of RNA is available and cannot be labelled *in vivo*. The authors estimate the sensitivity of the method as several picomoles[304], while the lower limit of spectrophotometric analysis is one nanomole. By studying the factors influencing the sensitivity of the method, Randerath achieved a level of sensitivity which proved to be sufficient for the detection of minor components of tRNA.[530,532,533] However, 2-*O*-methylnucleosides cannot be identified by this method, because they are not oxidised by periodate, and 4-thiouridine is converted into [^{3}H]uridine by reduction with borotritide[530,531,534]. In view of the instability of the borotritide, the reduction is carried out in an alkaline medium, where certain minor bases of tRNA are known to decompose[531,534]. The imidazole ring of 7-methylguanine is partly decomposed (about 35%) and 1-methyladenine is converted into N^6-methyladenine. 3-Methylcytosine also decomposes to the extent of 10—15%.[531,534,535]

Randerath employed his highly sensitive ultramicromethod for systematic studies on the composition of the bases of the tRNA isolated from various normal and neoplastic mammalian brain tissues[536]. The nucleoside derivatives are separated largely on cellulose layers.

Among other adsorbents giving satisfactory results in the fractionation of nucleic acid bases and nucleosides in a thin layer, mention may be made of polyamide[382,392,537]. Table 8 lists the R_f values for ten bases and nucleosides. The use of distilled water as a solvent greatly improves the mobilities of all the compounds, while the addition of a salt reduces the mobility[537]. Best results were achieved in aqueous sodium chloride solutions, although sodium

acetate or borate can also be used[537]. The polyamide layers can be employed repeatedly[537].

Chromatography in a thin layer of silica gel is sometimes used to separate the synthetic analogues and certain derivatives of nucleosides and bases[402,404,414,418,419,426,427,538,539]. Although silica gel layers are, in fact, used for the fractionation of the free bases and nucleosides[300,410,426], they give less satisfactory results than cellulose[300,426,427].

Table 8. The R_f values for bases and nucleosides in chromatography on polyamide layers[537].

Substance	Solvent*				Substance	Solvent*			
	I	II	III	IV		I	II	III	IV
Adenine	0.75	0.85	0.54	0.51	Inosine	0.32	0.30	0.23	0.85
Hypoxanthene	0.48	0.52	0.37	0.74	Guanosine	0.22	0.17	0.17	0.74
Guanine	0.00	0.00	0.00	0.44	Uridine	0.39	0.50	0.37	0.90
Uracil	0.58	0.72	0.54	0.83	Cytidine	0.30	0.37	0.23	0.90
Adenosine	0.65	0.80	0.50	0.65	Thymidine	0.56	0.75	0.51	0.78

*Solvent composition: I) heptane–butyl alcohol–acetic acid (4 : 4 : 1); II) carbon tetrachloride–acetic acid–acetone (4 : 1 : 4); III) toluene–pyridine–ethylene chlorohydrin–0.8 M NH_4OH (5 : 1 : 5 : 3); IV) 0.5 M aqueous NaCl.

2. PAPER ELECTROPHORESIS AND ELECTROPHORESIS IN A THIN CELLULOSE LAYER

The fractionation of nucleic acid bases and nucleosides by electrophoresis on paper or in a thin layer of cellulose has no special advantages over thin-layer or paper partition chromatography of these compounds. However, by combining this method with chromatography in thin cellulose layers, it is sometimes possible to improve the separation of certain mixtures containing, apart from the four main components, also minor components—methylated in the base moiety or in the 2′-hydroxy-group of ribose[382,484]. The most striking example of such application of electrophoresis and chromatography is provided by the separation of a mixture of five main and eight methylated bases with the aid of two-dimensional chromatography[484] (Fig. 8).

Deoxyribonucleosides and 2′-*O*-methylribonucleosides can be separated from ribonucleosides in a borate buffer at pH 9.2.[265,484] Borate complexes of ribonucleosides migrate as anions and the relative mobilities of adenosine, cytidine, guanosine, and uridine are respectively 0.64, 0.74, 0.88, and 1.0.[265] The four main ribonucleosides and deoxyribonucleosides are separated by paper electrophoresis at pH 3.2. The mobilities of uridine (thymidine), guanosine, and adenosine are respectively 0, 0.05, and 0.29 (the mobility of cytidine was adopted as 1.0)[265]. Adenine, guanine, cytosine, and uracil can also be separated by electrophoresis at pH 3.2.[265]

3. ION-EXCHANGE CHROMATOGRAPHY

The principles and methods of the separation of nucleic acid bases and nucleosides on ion-exchange resins have been described in fair detail in Cohn's papers and reviews[11,489,491,497]. Since all the data published hitherto on the fractionation of these components on ion-exchange resins proved to be comparable with one another and with Cohn's data (the same or similar ion-exchangers were employed in all cases), our discussions will be restricted only to those few ion-exchange resins which are used nowadays in micropreparative studies. The problem of the separation of nucleosides and bases by adsorption chromatography on gel filtration materials of the type of Sephadex and biogels, which have been recently used successfully for this purpose, will be discussed in somewhat greater detail in this Section.

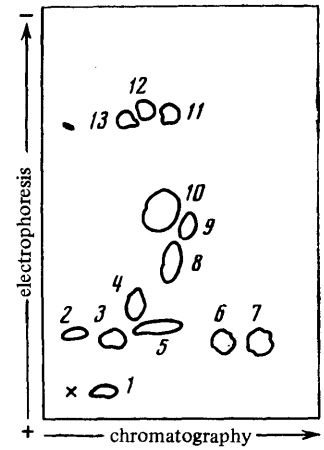

Figure 8. Separation of methylated bases on a thin layer of microcrystalline Pevikon cellulose. First direction: electrophoresis in 0.1 M sodium acetate at pH 3.5, 1000 V, and 20 mA for 3 h. Second direction: chromatography in the 65 : 16.7 : 18.3 isopropyl alcohol–HCl–water system[484]: 1) guanine; 2) 1-methylguanine; 3) 2-dimethylguanine; 4) adenine; 5) 2-methylguanine; 6) uracil; 7) thymine; 8) 6-methyladenine; 9) 6-dimethyladenine; 10) 2-methyladenine; 11) 5-methylcytosine; 12) cytosine; 13) 1-methyladenine.

In 1968 Cohn and coworkers modified Anderson's nucleotide analyser[498,499] and used it to separate nucleosides on cation-exchange resins such as Amberlite GG-120 (type III), Bio-Rad A-6, and Dowex 50 × 4.[540] The four main nucleosides obtained by the hydrolysis of RNA are readily separated on elution with 0.4 M ammonium formate at pH 4.65. The sequence in which nucleosides are eluted from the column is as follows: U > G > A > C. Minor nucleosides such as N^6-dimethyladenosine 7-methylguanosine, and N^2-dimethylguanosine are readily separated from one another and so do not interfere with the separation of the main nucleosides. Pseudouridine ribothymidine, uridine, inosine, and 4-thiouridine are incompletely separated. Although the authors investigated only the separation of nucleosides, a similar nucleoside analyser can probably also be used to analyse nucleic acid bases[502,541–543]. For example, a method was proposed in 1970 for the fractionation of a mixture of nucleotides, nucleosides, and bases on the cation-exchange resin Aminex A-4 [503] (Fig. 7). The separation was carried out using stepwise elution, initially with sodium citrate at pH 3.0 and then with 0.25, 0.50, and 1.00 M

sodium acetate at pH 6.4. All four 5′-mononucleotides are separated when the first buffer is passed through the resin. The second buffer gives rise to individual peaks of the nucleosides and nucleic acid bases. The employment of this cation-exchanger was also described previously for the separation of purine bases from pyrimidine bases and for the separation of hypoxanthine, guanine, and adenine[544].

A convenient method for the isolation and separation of purine bases from biological extracts using AG50W × 4 (H^+) resin has been proposed[545]. The elution is carried out with 0.05 *N* HCl, which results in the separation not only of purine bases but also of the entire nucleotide material present in the extract.

4. GEL FILTRATION AND ADSORPTION CHROMATOGRAPHY ON GELS

Gel filtration or fractionation of compounds on molecular sieves (dextran gels) of the type of Sephadex was described as early as 1959 [546] and has been widely used to separate various nucleic acid derivatives in accordance with their molecular weights. Thus nucleotides are readily separated from RNA or oligonucleotides[547,549] and are always eluted before nucleosides and bases, which constitutes a rapid and technically very simple method for the separation of these derivatives into groups of approximately equal molecular weights[549,550]. Sephadex, a relatively inert, insoluble, and hydrophilic material, is manufactured with different porosities (G-10, G-15, G-25, G-50, G-75, G-100, and G-200) and in the form of ion-exchange celluloses (CM- and DEAE-Sephadex), which combine the properties of molecular sieves and ion exchangers[551,552]. The elution of substances from columns is almost quantitative. About 3% is lost as a result of irreversible adsorption[553].

Soon after the introduction of gel filtration, Gelotte showed that nucleic acid derivatives are retained by the gel to different extents and are eluted from the latter by different volumes of the eluent, depending on the structure[553-557]. It was shown that, apart from the molecular weight, the separation of compounds on different types of Sephadex is greatly influenced both by the ionic strength and the pH of the eluting buffer and by the reversible adsorption of the substances[549,550,554-561]. The mechanism of the adsorption on Sephadex has not been established yet, but it is suggested that the adsorption involves the formation of hydrogen bonds between the heterocyclic bases and the ether bridges in the matrix[553,556,557]. Purine derivatives as a rule exhibit a greater affinity for different types of Sephadex than pyrimidine derivatives[549,550,553,556,557]. The separation on G-10, G-15, and G-25 is virtually the same for pyrimidine derivatives, while the use of more cross-linked gels, for example G-10, for purines results in an increased affinity for the matrix[549,550,553,556].

The relative volume of the eluent or the elution constant R_m for different derivatives is independent of the amount of gel and, when the conditions are standardised, can serve as the first criterion for the identification of the compound[556]. The elution constants for 50 purine and pyrimidine derivatives on a G-10 column in 0.01 ammonium carbonate at pH 9 are listed in the same report. In a single step it is possible to separate up to 16 compounds[556]. The elution constants of nucleosides and bases at other pH values have been published[559,561]. All four principal deoxyribonucleosides and ribonucleosides can be successfully separated on Sephadex G-25 or G-10.[141,547,550,562] The amount of each nucleoside in the mixture was $(1 - 10) \times 10^{-9}$ mole. The ratio of the column diameter to its height should be in the range 1:50–1:150 to ensure a clear-cut separation[547,562]. The sequence of the elution of the nucleosides from the column under these conditions is U(T) > C > G > A. The bases are separated in the same sequence, but in the presence of nucleosides the separation of adenosine and guanine is incomplete[553,556].

A mixture of nucleosides and bases can be analysed also in the presence of nucleotides, since the latter are eluted under these conditions as a separate peak ahead of nucleosides[547,553]. The amount of nucleotides should not exceed 50% of the total amount of substance injected. However, if longer columns are employed, then at lower rates of elution it is possible to separate a 12:1 mixture of nucleotides and nucleosides[547].

The fractionation of nucleosides and G-10 can be achieved also at neutral pH. However, an additional separation of uridine and cytidine, which overlap either partially (elution with phosphate buffer at pH 7.0) or completely (elution with water), is then necessary. Adenosine and guanosine are completely separated[549,558].

A similar behaviour has been observed at the same pH values also for nucleic acid bases[557]. Elution with 0.05 M phosphate buffer at pH 7.0 leads to a clear-cut fractionation of purine bases, including the minor bases, and to an incomplete separation of the pyrimidine bases. It is noteworthy that under these conditions not only hypoxanthine, xanthine, adenine, and guanine are separated, but also various methylated purine derivatives. The separation of methylated purines shows that the introduction of the methyl group decreases the degree of reversible adsorption of the compound[557].

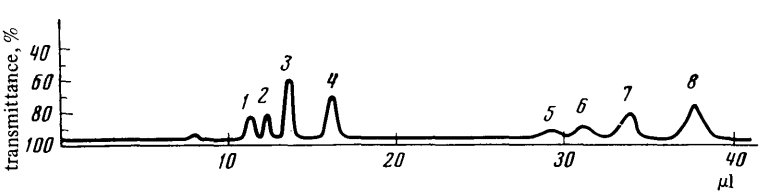

Figure 9. Chromatography of a mixture of deoxyribonucleosides and ribonucleosides on a fractionated Biogel P-2 (0.8 × 0.68 column); rate of elution 2.8 ml h^{-1}; volume of eluate 50 μl; 1) uridine; 2) guanosine; 3) deoxyguanosine; 4) thymidine; 5) cytidine; 6) adenosine; 7) deoxycytidine; 8) deoxyadenosine[566].

Guanylic and adenylic 2′:3′-cyclic phosphates can also be successfully separated on a G-10 Sephadex column[549]. Nucleotides are not separated from one another[141,557,562-565].

Another material most frequently employed recently for the separation of alkaline and acid DNA hydrolysates is polyacrylamide gel (Biogel P-2 and P-6).[136,158,566-574]. The advantage of polyacrylamide gel over different types of Sephadex is that a smaller volume of the gel is needed for separation, which shortens the elution time; the compounds are eluted in much smaller volumes and quantitatively[566]. It is recommended that nucleosides be separated on a fractionated Biogel P-2 at high pH.[158,566,572,573] The fractionation of the Biogel and the preparation of the columns have been described[566,572]. A mixture of ribonucleosides and deoxyribonucleosides was separated in a 0.1 M ammonium bicarbonate buffer with 1×10^{-3} M $Na_2B_4O_7$ at pH 10.1 (Fig. 9)[566,573]. The presence of nucleotides or high salt concentrations in the initial mixtures does not interfere with the separation of nucleosides, since both nucleotides and salts are readily separated from them[566,572,575,576].

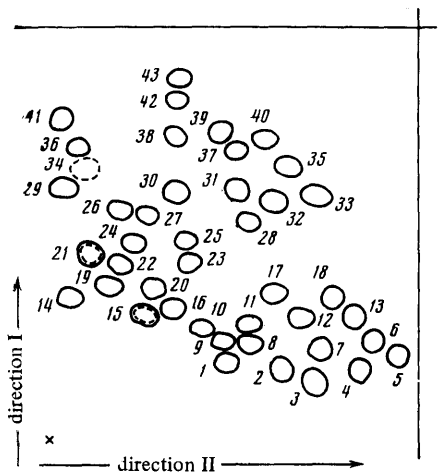

Figure 10. Two-dimensional chromatography of a complex mixture of nucleotides, nucleosides, and nucleic acid bases on a thin layer of cellulose. First direction: 6:3:1 n-propyl alcohol—25% ammonia—water system. Second direction: 2:79:19 isopropyl alcohol—sat.ammonium sulphate—water system[519]: 1) ATP; 2) GDP; 3) GTP; 4) ITP; 5) CTP + UTP; 6) CDP + UDP; 7) IDP + TTP; 8) GMP-5′; 9) TPN; 10) GMP-3′ + ATP; 11) GMP-2; 12) IMP-5′ + TDP; 13) CMP-5′ + CMP-2′ + CDPG + UMP-5′; 14) uric acid; 15) TPNH; 16) AMP-5′ + DPN + ADPG; 17) TMP-5′; 18) CMP-3′ + UMP-2′ + UMP-3′; 19) AMP-3′; 20) AMP-2′; 21) DPNH; 22) guanine; 23) orotic acid; 24) xanthine + GMP-2′:3′; 25) guanosine; 26) 7-methylxanthine; 27) deoxyguanosine + xanthosine; 28) 5-aminothymine; 29) adenine; 30) hypoxanthine; 31) inosine; 32) isocytosine; 33) uridine; 34) 2-aminopurine; 35) uracil + cytidine + cytosine + deoxyuridine; 36) adenosine; 37) 4-methyluracil; 38) 2-thiouracil; 39) thymidine + thymine; 40) 3-methylcytosine + deoxycytidine; 41) deoxyadenosine; 42) nicotinic acid; 43) nicotinamide.

VI. MIXTURES OF NUCLEOTIDES, NUCLEOSIDES, AND NUCLEIC ACID BASES

Partition[518,519] or ion-exchange thin-layer chromatography[438,577], electrophoresis[484,487], and ion-exchange[498-504,543] or adsorption[549,553,556,568,570] column chromatography can be used to fractionate complex mixtures of different nucleic acid components as well as for the separation of compounds of the same type.

Thin-layer chromatography on cellulose and cellulose ion-exchangers has been mainly used recently for the rapid analysis of microamounts of a mixture of nucleotides, nucleosides, and bases. Clear-cut fractionation of a large number of compounds on cellulose can be achieved with the aid of two-dimensional chromatography[518,519].

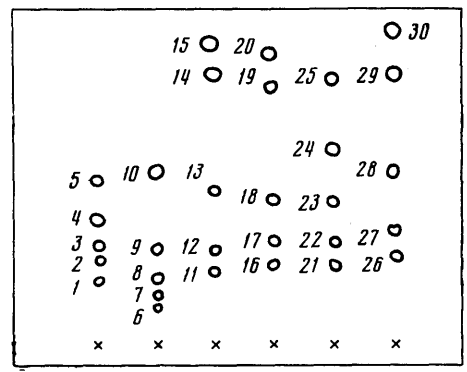

Figure 11. Chromatography of a mixture of nucleotides, and nucleosides, and bases on a layer of PEI-cellulose[577]; gradient: 0.6 ml of 0.1 M LiCl, 0.6 ml of 0.2 M LiCl, 0.6 ml of 0.5 M LiCl, 0.6 ml of 1 M LiCl, and 1.2 ml of 2 M LiCl: 1) ATP; 2) ADP; 3) AMP; 4) adenine; 5) adenosine; 6) GTP; 7) GDP; 8) GMP; 9) guanine; 10) guanosine; 11) UTP; 12) UDP; 13) UMP; 14) uracil; 15) uridine; 16) ITP; 17) IDP; 18) CMP; 19) cytosine; 20) cytidine; 21) ITP; 2) IDP; 23) IMP; 24) hypoxanthine; 25) inosine; 26) TTP; 27) TDP; 28) TMP; 29) thymine; 30) thymidine.

The separation of 22 compounds on MN-300 cellulose using the 57:4:39 isobutyric acid—concentrated ammonia—water solvent system in the first direction and the 7:3 methanol—1 M ammonium acetate system for two runs in the second direction may be quoted as an example[518]. Not only nucleoside mono-, di-, and triphosphates but also the 3′- and 5′-nucleotides are separated from one another fairly distinctly.

Fig. 10 illustrates the chromatographic separation of more than 60 nucleotides derivatives[519]. Special mention should be made of the satisfactory fractionation of the bases and the corresponding ribonucleosides, deoxyribonucleosides, the mono-, di-, and tri-phosphates of various nucleosides, and the 2′-, 3′-, and 5′-phosphates of ribonucleosides. Compounds with the same chromatographic mobility can be refractionated in another solvent.

Separation of the bases, nucleosides, and nucleotides with a high resolution has been achieved on PEI-cellulose using a salt gradient[578] (Fig. 11). Since the R_f values for nucleotides depend on the salt concentration[438], the bases and nucleosides can be readily separated from nucleotides by employing as the initial solvent distilled water or a 1:1 methanol—water mixture[438,442,578].

The separation of a complex mixture of bases, nucleosides, and nucleotides on columns has been described[498-500,503,504,543,549,553,556,557,568,570].

Gas—liquid chromatography (GLC), proposed initially only for the separation of acetyl, methyl, and isopropylidene derivatives of nucleosides[579] and methylated bases[580,581], has also been used recently to separate nucleic acid derivatives. In consequence of the low volatility and instability in the chromatographic process of the substances to be separated, these derivatives can be used only for qualitative analysis. The above difficulties were partly eliminated in the chromatography of trimethylsilyl derivatives of nucleosides[581-585]. Many modifications of the method are employed[581,583-591]. Chromatography of bis(trimethylsilyl)trifluoroacetamide derivatives has been most widely used[589,590,592-596]. However, in this case too certain nucleosides (cytidine, adenosine) give rise to several products after silylation[595,596]. For cytidine, this difficulty was obviated by modifying the cytidine derivatives with hydroxylamine derivatives before silylation[596]. GLC can be used to analyse the nucleotide composition of DNA and RNA,[589,593] but the sensitivity of the method is still insufficient (1—5 μg of nucleic acid per analysis). The GLC method can be usefully employed to analyse the compositions of synthetic oligonucleotides. The separation of rare nucleic acid components has been described[586,590,594,596,597].

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Chemical Treatment of Seeds and Its Application to Plant Growing

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Considerable attention is paid to the action on seeds of various plant-growth regulators and vitamins. A special place is occupied by the possibility of using chemicals to change the genetic peculiarities of plants, and also by the use of special polymer films as seed coatings. Great value attaches to the local introduction with the seeds of substances that protect both seeds and shoots from various pests and diseases. A list of 575 references is included.

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I. INTRODUCTION

As early as 1800 the founder of plant physiology, Jean Sénébier, remarked in his many-volume treatise that the attention of chemists must be drawn to processes of plant growth[1]. Only a hundred years later, in an address given at Moscow University in 1901 on "A Century of Progress in Plant Physiology", Timiryazev was able to state that "chemistry and physics, having come to the assistance of plant physiology, have given to man, over the course of a century, the possibility of extending his right to life and curtailing the power of death: no knowledge could have a more valuable application"[2].

The application of chemicals to the growing of plants has now acquired immense significance. This has been especially clearly shown in the treatment of problems connected with the root nutrition of plants and the production and application of fertilisers. During the past decade the attention of research workers has been attracted to the preparation and investigation of chemicals capable of controlling the growth and development of plants. The organisation of a laboratory for the preparation of physiologically active substances in 1946, by S.S.Nametkin at the Institute of Plant Physiology of the USSR Academy of Sciences, played an important part in the development of these investigations in the Soviet Union. High yields are at the present time unthinkable without the widespread application of various methods of plant protection.

One of the most convenient modes of application of the chemicals (pesticides) used in agriculture—in several cases the only method—is to treat the seeds. This plays an important part in the struggle against micro-organisms and pests, diminishing seed losses both during storage and during germination. The field germinating power of seeds is enhanced by enriching them before sowing with the vitally necessary compounds and substances controlling their germination and growth. The use of polymers to coat seeds is of considerable practical interest, and provides a solution to several important problems.

Although the production, properties, and application of pesticides are covered in a large number of reviews and monographs[3-8], insufficiently detailed consideration has been given during recent years to the whole complex of problems associated with the chemical treatment of seeds[9,10]†.

In the present Review, without claiming complete coverage of the literature and while disregarding problems connected with the biology of the germinating seed, we would like to examine the main classes of chemical substances employed for the treatment of seeds, together with certain aspects of their action. We have used information published mainly during the past 15–20 years both in original papers and in abstracts and books.

II. STIMULANTS AND INHIBITORS OF GERMINATION

Methods of treating seeds with growth regulators have been developed during the past forty years, and several groups of regulators, now being widely studied, were discovered only during the last two decades. The quantity of publications concerned with the action of regulators on germination is continually increasing. This information is being systematised to some extent in several monographs, reviews, and symposia[9,10,13-22].

Plant-growth regulators usually include stimulants and inhibitors, herbicides (substances causing destruction), desiccants (which dry up plants), and defoliants (causing leaves to fall). The last two groups are not used for treating seeds, and will not be discussed below.

Growth regulators are widely represented in plants, being products of normal metabolism. Such substances are often termed *plant hormones*. Synthetic products, by means of which it is also possible to control the vital activity of plants, are widely studied together with natural growth regulators. In this case stimulation is a consequence of the disturbance (usually only slight) of the normal functioning of the living system caused by the

† The first summaries of work on the treatment of seeds with various substances appeared in 1763 and 1876[11,12].

chemicals: the accompanying intensification of metabolism is a kind of protective reaction of the organism aimed at restoring its normal functioning as rapidly as possible[5].

The action of a regulator may vary with its concentration. Thus at low concentrations it has a stimulating effect, it retards metabolism with increase in concentration, and at doses exceeding the inhibiting dose it leads to destruction of the plant.

Various organic substances are mostly used as artificial regulators. The main groups of these compounds used for treating seeds before sowing are discussed below.

1. Auxins

An auxin was first isolated in 1931 by Kögl and Haagen-Smit[23]. They gave to the product the name *auxin*—a substance causing the growth and elongation of cells—and thereby introduced a new general term into scientific use. Some time later they isolated a second auxin, and then a third, termed a "heteroauxin", which on investigation proved to be indol-3'-ylacetic acid. This compound has since been detected in many plants. The ease with which indolylacetic acid can be synthesised explains its wide study as a stimulating regulator of plant growth.

It has since been found that auxin activity is possessed by other acids, e.g. those containing an aromatic carbocyclic or heterocyclic ring in the aliphatic radical[24]. The group of auxins most widely used for treating seeds are carboxylic acids derived from indole—indol-3'-yl-acetic, -propionic, and -butyric acids, as well as their esters, salts and amides.

Kholodnyi was the first Soviet worker to investigate[25] the effect of heteroauxin on the germination of seeds and the productivity of plants. Response to such treatment has since been confirmed by many investigators. Thus dipping rice seeds in auxin solutions before sowing was shown[26] to improve their germination in an unflooded soil, but this effect disappears on flooding. Indolylacetic acid increases the energy of germination of carrot and onion seeds by 9.0% and 9.4% respectively, and the germinating capacity by 5.6% and 13.7%.[27] It stimulates the germination of beans[28] and several other plants[29-31]. Keeping apple pips in a 0.01–0.001% solution for 30 min increases their germinating capacity by 10.6–18.1%.[32]

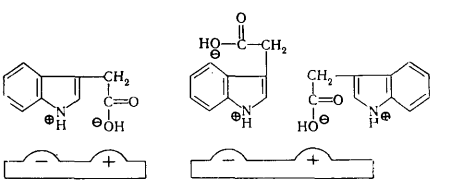
The intense physiological activity of auxins indicates that they are involved in the fundamental processes of metabolism. Thus indolylacetic acid plays a part in the phosphorus metabolism of plants[33], enhances the activity of 3'-nucleotidase[34], enhances oxidative phosphorylation, and activates the absorption of water[35]. It improves the binding of calcium by ribonucleic acid[36]. Activation of shoots of the cotton plant grown from seeds treated with the optimum concentration of auxin is accompanied by increased synthesis of nucleic acid and especially of ribonucleic acid[37].

The interconnection between the action of auxins and that of other growth stimulants is very interesting. Thus McLeod and Palmer have shown[38] that indolylacetic acid improves the conditions for the formation of α-amidase, which is dependent on the presence of gibberellins. The dependence of the action of gibberellic acid on the presence of auxins in plants has been confirmed[39]. The action of auxins on plants has been reviewed[40].

Many investigators were attracted by the discovery of auxins and by their great effectiveness in growth processes. The range of research on auxins has since been considerably extended: study of the responses of plants to treatment with auxins has been accompanied by attempts to synthesise new chemical compounds possessing auxin activity. In particular, the effect of introducing substituents into the heteroauxin molecule has been established. For example, auxin activity is suppressed by most substituents in the pyrrole ring[41]. Introduction of a 2-halogen, however, enhances it[42]. 2'-Substituted indolylacetic acids are considerably less active than their 3'-analogues[43]. Acids derived from naphthalene—naphth-1'-yl-acetic, -propionic, and -butyric acids—also exhibit auxin properties. On the other hand, 2-substituted naphthalenes are considerably less active[44]. Esters of the acids are used when a solution of the stimulant in a non-polar solvent is to be obtained. Naphth-1'-ylacetic acid is often used to treat seeds of various plants to stimulate germination and the development of shoots. It has been employed in particular to treat the seeds of wheat[45], tomato[44], red-currant[46], carrot[47], sunflower[29], and maize[48].

Acids containing a phenyl group, e.g. phenylacetic and phenoxyacetic, also exert a stimulating action. The nuclear-substituted acids often possess herbicidal properties, but at low concentrations even they have a stimulating effect. Thus 4'-chloro-2'-methyl-, 4'-chloro-2'-hydroxymethyl-, and 4'-chloro-2'-formyl-phenoxyacetic acids stimulate germination of seeds and development of the shoots of barley[49], tomato, and kidney-bean[50,51]. In low concentrations 2,4-dichlorophenoxyacetic acid (2,4-D) and its esters act as stimulants, e.g. on the seeds of pine, spruce, acacia, ash, and oak[52], annual weeds[53], and wheat[45]. Similar activity is developed also by substituted phenylbutyric acids[54] and indol-2'-ylglyoxylic esters[55].

Seeds and shoots are extremely sensitive to excess of auxins. This is apparent both in a diminution of germinating power and in the retardation of growth processes. A schematic model has been suggested to explain this phenomenon on the assumption of a two-point interaction between the auxin molecule and the enxymic centres with formation of a growth-stimulating auxin–receptor complex[56]:



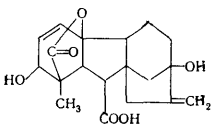
At high concentrations of indolylacetic acid two auxin molecules are adsorbed on the active site of the enzyme, and the required chemical conversion does not take place.

Study of the response of seeds to enrichment of their auxins has enabled the physiological role of auxins in the vital activity of seeds to be elucidated, and has also promoted the search for new plant-growth stimulants.

2. Gibberellins

The first gibberellin (subsequently termed gibberellin A_1) was obtained in 1937.[57] Several gibberellins were isolated, including gibberellin A_3—gibberellic acid—the most frequently used in practice and the most active of the 37 gibberellins known at the present time. Lona and Fioretti[58] have compared the activities of several gibberellins towards the germination of lettuce seeds.

Several new gibberellins have been described quite recently [16,59]. Gibberellic acid



like other gibberellins, is a fluorene derivative [320].

In industry, gibberellins are most often isolated from the fungus *Fusarium moniliforame* Sheld. A Soviet crystalline preparation of gibberellin A_3 contains gibberellic acid contaminated with certain other gibberellins, which widens the spectrum of its action and enhances its effectiveness. An inexpensive preparation—"gibberelate", containing ~10% of the active principle—has been manufactured in the Soviet Union since 1968. Its effectiveness has been demonstrated by trials [60]. Attempts are now being made to synthesise gibberellins [61].

Several surveys have appeared on the action of gibberellins [62-64]. The chemical structure of the compounds has been discussed in a review [65].

Although gibberellins are present in plants and seeds, the latter are extremely responsive to treatment with this plant hormone. Thus positive results have been obtained on treatment of the seeds of cotton [66,67], wheat [68,69], pea [69-71], barley [68,72], cucumber [73], maize [70,74], kidney-bean, parsley [70], lettuce [75,76], cabbage [77], radish [78], bean [71], belladonna [79-81], ginseng [82,83], and several other plants [84-90]. A large number of papers have dealt with the action of gibberellins on the germination of seeds of certain kinds of wood having seeds which germinate with difficulty (lime, ash, hornbeam) [91-99]. Such treatment with gibberellins increases the capacity for and vigour of germination of the seeds [68,71,78,91], and intensifies respiration [100]. Wheat and barley have shown rapid and harmonious growth with good development of the root system [68] (which is not usually characteristic of gibberellins). Beans and peaks have given good results with an increased moisture content in the soil [71].

The action of gibberellins can be promoted by preliminary chilling [84] and illumination [101] of the seeds. These and other facts suggest that a positive effect of gibberellins depends on the state of the seeds, the species of plant, and also the ambient conditions. Thus under identical conditions of treatment of the seeds, gibberellic acid stimulates the germination of cabbage but may depress that of carrots and tomatoes [77]. However, certain plants remained insensitive to such treatment [92]. Among 304 varieties of rice studied, seeds of southern origin were distinguished by a longer period of dormancy. These seeds proved especially sensitive to treatment with a gibberellin [102]. Early treatment of wheat grains undergoing prolonged storage was inadvisable, since it lowered the sowing qualities of the seeds [103]. The total quantity of gibberellins is determined photometrically [104] in practice, and the physiological activity of the preparations by means of a biological trial, e.g. on a dwarf pea [60].

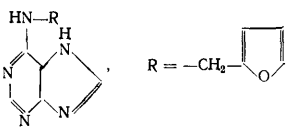
The mechanism of the action of gibberellins is illustrated by data published by Paleg [105] and Iomo [106] on the role of gibberellic acid in the formation of the hydrolytic enzymes of the endosperm of germinating barley. Work in this field has been continued very vigorously, and the main details of the mechanism have now been elucidated by researches on barley grains [38,107-113]. Zabolotskii has made a detailed survey of the regulatory mechanisms of the germination of seeds [114]. Formation of gibberellic acid during germination is assumed to be preceded by the synthesis of ribonucleic acid and of a protein in the embryo, which in turn are due to the activity of certain genes [21]. The synthesised gibberellin enters the endosperm, where it activates several enzymes—α-amidase, protease, ribonuclease, etc.—which reach the storage tissue, where they split up starch, proteins, and other materials. The cleavage products ensure normal growth of the shoot. Gibberellic acid also intensifies glycolysis and the activity of the ring in polycarboxylic acids [79]. Gibberellins promote plant growth by cell elongation, but do not stimulate cell division [86,115,116]. Such elongation assists better germination of the seeds.

Establishment of the presence in seeds of antagonists to gibberellins suggests that their favourable effect is due to the neutralisation of inhibitors [570]. A synthetic antagonist to gibberellins is chlorocholine chloride [117], which is used to oppose the flattening of wheat and other cultivated crops.

The treatment of seeds with gibberellins has provided a deeper insight into the favourable effects of light and low temperatures. The enrichment of seeds with this hormone replaces the stimulant action of light and temperature on germination [86,118]. These factors in the environment have been shown to stimulate the biosynthesis of gibberellins in seeds.

3. Kinins

During recent years the attention of research workers has been attracted by kinins, which are involved in the biosynthesis of proteins, chlorophyll, and other vitally necessary compounds [22,119]. Kinins are widely distributed in seeds, and have been detected in those of maize, sunflower, plum, peach, and other plants [120,121]. They are aminopurine derivatives, of which the best known is 6-fur-2′-ylmethylaminopurine or "kinetin"



Only eighteen years have elapsed since kinetin was obtained and its great physiological activity established [122], but many of its analogues have already been studied. Thus 6-benzylaminopurine surpasses kinetin in activity [123]. Another natural kinin—zeatin [R = $CH_2.CH:C(CH_3).CH_2OH$], isolated in 1967 from maize seeds [124]—also possesses very high activity. Many other purine derivatives have a stimulant effect, in particular those containing NRR′ and SR″ groups at position 6 (where R, R′, and R″ represent hydrogen or organic radicals). For example, 6-aminopurine and nitrogen-substituted aminopurines have proved active in experiments on the germination of horseradish and potato seeds [125]. 6-Benzylaminopurine raises the germinating capacity of lettuce seeds [126], as well as the long-keeping seeds of lupin, pea, maize, and barley [127,128]. Several other aminopurines have also been used to treat seeds [129]. Kinetin itself disrupts the dormancy of the seeds of beech, hazel, and mountain ash [130]; it stimulates germination of lettuce seeds [133] that have been treated with an inhibitor [131,132].

The initial effect of kinetin resembles that of gibberellins in enhancing the synthesis of nucleic acids. However, the second stage involves stimulating cell division, not elongation [134-138]. Kinetin and its analogues influence

mainly processes associated with the replication of deoxyribonucleic acid in cells. It intensifies the synthesis of ribonucleic acid and protein in cells, and stimulates the formation of ribosomes [139].

Kinins may delay the aging of plants. Thus treatment with kinetin has restored the colour of isolated yellowed leaves [140]. Finally, kinins restore the vital activity of irradiated plants. For example, viable ears could be obtained after the action of 6-benzylaminopurine on irradiated wheat grains [141].

Further study of the chemistry and biological action of kinins will be of great interest.

4. Vitamins

Seeds of all plants contain definite quantities of vitamins, which play an important part in germination and the development of shoots. The content of vitamins in seeds depends on many factors, in particular the ambient conditions. Therefore the quantity of vitamins necessary for germination sometimes accumulates in a seed; but sometimes the quantity present is insufficient. Although the vitamin content increases during germination, under unfavourable Spring conditions the accumulation of certain vitamins is insufficient for the normal course of the physiological processes. The presence in seeds of antivitamins and of enzymes which break down vitamins increases still further the deficiency of vitamins in germinating seeds. This makes it clear why supplying certain vitamins to such seeds will normalise metabolism and stimulate their germination.

Nicotinamide (vitamin PP) has been shown to act in this way towards the seeds of cotton [142,143], citrus [144], and vine [145]; pea, sorghum, cucumber, wheat, and beet seeds are also sensitive. Treatment raises the germinating power of the seeds, enhances development of the plant, and increases their yield [146-148]. This vitamin also improves the genetic properties of wheat, which is evident in a great development of vegetative parts, a higher grain content in the ear, increased weight of the seeds, and a higher protein content [149,150]. Treatment of the seeds of lemon, orange, and grapefruit considerably increases the number of seeds capable of giving several shoots [144].

Skrabka found [152] that wheat seeds of diminished germinating power and seeds germinating under anaerobic conditions contain lower contents of ascorbic acid and glutathione. The germinating capacity is raised appreciably by enriching the seeds with these two substances. Ascorbic acid has a favourable effect also on the germination of other seeds [88,153,155].

Seeds respond also to treatment with biotin, the sensitivity increasing during ripening. Seeds differing in quality react differently: seeds from the middle of the maize cob are usually more sensitive to enrichment with biotin, which is less active towards those from the upper part of the cob [156].

Treatment of the seeds of flax, pea, radish, buckwheat, and carrot with thiamine before sowing improves their germination and increases the yield [146]. This vitamin has a favourable effect on cotton seeds [143,158,159], whose growth processes are intensified by vitamin B_6. [142]

The observed biological action of vitamins involves not only normalisation of the metabolism in which a particular vitamin takes part but also an ensuing change in composition of the soil microflora [9]. For example, enrichment with thiamine, riboflavin, and nicotinamide of beans before sowing stimulates more intense formation of root nodules and nitrogen-fixing bacteria, which improves the supply of nitrogen to the plants and enhances growth processes and development of cultivated crops [146,161].

The above results indicate that seeds of several plants are deficient in certain vitamins. Timely treatment of such seeds with vitamins will therefore intensify metabolism, increase germinating capacity, and strengthen the growth and development of the plants.

5. Other Organic Compounds

Organic acids are widely represented in seeds, and are actively formed during germination [162]. The resulting organic acids are utilised in respiration, as well as for the synthesis of amino-acids and other vitally necessary compounds. In several cases, however, the quantities of such compounds remain insufficient for normal metabolism, and treating seeds with them has a favourable effect on growth processes.

Thus treatment of the seeds with succinic acid improves the germination of maize [163], cotton [164], pea [165], wheat [153,165,166], barley, and rye [166,167]. Improvement of germination and intensification of further growth are observed also with other plants [167-173]. The best results are obtained by treating seeds which are germinating in the presence of deficiencies of noisture and oxygen [166]. Not only succinic but also citric, malic, and fumaric acids increase the yield of wheat [153]. Succinic acid has a greater effect on radish and cucumber seeds than has fumaric acid [174]. Certain analogues of succinic acid, e.g. dodecylsuccinic acid, also have a stimulant effect [175]. The action of polycarboxylic acids on seeds has also been discussed in several papers [121,176-178].

Intensified germination of seeds is observed also on treatment with several other acids, e.g. amino-acids [179, 180,568], keto-acids [181], phenylboric acid [182], naphthenic acids [183-187], quinonecarboxylic acids [188,189], cinnamic acid [171,190], 1,2-benzocyclo-hept(and oct)ene-3-carboxylic acids [191], cedrenecarboxylic acid [192], and several others [193-195]. The seeds of wheat, barley, and several other plants are sensitive to formic and acetic acids (Ref. 10, p. 200). In some cases inorganic acids also accelerate germination [196,197].

Many substances belonging to other groups of organic compounds also affect the germination of seeds. Phenols (guaiacol, phloroglucinol, catechol) stimulate growth of the seeds of rye, beet, celery, carrot, and alder [198]; and quinol has a similar effect on wheat and pea [199]. In other cases phenols (tannin, guaicol, gallic acid, etc.) delay or completely suppress growth [200]. Vanillin and ferulic acid in small concentrations stimulate germination, increase the germinating capacity of seeds, and promote the development of shoots [171].

A method has been worked out for obtaining active furan derivatives, whose use for the treatment of wheat seeds produces better development of the root system together with an increased yield [201-204]. Derivatives of several other heterocycles also have a stimulant effect. Thus growth is stimulated, the yield of plants is raised, and resistance to wilting is improved by addition to seed disinfectants or use as a component part of steeping solutions. The greatest activity is exhibited by 1-cyano-2-methyl-5(6)-nitrobenzimidazole, 1-cyanoethyl-5(6)-nitrobenz-

imidazole, 5(6)-nitrobenzimidazole [205,206], 2-methyl-5(6)-nitrobenzimidazole, 5(6)-amino-2-methylbenzimidazole, 2-diethylaminobenzimidazole [171], and several other imidazoles [208]. Good results have been obtained by treating seeds with amino-, hydroxy-, and mercapto-derivatives of pyrimidine [209,210].

Development of the root system of maize, with simultaneous diminution of the height of the plants, is produced by the use of alkyl carbamates [211].

Halogenated alcohols—2-chloroethanol [67,212], 1,2-dibromo-3-chloropropanol [213], *N*-substituted chloroacetamides [214], dibromoethane [213], and *gem*-diarylcyclohexanol derivatives [215]—accelerate germination. In several cases preliminary treatment of the seeds with alcohols facilitates the penetration of moisture [216].

6-Aminopurine and several of its derivatives have a favourable effect on tomato and mustard seeds [217]. Salicylohydroxamic acid has proved useful for the germination of pea and tomato [218]. Wheat and pea germinate better after treatment of the seeds with derivatives of cyclohexane and cyclohexene containing hydroxy- and keto-groups [219], and seeds of grain crops with solutions of melamine and aminoethanol [220]. Seed germination has been enhanced by streptomycin [221], acetone [222], sucrose and hexoses [223], and chlorides of certain cyanine dyes [224].

Thiourea has a positive effect on the seeds of the Russian dandelion and of lettuce [225-228]. *N*-Alkyl-*N'*-arylthioureas, which have been tested on wheat grains, are more active [229]. The combined action of thiourea and indol-3'ylacetic acid on oats exhibits synergism [230]. The dry weight of the roots is increased by soaking peas, barley, and flax in glycothiourea solution [231], and cultivated lettuce seeds in methylurea solution [132].

Germination is stimulated also by certain nitrosulphonamides [232], mixtures of manganese salts of lower carboxylic acids [233], amines [101,234], and other synthetic compounds [235].

The supply of oxygen to seeds is of considerable importance. This is obviously responsible for the favourable effect of hydrogen peroxide on rice [236], sugar-beet [237], tobacco [238], and wheat [9]. Germination is accelerated and the percentage germination of seeds increased by the action of benzoyl peroxide, its halogenated derivatives, methyl hydroperoxide, and t-butyl perbenzoate [239].

Various products which protect plants from diseases and pests may also influence germination. Thus treatment of the seeds of certain crops with disinfectants has in several cases increased their germinating capacity [240-248]. Certain systemic pesticides have proved toxic to seeds [249]. Biologically active compounds containing sulpho-groups may also depress seeds [250].

It is interesting that ethylene is used to bring seeds out of their dormant state [126,251].

There are indications that certain inorganic substances—calcium cyanamide [9,252] and dilute alkalis [197]—may stimulate germination. Keeping seeds in solutions of salts of metals (potassium, calcium) and hydrohalic acids increases the accumulation of amino-acids [161,253].

The list of chemical compounds which have been tested for controlling the rate of germination of seeds could be considerably extended. However, most of the publications involve no knowledge of the mechanism of the action, but pursue the aim of determining whether a given compound stimulates germination and plant growth. Such work, of course, despite its usefulness, conveys little information on the germination of seeds and the mechanism of the action of particular compounds. Yet a solution of this problem would be invaluable for practical agriculture.

6. Inhibitors and Herbicides

A seed is a complicated biological system whose life is controlled by stimulants and inhibitors. The presence of the latter has long been known [254,255], and they have since been detected in many seeds [256-258]. Their quantity and nature depend both on genetic features of the plants and on the physiological state of the seeds. Thus extracts from 60-day green peas retarded the development of bean shoots more strongly than did extracts from ripe seeds [259]. Germination of seeds inside over-ripe fruits of the tomato, pumpkin, and water-melon is associated with a diminution in the content of inhibitors.

The retarding action of plant inhibitors is suggested by other facts. Germination of lime is delayed by extracts of the pericarp [260]. Flavonoid pigments, which inhibit the germination of cereals, have been found in the seed coat of barley [261]. Aqueous extracts of rice bran retard the germination and growth of rice and cultivated lettuce [262]. An extract of sugar-beet nodules greatly diminishes the germinating capacity of wheat [263].

Water-soluble substances from the leaves of steppe plants, which form a rosette at the roots, inhibited the germinating capacity of radish and poppy [211]; an onion paste delayed the germination of maize [224]. Extracts of several other plants exert an inhibiting effect on seeds [264-267].

Not only have several inhibitors occurring in plants now been identified, but in some cases the mechanism of their action has been established. Examples are coumarins in the seeds of sweet clover [268], cyanides in beans [269], parasorbic acid in the fruit of mountain ash [270], ferulic, vanillic, *p*-hydroxybenzoic, and *p*-hydroxycinnamic acids in sugar-beet seeds [271], and abscisic and paracoumaric acids in cotton seeds [173]. Abscisic acid has been detected in many seeds and plants [272-277]. It acts by inhibiting gibberellins and retarding the synthesis of nucleic acids. Several other inhibitors have been isolated from seeds [10,278].

A retarding and herbicidal effect on seeds and seedlings is exerted not only by natural inhibitors but also by many synthetic compounds. The considerable interest in this question led to study of the theoretical principles of the action of inhibitors and herbicides, which are antimetabolites of growth stimulants. Antimetabolites take the place of the most important metabolites in biological transformations during enzymic reactions and inhibit them. The antimetabolite, which is assumed to combine with the active centre of such a protein, forms a system which does not undergo the usual reactions, and the required products are not formed [279].

The structure of an inhibitor is often closely similar to that of the corresponding metabolite. The most active antimetabolites are those which show only slight structural differences from the corresponding metabolites. The main interrelationships in chemical structure between metabolites and antimetabolites have been established [279]. In particular, an inhibiting effect is produced by the replacement of e.g. carboxyl by sulpho, hydroxyl by alkoxyl, etc.

Antimetabolites can be divided into several groups according to the mechanism of their action [279]. Thus some inhibitors and herbicides—e.g. derivatives of phenoxy-, *p*-chlorophenoxy-, 2,4-dichlorophenoxy-, and *p*-methylphenoxy-propionic acids—suppress the activity of auxins and other growth stimulants [422]. A group of synthetic compounds which cause shortening of the stem, thickening of the cell walls, and intensification of leaf colour ("retardants") are antagonists of gibberellins [280,281].

The most widely known of such compounds is chlorocholine chloride ("CCC") $[ClCH_2.CH_2.N(CH_3)_3]^+Cl^-$, whose physiological action was first observed by Tolbert in 1960.[282] It was shown later that CCC is an antagonist of gibberellins[117,283,284]. A Soviet product TUR based on chlorocholine chloride is now available[285]. Plants are usually sprayed with chlorocholine chloride. Recently, however, seeds have also been treated with solutions or powders of retardants[286,287]. Thus the action of retardants on seeds of spring wheat, barley, oat[288-290], pea[291], and cotton[292] has been investigated. Treatment of seeds with CCC may determine the sex of plants[293].

Maleic hydrazide (brand MG-T) and its derivatives act as antagonists to plant-growth stimulants. The hydrazide inhibits cell division[294]. Gibberellins and maleic hydrazide have opposite effects when applied together[295]. These compounds are often used to treat seeds to prevent germination during storage. Maleic hydrazide inhibits the germination of cotton[296], beet[297], soya[298], peas, beans, cucumber, wheat, barley, maize, turnip, radish, tomato, and rye[300]. Analogous effects on metabolism are produced by hydrazides of several other acids—chloromaleic, methylmaleic, phthalic, and succinic[299]—*NN*-dimethylsuccinamic acid[296], 6-azauracil[300], and certain other uracil derivatives[301].

Halogenated aliphatic acids, which retard the biosynthesis of individual groups of enzymes, inhibit germination[279]. Thus investigations have been made on the action of sodium trichloroacetate on wheat and millet grains[302], of trichloroacetamidine on mono- and di-cotyledonous crops[303], of propionic acid, which protects grain forage of high moisture content from germination[304], and of chloral hydrate, which has a herbicidal action on the seeds of barley, millet, oats, mustard, and wheat[302].

Several other substances have an inhibiting action on seeds. Thus 3-acylated aminotriazines delay the germination of radish[305], sulphanilamide[306] and aminopteridine[307] that of maize and peas, diepoxides the germination of wheat, millet, and radish[308], and 1,3-diphenylprop-2-ylamine that of wheat and kidney-beans[309]. Vital activity is completely suppressed by isocyanates[310] and several other substances[311-316].

Study of the effect of physiologically active substances on the germination of various plants has shown that, whereas some seeds are destroyed by a particular compound, others are resistant. This has been used to develop ways of destroying the seeds of weeds in the soil. Thus many weeds are killed by introducing industrial herbicides into the soil before sowing.

Further study of the dependence of the inhibiting effect of synthetic antimetabolites on their chemical structure and examination of the mechanism of their action will permit the development of new types of selective weed-killers.

III. CHEMICAL MUTAGENS

Chemical compounds are able not only to stimulate or inhibit germination and plant growth but also to influence heredity[317]. The ability of chemical compounds to change genetic features was first observed as early as 1916.[318] A few new mutagens were discovered in the 1930s, when aziridine, diethyl sulphate, and several other substances were found to be highly active[318]. A broad investigation of this phenomenon was begun after valuable results had been obtained on barley and peas[3]. Whereas radiation methods became widely used in the 1930s to change heredity, nowadays chemical mutagens occupy the primary place[319].

The seeds are usually soaked in a solution of the mutagen of definite concentration[321]. *N*-Nitrosoethylurea, 1,8-bisdiazo-octane-2,7-dione, aziridinopiperidine[322-327], diazoacetic ester, bis-2,2-dichloroethyl hydrogen phosphate, *N*-nitrosomethylurea[328], ethyl methanesulphonate[329-334], *NN'N"*-triethyl-thiophosphoramide[335], diethyl dimethyl pyrophosphate, and tetraethyl dithiopyrophosphate[336] have found use for these purposes. Colchicine[337,338] and other substances[24] are employed as mutagens.

The largest number of publications have been concerned with obtaining valuable mutations in wheat and rice, as well as in maize[329], barley[330,333,339], sugar-beet[337], cotton[332], and peas[340].

Since traces of mutagens (or their decomposition products, e.g. ethyl hydrogen sulphate[341]) may have a deleterious effect, they are removed by washing with water, sometimes with the addition of chemicals, e.g. sodium thiosulphate[319]. Treatment and washing with water are followed by sowing.

The possibility of obtaining agriculturally valuable mutations of cultivated crops by treating the seeds with active compounds opens up new prospects for changing the genetic character of plants and will provide a deeper insight into the chemical nature of heredity[154].

IV. TREATMENT OF SEEDS WITH PLANT-PROTECTION AGENTS

Plants synthesise not only compounds that are directly involved in metabolic processes but also those which have a toxic effect on bacteria and fungi. The latter compounds were termed "phytoncides" by Tokin[342]. Investigation of the composition of gaseous and liquid examples showed that such products comprise various aldehydes, phenols, essential oils, and other compounds[343]. Available results indicate that treating seeds protects them from diseases caused by micro-organisms.

Thus during 1953–1954 it was found that treatment of clover and lucerne with the "phytoncides" of garlic had a protective effect on the seeds for a year[344]. Treatment of seeds of perennial grasses with onion "phytoncides" proved to be more effective. The morbidity of perennial grasses[345], barley, kidney-beans, peas, wheat, cucumbers, flax, and other plants[346] was lowered by applying analogues of pseudoallicin to their seeds. "Phytoncides" of onion, garlic, and horseradish lowered the incidence of vascular bacteriosis in cabbage, and of bacterial cancer in tomatos (seeds were treated before plants)[347,348]. Antimicrobial substances of mustard, horseradish, and eucalyptus protected cotton seeds from gummosis[346].

Treatment of tomato seeds with "phytoncides" from the fruit of nightshade completely eliminated morbidity due to bacterial disease[349], and of clover, lucerne, and tomato seeds with arenarin (a "phytoncide" of everlasting sandwort) tended to lower the susceptibility of the plants to bacteria, in some cases to fungi as well, and to a greater extent than treatment with Gramosan [an ethylmercuric chloride seed fungicide equivalent to Ceresan][346]. Fusariosis in melons is prevented by treating the seeds with anabasine (an alkaloid isolated from a leafless blackberry)[350]. Extracts of the seeds of certain kinds of wood (ash, acacia, wild rose) have a bactericidal effect on wheat grains[351].

Antibiotics have a special place in the fight against plant diseases. Streptomycin is the most widely used for disinfecting seeds. Thus tests on beet seeds in England gave such promising results that in 1960 almost all beet growers in that country had changed to treating seeds with a solution of streptomycin. It gave good results with oats, wheat, and barley [352]. However, products of the vital activity of organisms and plants have not found wide application for protecting seeds from fungal and bacterial diseases. This is due not only to the complexity of their isolation in considerable quantities but also to the inhibiting effect of some of them on germination.

Nevertheless, agriculture demanded readily available and effective agents to reduce the immense losses of production due to micro-organisms and pests. According to the most recent data, for example, the world losses merely of wheat are 85.6 Mt or 23.9% of the total production of this most important crop [353]. Comparable losses occur in stored grains and rice: in 1947 the United Nations estimated them to be 33 Mt, a quantity which would have fed a human population of 150 millions for a year [354].

A considerable proportion of plant disease is transmitted through the seed stock from generation to generation. Furthermore, the eggs of many insects are distributed with the seeds on sowing, so that the great attention paid to the chemical disinfection (decontamination) of seeds becomes understandable. This plays an important part also in the struggle against pests and micro-organisms inhabiting the soil, as well as against granary pests [3,355-359,160].

The local treatment of seeds with protective agents has considerable advantages over the continuous application of chemicals. Contamination of the soil with poisons is avoided. The introduction of protective agents is combined with sowing, which eliminates additional types of field operations, and considerably diminishes the quantities of pesticides required [360-363].

Although the disinfection of seeds with various chemical reagents has been employed for a long time, widespread use has occurred only during the past 30–40 years. At the present time hardly any seeds of agricultural crops are sown in developed countries without chemical treatment [364-366]. When especially injurious substances are applied, the seeds are dyed bright colours or are treated with compounds having a characteristic odour [367].

Substances used for plant protection can be divided according to their type of action into insecticides, fungicides, bactericides, zoocides (against rodents), nematocides (against roundworms—nematodes), repellents, and several others. The same substance can offer different types of protective action, but such pesticides are usually classified according to their most characteristic range of activity.

Below we shall survey the main classes of synthetic chemical compounds used for the protective treatment of seeds, primarily on the basis of their chemical structure, and secondarily their type of action.

1. Phosphorus Compounds

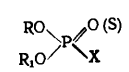
Phosphorus compounds form one of the chief classes of pesticides used for plant protection [368]. Several thousands of active phosphorus compounds are already known, among which about 80 are employed in agriculture. In the present Review, of course, it is impossible to consider all these products. We shall mention only the main phosphorus compounds used for the disinfection of seeds.

Although these are usually organophosphorus compounds, there are several active inorganic compounds, primarily zinc phosphide Zn_3P_2, which is used as a zoocide [4]. In several cases it also possesses insecticidal properties. Zinc phosphide has a strong disinfectant effect, but the substantial disadvantage of high toxicity towards farm animals: thus wheat, barley, and sunflower seeds remained toxic towards cows, calves, and pigs for 35, 43, and 96 days respectively after disinfection with zinc phosphide [369].

Organophosphorus compounds occupy a most important position among pesticides. Their total production now approaches that of chlorinated pesticides. Their useful properties include high activity, wide spectrum and rapidity of action, low consumption of products, and decomposition to give non-toxic or only slightly toxic products. An important aspect is that several of the organic compounds of phosphorus have a systematic effect [4].

The basis of the action of organophosphorus compounds is supposed to be inhibition of the enzyme choline esterase [4]. An impetus to a broad study of active organophosphorus compounds was given by the publication of Schrader's papers [370]. Soviet scientists have made a great contribution to developing the chemistry of organophosphorus compounds. Several reviews and monographs have appeared on the chemistry and application of organophosphorus pesticides [4,370,372,374].

Mel'nikov [4] made a detailed examination of the dependence of the pesticidal activity of organophosphorus compounds on their chemical structure. Compounds of general formula



are most often used, in which R and R_1 are organic radicals, usually lower alkyls (methyl, ethyl, isopropyl), while X is a group which can be replaced by a nucleophilic agent [371]. Increase in chain length leads to loss of activity. New active derivatives are therefore obtained by varying X. Replacement of oxygen by sulphur lowers the toxicity towards mammals without significant loss of pesticidal activity. The toxicity is still further reduced in derivatives of phosphorodithioic acids, which are more resistant to hydrolysis, so that the duration of their action is lengthened [4].

Among the large number of organophosphorus compounds for treating seeds use is made in particular of the products—2,2-dichlorovinyl dimethyl phosphate, 1,2-dibromo-2,2-dichloroethyl phosphate (Dibrom), dimethyl *N*-isopropoxycarbamoylphosphonate (Avenin, K-69-79), dimethyl 2,4,5-trichlorophenyl phosphorothioante (Ronnel, Trolene, trichlormetaphos, Etrolene, Dow ET-14, Korlan, Nankov), diethyl 2-isopropyl-4-methylpyrimidin-6-yl phosphorothionate (Dianisone), and 2-ethylthioethyl *OO*-dimethyl phosphorothioate (a mixture of isomers) (Meta-Systox, methyl demeton) for the treatment of grain [4,375]; *S*-1,2-diethoxycarbonylethyl *OO*-dimethyl phosphorothiolothionate (Carbophos, Malathion) for treating the seeds of kidney-bean, maize [4,376], barley, oats, rye, rice, sorghum, and wheat [4,377]; and *OO*-dimethyl *S*-*N*-methylcarbamoylmethyl phosphorothiolothionate (Phosphamide, Rogor, Dimethoate, BI-58) and pyrophosphoric octamethyltetra-amide (Octamethyl, OMPA, Tradane, Systam, Pestox-111) for the seeds of wheat, sugar-beet, and savoy [4,378]. Several other organophosphorus compounds are also used for disinfecting seeds [4,377-384].

Organophosphorus insecticides can be arranged in the sequence—Diazinon, Guthion, Ronnel, DDVP, Dibrom—according to the maintenance of the protective effect on the grain. Protection becomes weaker with increase in the moisture content and rise in the temperature of the grain.

Certain organophosphorus insecticides exert a stimulant effect on the germination of sugar-beet [378].

2. Mercury Compounds

Organic compounds of mercury occupy a leading position among means of protecting plants from fungal and viral diseases and from bacterioses. They possess the advantage of high toxicity towards micro-organisms and lack of toxicity towards seeds. In several cases, moreover, a stimulating effect on the growth processes of plants is observed [4]. Organic mercury compounds have already been widely used for several years in the disinfection of seeds. The history of and the prospects for their application have been discussed in several reviews [385,386]. Mercury preparations are considered to act by inhibiting the functioning of respiratory enzymes [387,388].

The compounds used as fungicides and bacteriacides usually have the formula R–Hg–X, where R is an unsubstituted or substituted aliphatic, aromatic, or heterocyclic radical, and X is an organic or inorganic acid radical [4,387]. The relation between the activity of these compounds and their chemical structure has been revealed by Mel'nikov [4]. Mercury compounds are often applied as components of combined disinfectants, but they also find independent usage. Many mercury compounds are used as seed disinfectants, of which only a few will be discussed here.

Ethylmercuric phosphate (NIUIF-1) is mostly used for the moist disinfection of seeds of various crops. However, other modes of disinfection are also applied. Thus a semi-dry treatment with ethylmercuric phosphate of the seeds of rye, winter wheat, and maize increases the yield, the energy of germination, and the germinating capacity [389]. Good results are obtained by immersing the seeds in a solution of the fungicide [390].

Methylmercury cyanodiamide (as the preparations Panogen, Aldrogen, Radogen [392]) is used in the form of solutions, often with mechanised treatment of the seeds [4]. This product gives favourable results for seed disinfection on flax [391], cereals, maize, tobacco, and vegetables [392].

Methoxymethylmercuric chloride (Ceresan Universal, Arethan) is a disinfectant for the seeds of grain, sugar-beet, and other crops [4].

Phenylmercuric acetate (Ceresan, PMATs, FMA, Tag, Quixane [4], Ruberone [393]) is sometimes supplied mixed with ethylmercuric chloride. Phenylmercuric acetate is used against kernel smut on seeds [393]. It can be mixed with a synergistic additive—dehydroabietylamine [394].

Phenylmercuric propionate is a bactericidal and fungicidal product [395].

Ethylmercuric chloride is the active principle of the disinfectant Granosan (NIUIF-2 [396]). It ensures decontamination of the seeds of almost all agricultural crops—cereals [397,398], fodder [400], industrial [399], horticultural, and ornamental [401]—from bacteria and fungi. Granosan increases the germinating capacity of the seeds of various crops [240].

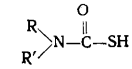
Among other mercury compounds used to disinfect seeds mention must be made of methylmercuric oxide [394], methylmercuric pentachlorophenoxide [402], and compounds of formula R'HgSR (where R' is a lower alkyl and R the residue of a polyhydric alcohol) [403]. The advantages of this group include the possibility of the advance treatment of wheat seeds with mercury-containing products [404], their comparatively high efficiency [405], and the possibility of application as oil emulsions [406].

Liquid disinfectants based on organomercury preparations have found wide application [357]: they are active not only on direct contact but also by the action of the gas phase. The best known are the above products Panogen and Aldrogen, as well as liquid preparations based on phenylmercuric acetate, mercury toluene-*p*-sulphonamide [407], and other products [408].

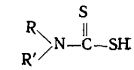
Czech workers have proposed an interesting method for obtaining small-volume arylmercury disinfectants by a series of ion-exchange reactions [409-412].

3. Thiocarbamates and Dithiocarbamates

A large group of seed disinfectants are derivatives of thiocarbamic acid



and dithiocarbamic acid

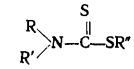


These compounds exhibit herbicidal activity, but they can also be used as fungicides or nematocides. Dithiocarbamates are the most widely used to disinfect seeds, although isolated publications have appeared on the use of derivatives of thiocarbamic acid to disinfect seeds of e.g. wheat and cotton [413].

Many papers have been published on the mechanism of the action of dithiocarbamates. It is assumed that their conversion products, isothiocyanates, possess toxic properties [387]. It is noteworthy that various isothiocyanates are used independently to treat seeds [414,415]. Discussions of the relation between the chemical structure of these compounds and their activity [4,387] reveal that the most active are those in which R and R' are methyl groups: lengthening the radical diminishes the activity.

The fungicidal properties of dithiocarbamic acids were discovered in 1934. [416] Many derivatives, primarily salts, are now used to treat seeds. Thus fungicidal activity is exhibited by the chelated dimethyldithiocarbamates of zinc [4,387,417] (marketed as Zineb), iron (Ferbam) [4,387], and manganese (Maneb) [4].

Another large group of derivatives of dithiocarbamic acid used for disinfecting seeds are compounds of general formula



where R'' may be various organic radicals, while R and R' both represent methyl. For example, compounds in which R'' = $SArX_nY_k$ (where X = NO_2; Y = H, Cl, cyclo-C_6H_{11}; and $n + k = 3$) are harmless to heat-resistant seeds and do not affect the properties of the grain [418]; compounds with R'' = $-\overline{N.CO.[CH_2]n.CO}$ are used to decontaminate rye seeds and possess slight phytotoxicity [419]; a preparation containing $(CH_3)_2N.NH.CO.S.S.CO.NH.N(CH_3)_2$ is used as a fungicidal disinfectant for the seeds of wheat and

oats[420]; and preparations containing a furan ring in the group R″ are applied to wheat and cotton seeds. Fungal diseases of wheat and cotton are resisted by treating the seeds with several heterocyclic derivatives of dimethyldithiocarbamic acid[413].

Derivatives of polymethylenethiocarbamic acids (usually ethylenethiocarbamic) form a separate group. The best known are manganese and zinc ethylenedithiocarbamates and bisdimethylthiocarbamoyl ethylenebisdithiocarbamate (Tekoram)[4]. Compounds of these salts with ethylenebis(thiuram disulphide) possess stronger fungicidal properties[4,421]. Tetramethylthiuram disulphide finds very wide application as a seed disinfectant, both alone and in various mixtures (Thiuram D, Thiuram, TMTD)[4]. It not only decontaminates the seeds of cereals, beans, and several other crops[397,423–425] but also raises the field germinating capacity of wheat, maize, and cotton[240,241]. The fungicidal and bactericidal properties of TMTD are strengthened by the addition of dehydroabietylamine[394].

4. Chlorinated Hydrocarbons

Chlorinated hydrocarbons (and more rarely other halogenated derivatives) form the main group of plant-protection agents, widely used both in the Soviet Union and abroad. They are employed mainly as effective insecticides and nematocides, although several also possess fungicidal properties. This class of compound is usually divided into three groups according to their chemical nature and mode of synthesis. The first group comprises halogen derivatives of aliphatic hydrocarbons, among which those which produce a sufficient concentration in the gas phase (fumigants) are usually applied to seeds.

The simplest member of the second group—halogenated aromatic hydrocarbons—is hexachlorobenzene, employed as a seed disinfectant in various mixtures against smut fungi of cereals, often together with the toxic ethylmercuric chloride[4]. Halogenated derivatives of diphenylmethane—primarily bis-*p*-chlorophenyl-2,2,2-trichloroethane (DDT)—have found considerably greater use. Several monographs have been published on the production, properties, and application of DDT.[426–428] In the treatment of seeds DDT is used mainly as a component of composite disinfectants, but references have been made to its independent application, e.g. for dusting the seeds of maize, kidney-bean, and ground-nut to protect them from pests. The germinating capacity of the treated seed was undiminished by storage in sealed vessels for up to 18 months[429]. In spite of the thorough study and adequate manufacturing capacity, the question of reducing the scale of production of DDT [4] arises from its considerable toxicity towards human beings and animals.

The third of these groups of seed disinfectants comprises halogenated alicyclic hydrocarbons. One of the most widely used insecticides of this group is hexachlorocyclohexane. Among its eight stereoisomers only the γ-isomer exhibits toxicity. A preparation containing 99–100% of the γ-isomer appears on the market as Lindane[4,430]. Hexachlorocyclohexane may also be a component of composite disinfectants. It can find independent application, e.g. to protect a seed stock from harmful insects[429]. The δ-isomer is used in disinfectant mixtures as a synergistic additive to certain fungicides[4].

Chlorinated derivatives of polycyclic compounds are widely used. Several effective products, which have found application in composite and in individual disinfectants, are obtained by diene synthesis, in particular with hexachlorocyclopentadiene as one of the reactants. Several of these products are listed below.

Allodan is 1,2,3,4,7,7-hexachloro-5,6-bischloromethylbicyclo[2,2,1]hept-2-ene

Endrin is 1,2,3,4,10,10-hexachloro-1,4 : 5,8-di-*endo*-methylene-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydronaphthalene

Aldrin is 1,2,3,4,10,10-hexachloro-1,4-*endo* : 5,8-*exo*-dimethylene-1,4,4a,5,8,8a-hexahydronaphthalene

Heptachlor is 1,4,5,6,7,8-heptachloro-4,7-*endo*-methylene-3a,4,7,7a-tetrahydroindene

Dieldrin is 1,2,3,4,10,10-hexachloro-1,4 : 5,8-di-*endo*-methylene-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydronaphthalene.

These products proved effective against harmful insects on treatment of the seeds of maize, sorghum, kidney-bean[431], carrot, onion[432], and cotton[433]. Dieldrin gives better results than other insecticides in protecting seeds from the Swedish fly[434]. These products are used also for several other plants.

Among other halogenated derivatives we must note the chlorothiophens, which are no less active than mercury preparations[435,571].

5. Other Groups of Seed Disinfectants

The earliest seed disinfectants were copper compounds, mainly organic derivatives. Copper 2,4,5-trichlorophenoxide is used[4], also constituting 20% of the disinfectant of the same name. The major portion of the product, marketed as a dust, is talc[355]. Copper trichlorophenoxide is employed e.g. for treating cotton[436] and soya[437] seeds. Another copper compound is the quinolin-8-yl oxide, the active principle of the disinfectant Quinolate-15 [438] (Quinolene-15 [439]).

Derivatives of trichloromethanethiol possess good fungicidal properties[440]. Attention was first directed by Kitleson[441] to the fungicidal activity of compounds containing a trichloromethylthio-group. Compounds of this series at present in use for treating seeds are tetrahydro-*N*-trichloromethylthiophthalimide (Captan)[4] and bistrichloromethyl trisulphide (possesses also stimulant properties)[242].

Among other groups of disinfectants used for treating seeds we must mention inorganic and organic arsenic compounds (e.g. calcium arsenite in Protas Preparation PD [355] and methylarsine sulphide[442]), tin compounds[443,444], and nitro-compounds, e.g. dinitrobenzene[397] and dihalogenonitrobenzenes[445,446].

The search for seed disinfectants less toxic than organometallic compounds led to the discovery of a large group of biologically active *N*-substituted carbamic esters, which were mainly highly active insecticides and herbicides. Derivatives of carbamic acid possessing also fungicidal activity are known[4,396,447]. These compounds have not yet found wide application for the treatment of seeds, but show promise in this respect[447].

Substances used to overcome pests and diseases by seed disinfection include pentachlorophenylmethanethiol and its zinc salt[449], *p*-hydroxyphenylazoformamide[450], lower 2,4-dihalogenophenyl halogenoalkanesulphonates[451], ethylenedisulphonic acids[452], 2-methoxyethylamine[453], methanol[454–456], various heterocyclic derivatives—of isothiazole[457], benzimidazole[458], benzoxazolinone[459], and thiophen[460]—oxathi-in derivatives (in particular

3-carboxyanilido-5,6-dihydro-2-methyl-1,4-oxathi-in—Vitavax)[461,572-575], substituted maleimides[462], sorbic acid[463], and several other substances[454,464]. In particular sorbic acid diminishes considerably the disease of fusariosis in cotton seeds.

Great attention has recently been paid in seed treatment to disinfectants containing more than one active principle, e.g. one or two fungicides, an insecticide, sometimes with the addition of trace elements and other active substances[157]. Such preparations are highly efficient[207,373,379,448,508]. In individual cases mixtures of different insecticides are used[151].

A mixture of the disinfectants—tetramethylthiuram disulphide and γ-hexachlorocyclohexane—is most often employed, against pathogenic fungi and bacteria, by treating seeds of grain crops[241,439,465], peas[466], and maize[246,467]. The mixture is marketed as the composite disinfectants Thiuram-gamma (50% TMTD + 20% γ-isomer + filler)[465-467], Germal (50% TMTD + 40% γ-isomer + filler)[439], and Thiramin[468]. Other mixtures are also used[241]. Manganese sulphate may be introduced into such a composition[246].

Tetramethylthiuram disulphide (40%) and γ-hexachlorocyclohexane (20%) are widely used in combination with copper trichlorophenoxide (10%) as the disinfectant Phenthiuram (containing also 5% of sulphite–alcoholic residue + 3% of carboxymethylcellulose + 20% of kaolin), employed for treating seeds of cotton and cereal–legume crops[439,469-472]. Phenthiuram possesses a broader fungicidal and bactericidal action than tetramethylthiuram disulphide[4]. Phenthiuram mixed with 8% of ammonium molybdate is marketed as Phenthiuram Molybdate[4], which gives good results against pea ascorosis[473].

Mercurhexane (containing 1% of ethylmercuric chloride + 15–20% of hexachlorobenzene + 15–20% of γ-hexachlorocyclohexane + talc + kaolin) has found widespread application as a composite disinfectant. It possesses high fungicidal activity, together with insecticidal properties[471,474-476]. Other composite disinfectants containing mercury include a mixture of Granosan and Hexachloran used for treating sugar-beet seeds[477], the preparation VV (a mixture of Lindane and organomercury compounds) for the seed treatment of wheat[478], a fungicidal mixture of ethylmercuric chloride and tetramethylthiuram disulphide stabilised with thioglycerol for preventing the infestation of seeds with fungi[479], and a mixture of tetramethylthiuram disulphide and methylmercuric dicyanodiamide[480] for grain.

Other composite disinfectants—e.g. mixtures of copper trichlorophenoxide and γ-hexachlorocyclohexane[481], tetramethylthiuram disulphide and pentachloronitrobenzene[482], zinc chromate and Heptachlor[467], tributyltin and chlorinated aliphatic compounds[483], and of tetramethylthiuram disulphide, chlorinated hydrocarbons, glycols, and quinones[484]—are also used for treating seeds to protect them from various pathogens.

Seeds are treated also with active vapours to protect them from pests and diseases. Halogenated lower hydrocarbons are most widely used in this way (as fumigants). They are applied to the seeds of sunflower[485,486] wheat[487,488], pea[489,490], barley[491-493], maize[491,494], oats[491,492], flaz[494], sorghum[491], carrot, cabbage, radish, and turnip[495].

Methyl bromide, which destroys nematodes as well as certain injurious insects, is most often used[185,485,488,490-497]. However, several disadvantages are entailed: being an alkylating agent, methyl bromide may act as a mutagen, disturbing the growth processes of plants[4] and in several cases retarding the germination of seeds[242]. Furthermore, this compound may also impair the quality of the oil obtainable from treated seeds of oil-yielding crops[486]. In this connection, the brief application of high concentrations is more effective than prolonged exposure at lower concentrations[491].

Among other halogenated hydrocarbons used for fumigation we must mention chloroform[487,498], carbon tetrachloride[485,487,499], dichloromethane[498], dichloroethane[485,499], dibromoethane[485,497], and dichloropropene (the active principle of the fumigants DD and Telon[497]), as well as dichloroethylene, trichloroethylene, dibromoethylene[499], and 1,2-dibromo-3-chloropropene[497]. The application of mixtures of these halogenated hydrocarbons has been reported. In some cases better results are given by halogenated nitro-hydrocarbons, such as chloropicrin and dichloro-1-nitroethane[490,500].

Other groups of compounds are also used as disinfestants in fumigation. Thus aluminium phosphide pellets, which evolve phosphine on hydrolysis, lead to complete destruction of granary weevils[498,501]. Sulphur derivatives—carbon disulphide[499], sulphuryl fluoride[502], sulphur dioxide, and volatile sulphur-containing decomposition products of coal[503]—are used for fumigation. This has been effected also by means of hydrogen cyanide[504] and oxiran[490]. Application of morpholino-α-methylacetonitrile and 2,2-dichloro-1-hydroxyvinyl dimethyl phosphonate showed high activity[505].

To prevent infestation with insects it is recommended that grain should be stored in an atmosphere of an inert gas, e.g. carbon dioxide or nitrogen[506], or else heptane[498].

Special attention is paid to the preservation of seeds of high moisture content[485,500,507] as well as seeds of oil-yielding crops[486,509-514], which are sensitive to several fumigants.

Repellents—in particular a mixture of 2-methylquinoline and naphthenic acids[515], cycloheximide[516]—are used against insects and rodents in the storage of grain reserves, as well as bird repellents[569].

Thus the combined efforts of plant growers and chemists have led to the manufacture of effective products that have greatly reduced crop losses. An intense search has recently been made for compounds possessing a wide spectrum of action and high activity but yet harmless to man, animals, and useful insects, as well as decomposing within required periods of time. For these reasons, in particular, interest has diminished in chlorinated, copper, and mercury products, and the use of derivatives of carbamic acid and certain other substances has increased[364,365,517].

V. APPLICATION OF CHEMICALS TO SEEDS

The seeds of certain plants are small (carrot, onion, tomato, parsley, etc.), and contain little of the reserve materials required for germination. Owing to the small size it is difficult to mechanise sowing: considerable quantities of these expensive seeds must be sown, and the shoots thinned after germination, which makes large demands on labour. As a consequence, the size of such seeds has been increased by covering their coats with bulky materials[518-524]. Such treatment (seed pelleting) was undertaken in the Soviet Union by Peterburgskii[525], who coated seeds with superphosphate mixed with starch paste. Peat, humus, feldspar, bentonite, and several other inert bulking materials are most often used for

pelleting[526,527]. The supply of mineral nutrients to the germinating seeds is improved by introducing major and minor fertilisers[528,529], as well as pesticides, into the pellet.

The experience which has accumulated shows that pelleting is a promising method, reducing the consumption of seeds, improving their germination and the development of shoots, and increasing the yield[519-521,526,530]. An important advantage over steeping seeds is that they can be prepared long before sowing, whereas soaked seeds must be sown immediately.

Protective substances are usually applied in three ways—dry, semi-dry, and moist disinfection—and usually in special equipment—disinfectors[4,356].

In dry disinfection the surface of the seeds is covered with a thin layer of the dry product. A dust is often used for this purpose, consisting of the active principle and an inert filler (kaolin, bentonite, gypsum, talc, etc.); the active part is applied from solution with subsequent evaporation of the solvent or with joint grinding[4]. In spite of the cheapness and convenience of application, dry treatment has several substantial disadvantages, primarily poor adhesion of chemicals, increased consumption thereof, and the dispersion of substances into the air, which impairs the hygienic conditions of the work[356]. Better results are obtained by applying substances in an electrostatic field, but this procedure has not been widely used[531].

"Semi-dry" disinfection improves adhesion to the seed surface and diminishes dispersion of the materials in the air[356]. This implies treatment of the seeds with moistened products and a liquid consumption usually not exceeding 30 litres per tonne of seeds. With a larger quantity of liquid such treatment is termed "moist disinfection". This is not usually applied to large batches of seeds, and requires preliminary slight drying before sowing or storage[356].

A great problem is retention of the chemical on the surface of the seeds. So called stickers are used to improve adhesion, among them a concentrate of sulphite–alcoholic residues[532], sulphite lye[533], silicate cement, flour paste, skimmed milk, molasses, liquid manure[534,535], oils[536], and alabaster[537].

The quality of the applied coating of pesticides is considerably improved by introducing a polymeric film-forming agent into the composition. This is most often a water-soluble polymer—polyacrylamide[538], methylcellulose[539], carboxymethylcellulose[540], a vinylpyrrolidone polymer or copolymer[540,541], partly hydrolysed poly(vinyl acetate)[542], polyvinyl alcohol[526], or a urea—formaldehyde resin[543]—usually amounting to a few percent. However, there are references to the use of compositions containing up to 15% of the polymer, e.g. polyvinylpyrrolidone, polyvinylimidazole, polyvinyloxazolidone, or their mixtures[544,545], epoxide resins, poly(vinyl chloride), polyethers, polyesters, polyurethanes, poly(vinyl acetate), and synthetic rubber[546]. These compositions can be applied from solution or from a dispersion in kerosene[544].

Polymeric materials are also applied that possess intrinsic fungicidal, bactericidal, and herbicidal properties without the addition of active agents of low molecular weight. Thus the polymeric complex of polyvinylpyrrolidone and iodine[547] and ligninacetic acid[548] have a bactericidal action, the product of the condensation of aminoethanol with formaldehyde is fungicidal[547], and poly(vinyl aryloxyacetates), obtained by polymerisation of the monomeric vinyl esters or by aryloxyacetylation of polyvinyl alcohol, are herbicidal[549].

Wetting powders—products giving stable suspensions when mixed with water—have recently occupied an important place among preparations applied to seeds. They are produced by introducing surface-active agents into the compositions[4,550-553].

It has long been established that seeds of many crops, after having been subjected to the action of low temperatures, will give more productive plants: they ripen sooner and give a higher yield. However, practical application of these results encountered considerable difficulties, since seeds sown early in Spring, on germinating, were destroyed by Spring frosts. In this case germination could be delayed by coating the seeds with water-repellent films. By restricting the entry of water into the seeds, such films thereby delay the metabolic processes governing germination. The application of hydrophobic films is especially important for Spring wheat, whose cultivation encounters certain difficulties in several regions. The use of water-repellent seed coatings enables Summer crops to be sown not in Spring but in Autumn, even before the soil is frozen.

Attempts were made to use paraffin wax and a liquid silicone to effect such water-repellency[554-557], but polymeric seed coatings were found to be more promising. Even previously pelleted seeds can be coated with such polymer films. In particular, the presowing treatment of pelleted vegetable seeds with copolymers of vinyl chloride and vinylidene chloride has been reported[558].

Polymer coatings comprising several layers are used for seed treatment[559,560]. The outer, poly(vinyl chloride) film, by disintegrating under the influence of variable temperatures, frees the inner, hydrophilic layers, thereby promoting penetration of moisture into the seeds. Cellulose derivatives have been used as the second layer. The application of such coatings enables the yield to be raised by 15–16% and more convenient sowing times to be used for Spring crops. Plants were found to bush more intensely, have a shorter and stronger culm, ripen two weeks sooner, and give a grain of enhanced protein content.

Union Carbide has proposed an interesting method for controlling germination, by the factory sealing of the seeds into a continuous polymer ribbon which, when placed in the soil, will dissolve within a short period (from 1 min to 1 h). Use of such a ribbon facilitates the sowing of vegetable crops, assists the production of harmonious seedlings and uniform plant growth, increases the yield, and improves the quality of production[561].

It is seen that polymers are finding increasing application for improving the sowing qualities of seeds. In the future the coating of seeds with special films may occur on a larger scale.

A solution in water or in an organic solvent is usually employed for the coating of seeds with polymers. Organic solvents are used also for the application of compounds of low molecular weight. The solvents employed have been acetone, methanol and ethanol[562], halogenated hydrocarbons[4], dimethyl sulphoxide, dimethylformamide, and dimethylacetamide[450]. The germinating power of the seeds may be affected by the organic solvent[563,564].

References have been made to the possibility of the direct polymerisation of monomers on the seed surface. Thus Kozlov and Tarusov polymerised vinylpyrrolidone on the surface of irradiated seeds in aqueous solution at 30–70°C for 2–24 h.[566,567]

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The facts reported here indicate the wide possibilities of the application of chemicals to the treatment of seeds. These include disruption of their dormancy, stimulation of germination, increase in field germinating capacity, and heightened resistance to pathogenic micro-organisms and unfavourable weather conditions. Further cooperation of chemists with physiologists and growers may not only promote a more fundamental study of the processes occurring during storage and germination but also yield new possibilities of controlling the vital activity of seeds.

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Unstable Silicon Analogues of Olefins and Ketones

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In contrast to carbon, silicon does not tend to form multiple bonds. Until recently it was believed that compounds with multiple bonds at the silicon atom do not exist, but in recent years results were obtained which permitted a new approach to this interesting and important problem in the chemistry of organosilicon compounds.
The present review considers unsaturated compounds the compositions and properties of which may be described in terms of the hypothesis that the silicon atom forms $(p-p)_\pi$ double bonds.
The bibliography includes 81 references.

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I. INTRODUCTION

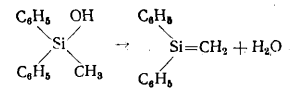
Silicon, the closest analogue of carbon has a similar structure of the outer electron shell: $2s^2 2p^2$ for carbon and $3s^2 3p^2$ for silicon. In most of its compounds silicon is quadrivalent owing to the transition of one $3s$ electron to the $3p_z$ orbital. Like carbon, silicon readily forms compounds with single bonds as a result of the overlapping of the hybridised $3sp^3$ orbitals. On the other hand, it is striking that compounds with multiple bonds of the type $(p-p)_\pi$ are very common in carbon compounds but are completely absent from silicon compounds stable under the usual conditions[1,2]. However, silicon has unfilled $3d$ orbitals which might form bonds of the $(p-d)_\pi$ type with substituents containing lone electron pairs, which would increase the multiplicity of the single bond[2].

The present review deals only with silicon compounds the structure of which can be described in terms of the hypothesis that a multiple bond is formed at the silicon atom. These are the silicon analogues of olefins (R_2Si = = SiR_2; R_2Si = CR_2) and ketones (R_2Si = O). The analogous compounds of bivalent silicon (for example SiO) are not considered, since their properties are largely determined by the presence of the lone electron pair[3].

Until recently it was believed that such unsaturated silicon compounds do not exist. However, the results obtained in recent years give grounds for a modification of this view.

The characteristics of the methods of synthesis of the organosilicon compound belonging to this new class and evidence for their existence are given in the present review and their structures and possible use in syntheses are considered. The employment of the symbol for the double bond, for example, R_2Si = CH_2, in this and in the majority of the studies quoted should be regarded as representing one of the possible structures which explains many of the reactions of these compounds, although the alternative structures $R_2\dot{S}i-\dot{C}H_2$ and $R_2\overset{+}{S}i-\overset{-}{C}H_2$ are also quite possible.

A structure with multiple bonds at the silicon atom was put forward for the first time by Gattermann[4] in 1889 for compounds obtained by treating silicon tetrachloride, trichlorosilane, etc. with ammonia (HN = Si = NH; N = Si = = NH_2). In 1912 Schlenk and Renning[5] reported the synthesis of a stable compound with a silicon-carbon double bond via the mechanism



However, later these results were disproved by Kipping[6], who, having repeated the experiment, showed that Schlenk and Renning[5] did not obtain an individual compound but a mixture of dimethyldiphenylsilane, methyldiphenylsilanol, and biphenyl. In general, towards the end of the 1920s it became clear that the earlier studies[7] where structures with multiple bonds at the silicon atom were attributed to stable compounds must have been erroneous. Moreover, it was shown that the reactions usually employed to form multiple bonds between carbon atoms are unsuitable for the synthesis of the corresponding silicon compounds. Thus the loss of a single water molecule by a tertiary silanol does not occur at all. Disiloxanes are formed instead. Nor are silicon analogues of olefins formed as a result of the dehydrochlorination of silyl chlorides. The latter are extremely stable and can be distilled without decomposition (even in the presence of quinoline). The formation of unsaturated silicon compounds by treating tertiary silyl chlorides with Grignard reagents is also unknown, although many tertiary halogenomethanes do form olefins. Other attempts to prepare stable compounds with a multiple bond at the silicon atom were also unsuccessful[8].

Towards the end of the 1940s and the beginning of the 1950s, the problem of the instability of compounds with multiple bonds at the atoms of elements in the Third and succeeding Periods began to be considered in terms of graphical representations of orbitals and quantum-mechanical calculations (see Section V).

In 1952 Andrianov and Sokolov[9] reported the detection of the dimethylsilanone ion in the mass spectrum of octamethylcyclotetrasiloxane and also the mass spectrometric identification of several dialkylsilanones formed when organopolysiloxanes are heated to 150–200°C and in the gas-phase hydrolysis of dichlorodimethylsilane.

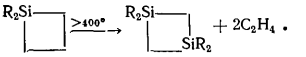
Nevertheless the earlier ideas concerning the possibility of the existence of stable compounds with multiple bonds at the silicon atom were so attractive that even in the 1960s they resulted in the publication of two erroneous communications: concerning the preparation of $Me_3SiCH = SiMe_2$ [10] and of the silicon analogue of benzene[11]. It was soon shown that, instead of the former compound, the authors obtained 1, 1, 3, 3-tetramethyl-1, 3-disilacyclobutane, which was mistaken for an unsaturated compound by virtue of its ability to combine with bromine[12]. The structure of the second compound was not confirmed either[13].

In later studies compounds with double bonds at the silicon atom were regarded only as short-lived species responsible for the formation of particular reaction products. Thus dimethylsilanone was postulated as an intermediate in the cleavage of polysiloxanes by the Iotsich reagent[14]; $MeHSi = CH_2$ was regarded as a product of the carbene–olefin isomerisation of dimethylsilylene[15] and the biradical $Me_2\dot{S}i-\dot{C}H_2$ was introduced into the mechanism of the thermal decomposition of tetramethylsilane to account for the formation of 1, 1, 3, 3-tetramethyl-1, 3-disilacyclobutane[16]; here mention may also be made of the study of Müller and Müller, who considered the dechlorination of chloromethanes in the presence of a silicon–copper alloy[17]. However, all these cases involved complex non-selective processes in which other interpretations of the mechanism are equally probable.

In 1965 the present authors discovered the selective thermal decomposition of monosilacyclobutanes[18,19] via the formation of silicon analogues of olefins. The study of this reaction yielded for the first time kinetic and chemical evidence for the existence of an intermediate compound with a silicon-carbon double bond[20–22] and led to methods for their stabilisation. As a result, these species and other compounds with double bonds at the silicon atom again attracted the attention of chemists, as can be judged from the publication of numerous studies on this subject in recent years. The results of this new stage in the development of the chemistry of silicon analogues of unsaturated compounds are discussed below.

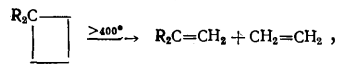
II. MONOSILICON ANALOGUES OF OLEFINS

In a study of the pyrolysis of a number of monosilacyclobutanes we observed the elimination of ethylene and the formation of 1, 3-disilacyclobutanes[18,19].

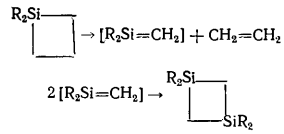


For example, in the pyrolysis of 1, 1-dimethyl-1-silacyclobutane the only reaction products were ethylene and 1, 1, 3, 3-tetramethyl-1, 3-disilacyclobutane. The yield of 1, 3-disilacyclobutane was lower when chlorine atoms were attached to the silicon atom. However, it amounted to 34.8% even for 1, 1-dichloro-1-silacyclobutane, which was of preparative interest for the synthesis of 1, 1, 3, 3-tetrachloro-1, 3-disilacyclobutane which is otherwise difficult to obtain.

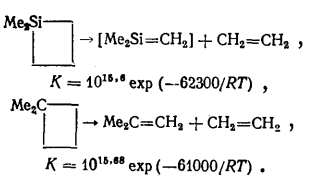
For the analogous thermal decomposition of compounds of the cyclobutane series[23],



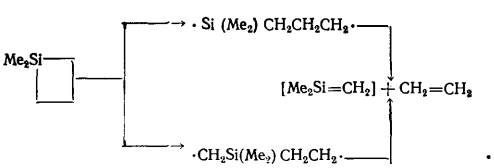
we assumed that the reaction proceeds via an intermediate unstable compound — a silicon analogue of an olefin, which is in fact responsible for the formation of 1, 3-disilacyclobutane[20]:



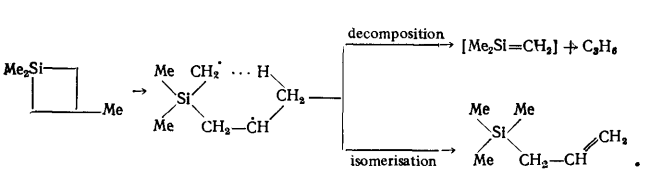
Indeed, kinetic data for the thermal decomposition of 1, 1-dimethyl-1-silacyclobutane proved to agree well with this hypothesis[21,22]. The reaction was of first order with respect to monosilacyclobutane and was homogeneous and the variation of the decomposition rate constant with temperature was very close to the corresponding variation for the thermal decomposition of 1, 1-dimethylcyclobutane[24]:



The closeness of the Arrhenius parameters of these reactions suggests that they have the same mechanism, namely the reaction begins with the dissociation of one bond in the ring (Si–C or C–C) and a consequent formation of a biradical, which decomposes spontaneously to a short-lived compound and ethylene (the biradical mechanism provides a satisfactory explanation of the characteristics of the thermal decomposition of cyclobutanes[25]):



The dissociation of the ring C–C bond is consistent with the isomerisation of 1, 1, 3-trimethyl-1-silacyclobutane[26,27] to allyltrimethylsilane during its thermal decomposition †. Such isomerisation is probably due to the 1, 5-migration of a hydrogen atom in the biradical:



† We may note incidentally that the above reaction is the first instance of the isomerisation of monosilacyclobutanes to silaolefins.

A subsequent investigation established[28] that in the pyrolysis of 1,1-dimethyl-1-silacyclobutane in a flow reactor at low pressures the processes involving the formation and disappearance of the silicon analogue of an olefin can be separated. Thus we found that, when the pyrolysis is carried out at pressures below 1 torr, the region where $Me_2Si = CH_2$ undergoes cyclodimerisation moves to an increasing distance beyond the reactor, as shown by the increase of the ratio $[C_2H_4]/[Me_2SiCH_2)_2]$ by two powers of ten on reducing the pressure to 10^{-3} torr (Fig. 1) owing to the formation by the silicon analogue of isobutene of a polymeric product $(-Me_2SiCH_2-)_x$ on the cold surface.

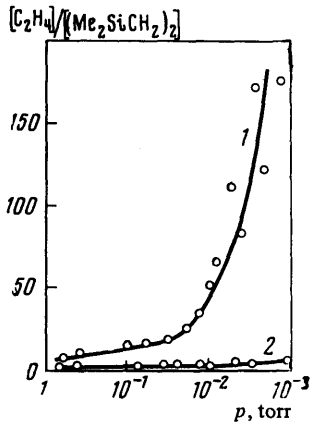
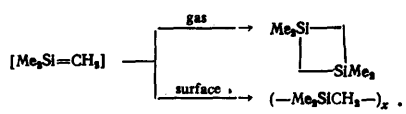


Figure 1. Variation of $[C_2H_4]/[(Me_2SiCH_2)_2]$ with pressure in the pyrolysis of 1,1-dimethyl-1-silacyclobutane in a flow reactor; distance between the pyrolysis and condensation zones: *1*) 30; *2*) 250.

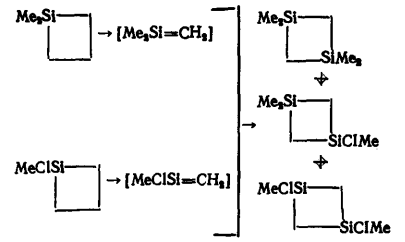
Walsh[29], who employed our kinetic data for the pyrolysis of 1,1-dimethyl-1-silacyclobutane and Davidson and Lambert's data[30] for the pyrolysis of trimethylsilane, found that the π-bond energy in the silicon analogues of olefins is in the range 30–42 kcal mole^{-1} and Barton and McIntosh[31], who investigated the pyrolysis of 1,1-dimethyl-1-silacyclobutane at -196°C by infrared spectroscopy, observed a band at 1407 cm^{-1} which they believe to be due to the presence of $Me_2Si = CH_2$. The methylenediamethylsilane ion is also formed in the dissociative ionisation of 1,1-dimethyl-1-silacyclobutane[32,33] (the peak of this ion is the most intense in the mass spectrum).

Certain reactions of the silicon analogues of olefins, which may be regarded as chemical evidence for the existence of these compounds, are discussed below in relation to $Me_2Si = CH_2$.

It has already been mentioned that, in the absence of trapping agents, cyclodimerisation takes place in the gas phase and polymerisation on the cold surface:

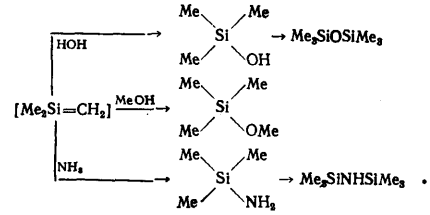


Products of direct and cross cyclodimerisation are formed in the pyrolysis of two different monosilacyclobutanes[20,34]:

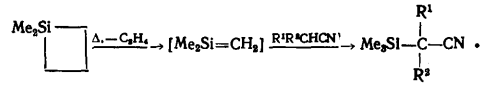


One should note that we never observed among the reaction products dimers of the "head to head" type or cyclic trimers.

Trapping agents form adducts with silicon analogues of olefins. Chemical trapping of $Me_2Si = CH_2$ was first achieved with the aid of water and ammonia in the pyrolysis of 1,1-dimethyl-1-silacyclobutane in their presence[21,22]. The reaction with alcohols occurred similarly:



Quite recently Sommer and coworkers[35] carried out this reaction with acetonitrile and its derivatives:



Another reaction of silicon analogues of olefins is cycloaddition to olefins. However, since the rate constant for this reaction is low compared with the cyclodimerisation rate constant, its contribution can be observed only at olefin concentrations greatly exceeding that of the intermediate. For example, this reaction results in a decrease of the rate constant for the thermal decomposition of 1,1-dimethyl-1-silacyclobutane at conversions in excess of 60%[22]. Kinetic evidence for the cycloaddition of $Me_2Si = CH_2$ to ethylene was obtained in a study of the pyrolysis of 1,1-dimethyl-1-silacyclobutane in the presence of added ethylene[22]. Indeed the apparent first-order reaction rate constant was found to depend on ethylene concentration, in agreement with the kinetic mechanism involving a reversible first stage of the thermal decomposition:

$$A \underset{k_3}{\overset{k_1}{\rightleftharpoons}} B + C$$

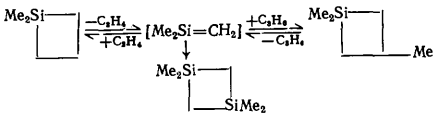
$$2B \xrightarrow{k_2} D$$

$$-\frac{d\ln A}{dt} = k_1\left\{1 - \frac{k_3 C}{(2k_1k_2)^{1/2}A^{1/2}}\left(1 - \frac{k_3 C}{2(2k_1k_2)^{1/2}A^{1/2}}\right)\right\} .$$

where A = 1,1-dimethyl-1-silacyclobutane, B = Me_2Si = $= CH_2$, C = ethylene, and D = 1,1,3,3-tetramethyl-1,3-disilacyclobutane [or the corresponding concentrations (Ed. of Translation)] variation of the apparent first-order reaction rate constant with $(C/A^{1/2})[1-k_2/2(2k_1k_3)^{1/2}-C/A^{1/2}]$ should be linear, which was in fact observed experimentally at different temperatures (Fig. 2). It was also possible to estimate the ratio $k_2/k_3^{1/2}$ and $E_2 - \frac{1}{2}E_3 = 14.5 \pm 4$ kcal mole^{-1}.

The formation of 1,1,3-trimethyl-1-silacyclobutane in the pyrolysis of 1,1-dimethyl-1-silacyclobutane in the

presence of a 15–20-fold excess of propane and the formation of 1,1-dimethyl-1-silacyclobutane in the pyrolysis of 1,1,3-trimethyl-1-silacyclobutane in ethylene constituted chemical evidence for the reversibility of the first stage of the thermal decomposition[36,37]:



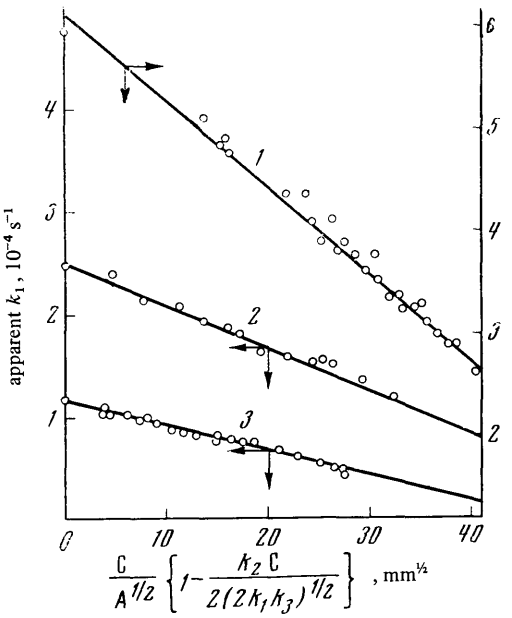
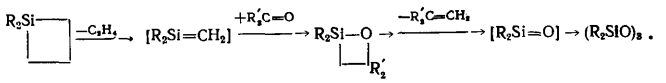


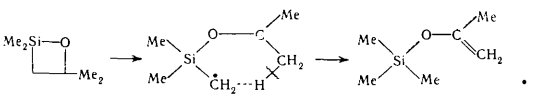
Figure 2. Variation of the apparent rate constant for the thermal decomposition of 1,1-dimethyl-1-silacyclobutane with the concentration of added ethylene (in terms of the coordinates corresponding to the kinetic equation quoted); temperature (°C): *1*) 450.7; *2*) 437.1; *3*) 423.

Silicon analogues of olefins readily undergo cycloaddition to the double bond of the carbonyl group. Cyclosiloxanes (mainly the cyclic trimer), ethylene, and new olefin are formed in the pyrolysis of 1,1-dimethyl-1-silacyclobutane in the presence of isobutyl methyl betone[38] and in the pyrolysis of 1,1-diphenyl-1-silacyclobutane in the presence of 2-pentanone, 2-heptanone, and benzophenone[39]:

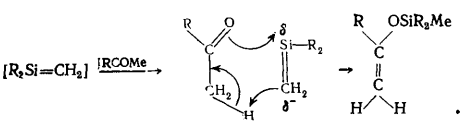


The cycloaddition product (silaoxetan) was not isolated, although Barton and Kline[38] reported its mass-spectrometric identification. We isolated a compound with the corresponding composition in the pyrolysis of 1,1-dimethyl-1-silacyclobutane in the presence of acetone (*m/e* 130), but its spectrum showed bands due to a double bond and the band due to the Si–O bond was in the usual region (1050 cm^{-1}) (in strained rings, this band should undergo a pronounced bathochromic shift — 100 cm^{-1} and more). This made it possible to assign the isomeric structure $Me_3SiOC(Me)=CH_2$ to the product.

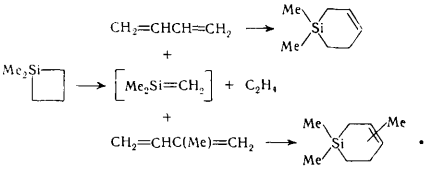
The formation of isopropenyloxytrimethylsilane can be readily represented as a result of the isomerisation of the silaoxetan, which is unstable under the reaction conditions, via the 1,5-migration of the hydrogen atom in the biradical formed on dissociation of the C–C bond of the four-membered ring:



The mechanism of the formation of analogous products based on the addition of the enolised form of the ketone of the silicon–carbon double bond[39] appears more likely. The argument based on the fact that the reaction does not occur in the presence of benzophenone is not convincing, since the 1,5-migration of hydrogen in the biradical is also impossible in this case. In his latest investigations[35,40] Sommer proposes an essentially new mechanism, which includes a six-centre transition state, but, in contrast to our mechanism, no account is taken of the formation of the intermediate silaoxetan:



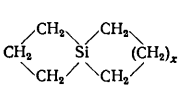
Silicon analogues of olefins are effective dienophiles; they readily enter into the diene synthesis reaction. Thus the corresponding Diels–Alder adducts are formed in the pyrolysis of 1,1-dimethyl-1-silacyclobutane in the presence of butadiene[37], isoprene[37], or 2,3-dimethylbutadiene[41]:



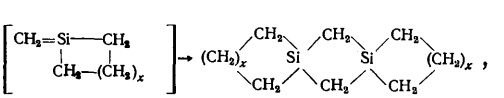
The formation of a single adduct with butadiene and of two adducts with isoprene suggests that the reaction proceeds via a single-state 1,4-cycloaddition mechanism.

Thus there are many reactions demonstrating the existence of short-lived silicon analogues of olefins. The pyrolysis of 1-methyl-1-vinyl-1-silacyclobutane[26] and 1,1-diphenyl-1-cyclobutane[39] proceeds similarly.

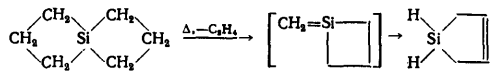
We observed an interesting feature in a study of the thermal decomposition and dissociative ionisation of silaspiroalkanes[43] containing the monosilacyclobutane ring:


(where x = 1, 2, or 3).

Whereas 4-silaspiro[3,4]octane (x = 2) and 4-silaspiro[3,5]nonane (x = 3) form the corresponding 1,3-disilacyclobutanes,



4-silaspiro[3,3]heptane ($x = 1$) behaves anomalously in the pyrolysis[23,43]. Oily products with the composition corresponding to that of the initial compound after the elimination of an ethylene molecule are mainly formed in a flow system in an atmosphere of helium. On the other hand, *in vacuo* this compound decomposes into hydrogen, ethylene, propene, butadiene, and 1-silacyclopent-3-ene, the relative contents of which depend on temperature (Fig. 3). It is significant that compounds with 1,3-disilacyclobutane rings were not formed and the precipitation of elemental silicon on the reactor walls was noted. We believe that these characteristics of the thermal decomposition are in many ways determined by the specific features of the behaviour of the methylenecyclobutane analogue formed from this silaspiroheptane, which is capable of isomerising, in contrast to other compounds of this type:



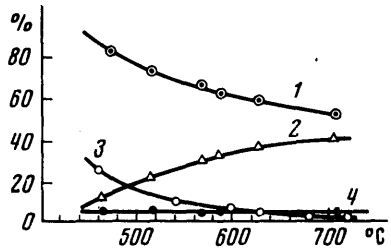
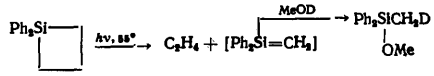


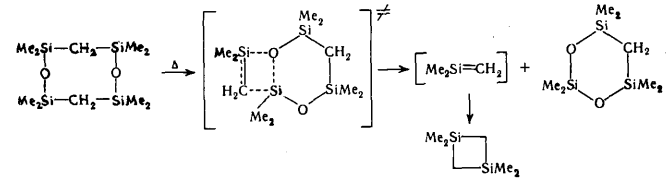
Figure 3. Temperature variation of the relative contents (%) of the decomposition products in the pyrolysis of 4-silaspiro[3,3]heptane: *1*) ethylene; *2*) butadiene; *3*) 1-silacyclopent-3-ene; *4*) propene.

In conclusion of the discussion of the thermal decomposition reactions of monosilacyclobutanes as a method for the generation of silicon analogues of olefins, we may mention that in the series of compounds (where E = C, Si, or Ge) the selectivity of the olefin decomposition process is maintained only for the first two members of the series. The reaction of the germanium compound is significantly complicated by a carbenoid decomposition[44], which precludes its employment for the selective generation of germanium analogues of olefins.

Monosilacyclobutanes are also effective sources of silicon analogues of olefins in the liquid-phase photochemical decomposition reaction[45], as can be seen from the formation of an adduct with deuteriomethanol (yield 80%):

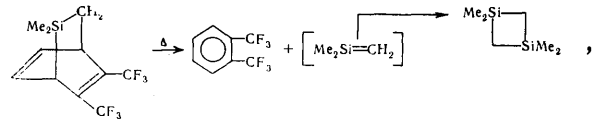


We noted the formation of a silicon analogue of isobutene in the pyrolysis of eight-membered cyclocarbasiloxanes containing siloxane and silmethylene groups[46,47], for example:



However, an alternative decomposition with formation of dimethylsilanone also takes place in this case (see Section IV).

Bicyclo[2,2,2]octa-2,5-dienes proved to be extremely promising for the generation of silicon analogues of olefins. Barton and Kline[48] found that the pyrolysis of 7,7-dimethyl-2,3-bis(trifluoromethyl)-7-silabicyclo[2,2,2]octa-2,5-diene takes place at 400°C in the gas phase with formation of *o*-bis(trifluoromethyl)benzene and 1,1,3,3-tetramethyl-1,3-disilacyclobutane via the mechanism



and the photolysis of this compound at 77° and 28°K resulted in the formation of a large amount of the first product and only of traces of the second. The latter is probably due to the polymerisation of $Me_2Si = CH_2$ in the condensed phase. $Et_2Ge = CH_2$, formed as a result of the pyrolysis, gives rise to 1,3-digermacyclobutane and in the presence of 2,3-dimethylbuta-1,3-diene the product is 1,1,3,4-tetramethyl-1-germacyclohexene.

* * *

The formation of silicon analogues of olefins was also postulated in a number of gas-phase thermal decomposition reactions of cyclic organosilicon compounds. However, in contrast to the majority of the cases which have been discussed, these reactions are not selective and the yield of products due to the formation of unstable species with a multiple bond at the silicon atom is usually low. The thermal decomposition of tetramethylsilane[18], where the formation of 1,1,3,3-tetramethyl-1,3-disilacyclobutane and 1,1,3,3,5,5-hexamethyl-1,3,5-trisilacyclohexane was attributed to the cyclodimerisation and cyclotrimerisation of the silicon analogue of isobutene, was mentioned above:

$$Me_4Si \rightarrow Me_3Si\cdot + Me\cdot ,$$
$$Me\cdot + Me_4Si \rightarrow Me_3SiCH_2^{\cdot} + MeH ,$$
$$Me_3SiCH_2^{\cdot} \rightarrow [Me_2Si{=}CH_2] + Me^{\cdot} .$$

The authors[16] suggest that the intermediate is formed as a biradical species in the decomposition of the trimethylsilylmethyl radical. However, Davidson and Lambert[30,50], who investigated the thermal decomposition of trimethylsilane, showed that the disproportionation of the radicals is more important under these conditions:

$$HMe_2Si^{\cdot} + \dot{C}H_2SiMe_2H \rightarrow Me_2SiH + [CH_2{=}SiMeH] ,$$
$$Me_3Si^{\cdot} + \dot{C}H_2SiMe_2H \rightarrow Me_3SiH + [CH_2 = SiMe_2] ,$$
$$2\,\dot{C}H_2SiMe_2H \rightarrow Me_2SiH + [CH_2{=}SiMe_2] .$$

The competing radical recombination reaction proceeds less vigorously at elevated temperatures owing to the low

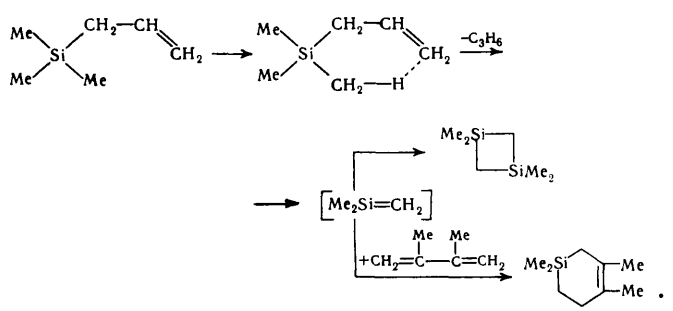
stability of disilanes. The cyclodimerisation of the above olefin analogues leads to the formation of the corresponding three 1,3-disilacyclobutanes. It is important to note that the formation of a cyclic trimer was not observed in this case either.

Moreover, a recent study of the kinetics of the thermal decomposition of tetramethylsilane[51] showed that the disproportionation of silyl radicals

$$2\,Me_3Si^{\cdot} \rightarrow Me_3SiH + [Me_2Si=CH_2]\ ,$$

plays an important role among the reactions involving the formation of $Me_2Si=CH_2$. In particular, whereas at 900°K the ratio of the disproportionation and recombination rate constants for trimethylsilyl radicals is 1.2,[51] at 300°K it is less than 10^{-3}.[52] This corresponds to a disproportionation activation energy of 6–7 kcal mole^{-1}.

According to Bailey and Kaufmann[41], $Me_2Si=CH_2$ is an intermediate in the pyrolysis of allyltrimethylsilane. Together with other products, 1,1,3,3-tetramethyl-1,3-disilacyclobutane is formed in the process and pyrolysis in the presence of 2,3-dimethylbuta-1,3-diene gives 1,1,3,4-tetramethyl-1-silacyclohexene:



However, Sakurai et al.[53] found that the thermal decomposition of allyltrimethylsilane occurs at a low as 500°C. Under these conditions, the main reaction is α-elimination of methylene:

$$Me_3SiCH_2CH=CH_2 \xrightarrow{\Delta} Me_3Si\cdots CH=CH_2 \rightarrow Me_3SiCH=CH_2 + CH_2:\ .$$

Comparison of the results of these studies suggests that the formation of $Me_2Si=CH_2$ in the first case is more likely to be associated with the decomposition to the trimethylsilyl radical and its disproportionation:

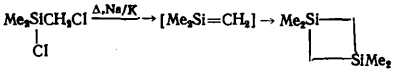
$$Me_3SiCH_2CH=CH_2 \xrightarrow{\Delta} Me_3Si^{\cdot} + CH_2{\cdot}{\cdot}{\cdot}CH{\cdot}{\cdot}{\cdot}CH_2\ ,$$
$$2\,Me_3Si^{\cdot} \longrightarrow Me_3SiH + [Me_2Si=CH_2]\ .$$

This is consistent with the non-selectivity of the reaction noted by Bailey and Kaufmann[41].

According to the latest results[54,55], the pyrolysis of hexamethyldisilane in a flow system at a low pressure proceeds with formation of trimethylsilane, $Me_3SiCH_2Si(H)Me_2$, and 1,1,3,3-tetramethyl-1,3-disilacyclobutane via $Me_2Si=CH_2$:

$$R^{\cdot} + Me_3SiSiMe_3 \rightarrow RH + Me_2SiSiMe_2CH_2^{\cdot}\ ,$$
$$Me_2SiSiMe_2CH_2^{\cdot} \rightarrow Me_2SiCH_2\dot{S}iMe_2\ ,$$
$$Me_2SiCH_2\dot{S}iMe_2 \rightarrow Me_2Si^{\cdot} + [Me_2Si=CH_2]\ .$$

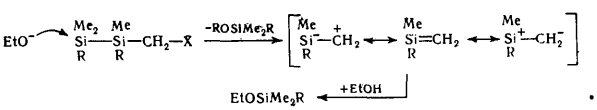
Among other ways of generating intermediates with a double bond at the silicon atom, mention may be made of the gas-phase dechlorination of chloromethyldimethylchlorosilane by sodium and potassium vapours[56]:



and of the photolysis of methylsilane[57,58] by vacuum ultraviolet radiation.

* * *

The hypothesis of the formation of silicon analogues of olefins was also used in the treatment of the mechanisms of certain liquid-phase reactions. Thus Kumada et al.[59] suggested that, when sodium ethoxide is allowed to react with 1-chloromethylpentamethyldisilane and other halogenomethyldisilanes in ethanol solution, there is a synchronous β-elimination of $Me_2Si=CH_2$, which is trapped by ethanol:

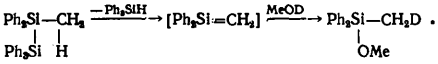


and Jarvie and Rowley[60] introduced this intermediate into the mechanism of the anomalous reaction between dimethylsilylmethylmagnesium bromide and benzophenone:

$$Ph_2C=O + Me_2Si(H)CH_2MgBr \rightarrow Ph_2CHOMgBr + [Me_2Si=CH_2]\ ,$$
$$[Me_2Si=CH_2] + Ph_2CHOMgBr \rightarrow Me_2SiCH_2MgBr \xrightarrow{+H_2O} Me_2SiOCHPh_2\ ,$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad OCHPh_2$$
$$[Me_2Si=CH_2] + Me_2Si(H)CH_2MgBr \xrightarrow{+H_2O} HMe_2SiCH_2SiMe_3\ .$$

However, one should note that in both cases there are alternative reaction mechanisms[60,61] which do not involve the formation of species with a double bond at the silicon atom.

From our point of view, the most convincing studies demonstrating the generation of silicon analogues of olefins in liquid-phase reactions are the investigation of the photolysis of 1,1-diphenyl-1-silacyclobutane already discussed[47] and a study of the photochemical dehydrosilylation of methylpentaphenyldisilane[62], where it was shown that the photolysis of this compound in methanol-d_1 leads to the formation of triphenylsilane and $Ph_2(CH_2D)SiOMe$ in 60% yield. The formation of these products is indeed consistent with the dehydrosilylation mechanism in which the intermediate compound is trapped by deuteriomethanol:

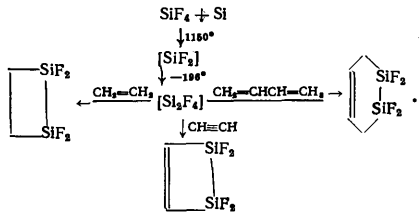


Likewise photolysis of $Ph_2(CD_3)SiSiPh_3$ in methanol yields $Ph_2(CD_2H)SiOMe$ and triphenyldeuteriosilane.

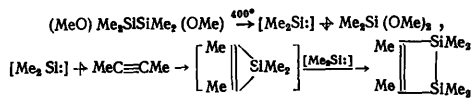
III. DISILICON ANALOGUES OF OLEFINS

After considering data on the joint condensation of difluorosilylene with unsaturated compounds and also the

low-temperature infrared and ESR spectra of difluorosilylene, Margrave and Wilson[63] suggested the formation of the biradical Si_2F_4 at -196°C:



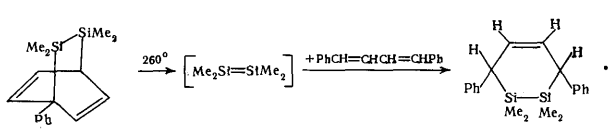
A similar conclusion was reached in a study of the reactions of difluorosilylene with BF_3, benzene, methylacetylene, and dimethylacetylene. However, the reactions of difluorosilylene with methanol, water, hydrogen sulphide, iodine, and germane could not be accounted for by the involvement of the dimeric biradical. It is therefore interesting to note a recent investigation[64] in which a reaction analogous to that described above was also explained without postulating the involvement of Si_2F_4:



Moreover, the observation of the ESR spectrum of singlet difluorosilylene condensed on a cold surface probably cannot be regarded as evidence for the triplet structure of Si_2F_4. This spectrum may be due to the polymeric species $\cdot SiF_2(SiF_2)_xSiF_2\cdot$, where $x = 1, 2, 3\ldots$, and not to Si_2F_4.

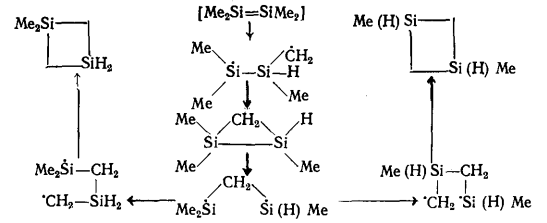
Thus, although there is no doubt about the possibility of the formation of olefin analogues by the dimerisation of silylenes and the structures of the products of the cocondensation of difluorosilylene with alkenes, alkynes, and butadienes can be described in terms of the Woodward–Hoffmann rule as a result of the cycloaddition of tetrafluorodiselene[65], the involvement of the latter as well as its biradical in the above reactions requires additional evidence.

More convincing data concerning the existence of disilicon analogues of olefins were obtained in a study of the thermal decomposition of 7,8-disilabicyclo(2,2,2]octa-2,5-dienes. Peddle, Roark, and coworkers[66,67] found that the pyrolysis of 7,8-disilabicyclo[2,2,2]octa-2,5-dienes leads to the formation of the intermediate $Me_2Si = SiMe_2$, which may be captured by anthracene, naphthalene, and *trans*, *trans*-1,4-diphenylbuta-1,3-diene to form adducts, for example:



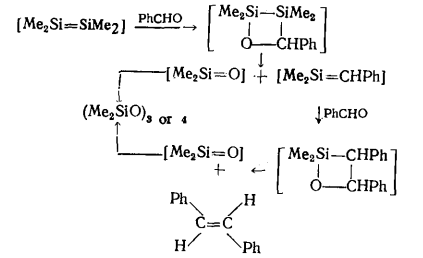
The $Me_4Si_2^+$ ion is the main species also in the mass spectra of these compounds.

In the absence of trapping agents, 1,1-dimethyl-1,3-disilacyclobutane (30%), 1,3-dimethyl-1,3-disilacyclobutane (10%), and a polymer were formed[67]. The mechanism of the formation of 1,3-disilacyclobutanes proposed by the authors is given below:



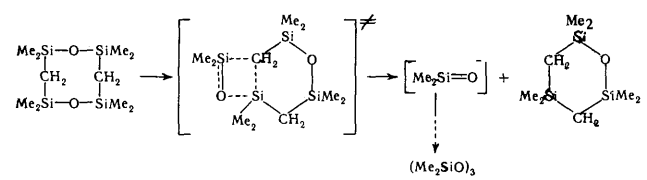
Since the short-lived compound is formed in a thermally activated concerted retrodiene synthesis reaction, it should be in the singlet form, provided that the repulsion of the vicinal methyl groups does not exceed the π-bond energy.

Barton and Kilgour[68] found that the joint pyrolysis of 7,7,8,8-tetramethyl-1-phenyl-7,8-disilabicyclo[2,2,2]octa-2,5-diene or 7,7,8,8-tetramethyl-5,6-benzo-7,8-disilabicyclo[2,2,2]octa-2,5-diene with an excess of benzaldehyde leads to the formation of *trans*-stilbene and cyclosiloxanes together with biphenyl or naphthalene. The following mechanism involving the formation and reactions of $Me_2Si = SiMe_2$ was proposed:



IV. SILICON ANALOGUES OF KETONES

In a systematic study of the pyrolysis of organosilicon compounds, we found that eight-membered cyclocarbosiloxane decompose with formation of products resulting from the elimination of monomeric units[46,47,69]. In particular, it was shown that one of the decomposition pathways involves the scission of dimethylsilanone:



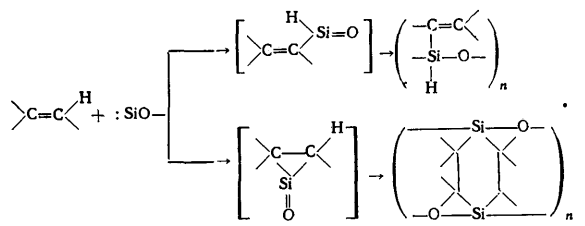
We obtained similar results also in a study of the mechanism of the thermal decomposition of cyclosiloxanes $D_n (n = 3-7)$[70,71]. It was found that in the initial stages of the reaction the main monomolecular decomposition products are compounds of the type D_{n-1} and that virtually the only example of products of the type D_{n+m} is D_{n+1}. This is consistent with the scission of dimethylsilanone, which either forms a cyclic trimer or is inserted in the Si–O bond of the initial compound, yielding D_{n+1}:

$$D_n \rightarrow [Me_2Si=O] + D_{n-1},$$
$$[Me_2Si=O] + D_n \rightarrow D_{n+1},$$
$$3[Me_2Si=O] \rightarrow (Me_2SiO)_3.$$

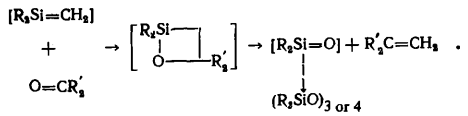
While the scission of dimethylsilanone is characteristic of the cyclic tetramer and pentamer, for higher cyclosiloxanes direct decomposition into D_3 or D_4 is energetically more favourable.

Similar results were obtained by Davidson and Tomson[72], who later investigated the pyrolysis of octamethylcyclosiloxane. The main reaction products D_3 and D_5 were detected in proportions of 1.3 : 1, which is consistent with the above mechanism. As was to be expected, their activation energy for the decomposition reaction (71.9 kcal $mole^{-1}$) was higher than for the cyclic pentamer (61 kcal $mole^{-1}$)[70,71]; they estimated the lower limit of the π-bond energy in dimethylsilanone as 38 kcal $mole^{-1}$).

Silanones are probably also formed in the joint condensation of silicon monoxide with organic compounds at 196°C.[3] However, in contrast to the compound discussed above, they undergo uncontrollable polymerisation:



As already mentioned above, the thermal decomposition of silaoxetans (see Section II), formed in the reaction of $R_2Si = CH_2$ with ketones and aldehydes, is a very effective reaction for the generation of silicon analogues of ketones:



The reaction with aromatic carbonyl compounds follows a more specific pathway[40]. In the case of aliphatic ketones and aldehydes the decomposition of the silaoxetan is accompanied by its isomerisation to the corresponding alkenyloxysilane. A similar reaction was observed in the decomposition of the adduct of $Me_2Si = SiMe_2$ with benzaldehyde[68] (see Section III).

V. THE STABILITY OF SILICON ANALOGUES OF UNSATURATED COMPOUNDS

As can be seen from the studies discussed above, there are numerous data in agreement with the hypothesis of the existence of silicon analogues of olefins and ketones as short-lived species. Their number increases still further if mass-spectrometric data are included. Only some of these were mentioned in the present review, while others can be found in Orlov's review[73].

In contrast to unsaturated carbon compounds, their silicon analogues exhibit an enhanced reactivity in bimolecular reactions, which hinders their isolation in a monomeric form. The latter can be stabilised only at low temperatures.

On the other hand, compounds of this type are extremely resistant to monomolecular decomposition. Among the examples discussed above, the only exception was methylenesilacyclobutane, formed in the pyrolysis of 4-silaspiro[3, 3]heptane; it undergoes a more profound decomposition or isomerises as a result of its specific structure.

A number of attempts have been made to explain the low stability of the π-bond in double-bonded compounds of elements in the Third and subsequent Periods. On the basis of a graphical representation of orbitals, Pitzer[74] postulated that the low stability of the multiple bonds in such molecules is due to the appreciable repulsion between the bonding orbitals and the filled inner shells of these atoms (*inner shell repulsion*). However, Mulliken[75,76] demonstrated by calculations of overlap integrals that this repulsion is no greater for elements of the Third Period than for elements of the Second Period and therefore it cannot be the cause of the absence of π-bonds in compounds of heavy elements. According to Mulliken, a possible explanation of this phenomenon is that the formation of two σ bonds is more favourable than the formation of a double bond, i.e. there should be a greater tendency towards the formation of a polymeric form than towards the formation of a monomeric form.

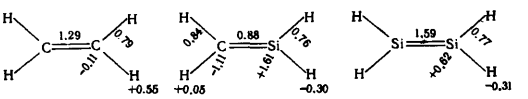
On the basis of the structure of the energy bands in diamond and crystalline silicon, Levin et al.[77] estimated the extent of $(p-p)_\pi$ interaction between carbon and silicon atoms and showed that the corresponding resonance integral for silicon is smaller by a factor of approximately two than for carbon. The authors regard this finding as a possible cause of the absence of silicon compounds with multiple bonds.

Quite recently Curtis[78] carried out calculations on the $H_2Si = CH_2$ and $H_2Si = SiH_2$ molecules using the extended Hückel molecular orbital method and found that 3*d* orbitals contribute significantly to the π-overlap population. Moreover the contribution of the $(p-d)_\pi$ bond actually exceeds that of the $(p-p)_\pi$ bond:

π-Overlap populations

	$(p-p)_\pi$	$(p-d)_\pi$	$(d-d)_\pi$	Σ
$CH_2=SiH_2$	0.130	0.197	—	0.327
$H_2Si=SiH_2$	0.277	0.348	0.038	0.663

The π-overlap populations and atomic charges in ethylene and its silicon analogues are quoted below (after Curtis)[78]:



Evidently the silicon–carbon double bond is extremely polar. The high polarity of this bond also follows from a CNDO calculation on $H_2C = SiH_2$ [79]; the dipole moment of this molecule has been estimated as 2.99 D. The barrier to rotation about the π-bond (and hence the π-bond energy) increases in the following sequence: C = Si < Si = Si < C = = C, and the low stability of the C = Si bond is explained by the energy discrepancy between the carbon and silicon *p* orbitals. Damrauer and Williams[80] carried out CNDO calculations on the $H_2Si = CH_2$, $F_2Si = CH_2$, $H_2Si = CF_2$, and $F_2Si = CF_2$ molecules in order to determine the influence of the positions of the fluorine atoms on the strength of the π-bond. Their high π-bond orders and the small lengths of the silicon-carbon bonds (1.75 Å in $H_2C = SiH_2$ and $H_2C = = SiF_2$; 1.80 Å in $F_2C = SiF_2$ and $F_2C = SiH_2$) indicate the olefinic character of these compounds. The FSiF and FCF angles are 110° and ∠ HSiH and ∠ HCH are 120°. Calculation showed that, in contrast to $H_2Si = CH_2$ and $F_2Si = = CH_2$, the $H_2Si = CF_2$ and $F_2Si = CF_2$ molecules have less polar π-bonds. It is interesting to note that analysis of the reactivities of the above compounds by electrostatic methods led to the conclusion that the formation of 1, 2-disilacyclobutane from $H_2Si = CF_2$ should be more favourable than the formation of 1, 3-disilacyclobutane.

In conclusion of this section, we should note that the stability of the silicon analogues of olefins is in general correlated with the lack of tendency of the silicon atom towards sp^2 hybridisation noted in recent publications[81] on the structure of silyl radicals. It was found that, in contrast to the methyl radical, the silyl radical is non-planar and has a pyramidal configuration. The substitution of a hydrogen atom by methyl group has only a slight influence on the geometry of the radical.

Nevertheless the nature of the bonds in silicon analogous of unsaturated compounds still remains one of the unsolved problems of chemistry. The advances achieved in the stabilisation of compounds of this class, which made possible spectroscopic and other physical studies on these compounds, are promising in this connection.

* * *

The results discussed above have shown that monosilacyclobutanes still remain some of the most effective and most readily available sources of silicon analogues of olefins. Mono- and di-silabicyclo[2, 2, 2]octa-2, 5-dienes are particularly convenient for this purpose. There is no doubt that the discovery of new selective and simple methods for the synthesis of silicon analogues of unsaturated compounds will permit a wider employment of the interesting synthetic possibilities of this new class of organosilicon compounds.

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Ultraviolet Spectroscopic Determination of the Stabilities of Weak Organic Complexes

E.G.Polle

The methods described in the literature for the determination of the stability constants K and extinction coefficients ϵ of weak organic electron-donating and electron-accepting complexes are discussed. It is shown that the majority of the methods based on a combination of the Bouguer-Beer-Lambert law and the law of mass action and involving the use of an excess of one component suffer from the same disadvantages as the parent spectrophotometric method—the Benesi-Hildebrand method (the inconsistency between K and ϵ, the appearance of negative values of K, the dependence of K on the wavelength used, the dependence of K and ϵ on the relative amounts of the donor and acceptor, etc.). The reliability criteria of Pearson and Deranleau are discussed and their limitations are demonstrated. It is suggested that the absolute values of K and ϵ obtained spectrophotometrically are of interest only from a comparison of complex formation in series of organic compounds with similar structures and that all measurements should as far as possible be made under identical conditions. The review covers studies published up to the middle of 1973.
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I. INTRODUCTION

Numerous reviews[1-6], dealing mainly with the stable inorganic and organic-inorganic complexes, have been devoted to studies on the stabilities of complexes in solution. There have also been a fair number of publications on weak organic electron donor–acceptor complexes[7-17], but attention has been concentrated on the properties of the complexes and not on the calculation of the stability constants. The group of complexes under consideration ($K \leqslant 20$ litre mole^{-1}) exhibit a specific absorption in the electronic spectrum. Even very weak complexes frequently give rise to an appreciable deviation from additivity of optical densities in the spectrum of a mixture of the reacting molecules. The reasons for this phenomenon are being widely discussed—it may be due to a charge-transfer band, or to a singlet–triplet absorption by the donor, or to the resolution of latent bands of the acceptors, etc.—and in the present review they will not be considered. However, the appearance of a new absorption following interaction has led to a very frequent application of spectrophotometric methods. On the other hand, there is not in the literature even one critical study of the entire series

of methods used to investigate weak molecular complexes. Such an examination is particularly necessary, since the determination of the stability constants was not the main aim of the majority of investigators; one may say that, for organic chemists dealing with syntheses, the constant K provides a comparison of the complex-forming capacities of new substances with those investigated previously, etc. A method widely described in the literature, usually the Benesi–Hildebrand method [18] (or its modifications) which is very easy and clear-cut, is employed.

The aim of the present review is to demonstrate the limitations of the spectrophotometric methods for the determination of K and ϵ and the necessity for much caution in the assessment of the results.

II. SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF THE STABILITY CONSTANTS OF WEAK ORGANIC COMPLEXES

Spectrophotometric methods for the investigation of the stability of organic complexes have been known for a long time (see, for example, Halban and Zimpelmann [19] and Michaelis and Granick [20]), but the methods became widely used only from the beginning of the 1950s. This was stimulated by Mulliken's theoretical studies [21–24], partly based on the experimental data of Benesi and Hildebrand [18,25]. The basic postulates used in the analysis of complex-forming systems by the Benesi–Hildebrand (B–H) method [18] can be formulated as follows: (a) the system is in a state of equilibrium; (b) the optical density of the solution is due to a molecular compound; (c) only one complex is formed in solution; (d) the absorption by the complex obeys the Bouguer–Beer–Lambert law.

For the reaction

$$A + nB \rightleftarrows AB_n \quad , \tag{1}$$

we have

$$K = C_{AB_n}/C_A \cdot C_B^n \quad , \tag{2}$$

where A and B are the components, K is the stability constant, C_{AB_n} the concentration of the complex at equilibrium, $C_A = a - C_{AB_n}$, and $C_B^n = (b - C_{AB_n})^n$, a and b being the initial acceptor and donor concentrations and C_A and C_B the equilibrium concentrations.

According to the Bouguer–Beer–Lambert law, one can write for the complex

$$D = C_{AB_n}\epsilon_{AB_n}l \quad , \tag{3}$$

where D is the optical density of the solution, ϵ_{AB_n} the molar extinction coefficient of the complex, and l the optical pathlength.

On combining Eqns. (2) and (3), Benesi and Hildebrand arrived at the expression

$$al/D = (1/K \cdot \epsilon_{AB_n})(1/b^n) + 1/\epsilon_{AB_n} \quad . \tag{4}$$

The plot of al/D against $1/b^n$ is linear, $1/\epsilon_{AB_n}$ being the slope and $1/\epsilon_{AB_n}K$ the intercept. Three possibilities arise for this linear plot: (a) the intercept is positive, i.e. ϵ_{AB_n} and K are positive and non-zero; (b) the intercept is zero, i.e. $\epsilon_{AB_n} = \infty$ and $K = 0$; (c) the intercept is negative, i.e. $\epsilon_{AB_n} < 0$ and $K < 0$.

As an illustration we shall consider the *m*-dinitrobenzene (DNB)–*o*-bromoaniline and *m*-dinitrobenzene–2-methylnaphthalene systems [26] (Figs. 1 and 2). In both systems different straight lines are obtained at different donor concentrations. In the presence of a 60–124 and 124–200-fold excess of *o*-bromoaniline the first system gives rise to straight lines *a* and *b* respectively in Fig. 1. In the presence of a 40–120- and 120–320-fold excess of 2-methylnaphthalene the second system gives rise to straight lines *a* and *b* respectively in Fig. 2.

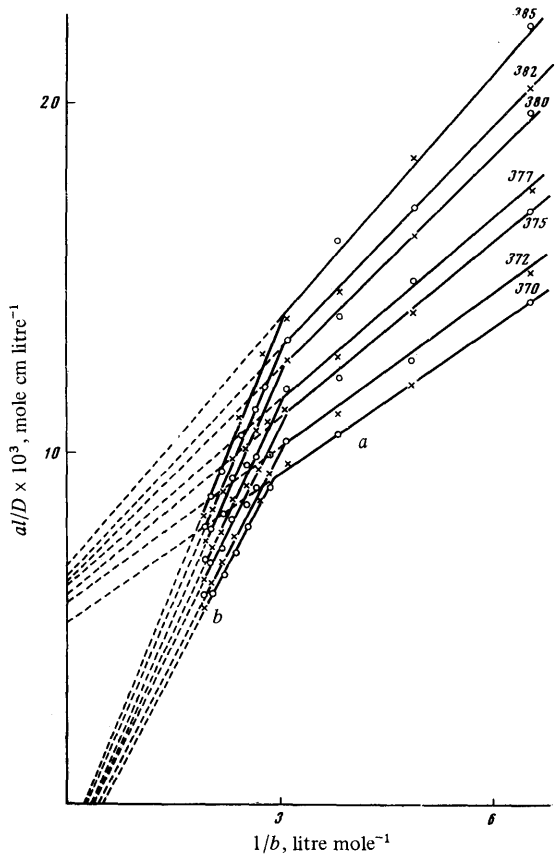

Figure 1. Application of the Benesi–Hildebrand method to the *m*-dinitrobenzene–*o*-bromoaniline system [26] in methanol; the numerals against the plots represent wavelengths (nm).

The Benesi–Hildebrand method is most commonly used at present [25,27] and the investigators do not always treat the results critically. The equation of Ketelaar et al. [58], which differs from the Benesi–Hildebrand expression by taking into account the absorption by the acceptor, is more accurate for the calculation of K and ϵ_{AB}:

$$1/(\epsilon_a - \epsilon_A) = 1/K \cdot b \quad (\epsilon_{AB} - \epsilon_A) + 1/(\epsilon_{AB} - \epsilon_A) \quad , \tag{5}$$

where $\epsilon_a = D/la$. The plot of $1/(\epsilon_a - \epsilon_A)$ against $1/b$ is linear and permits the determinations of K and ϵ_{AB}. [59–62] Landauer and McConnell [63] derived an expression for the estimation of K_1 and K_2 for 1 : 1 and 1 : 2 complexes present

simultaneously in solution[51,60,64-73]. An effective extinction coefficient is introduced: $\bar{\epsilon} = D/al$, where D is the total optical density of the solution. If $l = 1$, then

$$D = a\bar{\epsilon} = \varepsilon_A \; C_A + \varepsilon_{AB} \; C_{AB} + \varepsilon_{AB_2} \; C_{AB_2} \; , \qquad (6)$$

since

$$a = C_A + C_{AB} + C_{AB_2}$$

or

$$a = C_A(1 + K_1 b + K_2 b^2) \; . \qquad (7)$$

Putting

$$Q = b/(\bar{\epsilon} - \epsilon_A) \qquad (8)$$

and using Eqns. (6) and (7), we obtain

$$Q = \frac{1 + K_1 b + K_2 b^2}{(\varepsilon_{AB} - \varepsilon_A) K_1 + (\varepsilon_{AB_2} - \varepsilon_A) K_2 b} \; . \qquad (9)$$

It is assumed that $C_{AB} \gg C_{AB_2}$ and therefore to a first approximation one can neglect the term containing K_2, i.e.

$$Q = (1 + K_1 b)/(\varepsilon_{AB} - \varepsilon_A) K_1 \; . \qquad (10)$$

Q varies linearly with b and K_1 and ϵ_{AB} can be obtained from the plot. Knowing them, it is possible to estimate K_2 and ϵ_{AB_2}:

$$(1 + K_1 b)/Q = (\varepsilon_{AB} - \varepsilon_A) K_1 + (\varepsilon_{AB_2} - \varepsilon_A) K_2 b \; .$$

After substitution of Q from Eqn. (8) and a slight rearrangement, Eqn. (10) becomes

$$al/(D - \varepsilon_A l) = 1/(\varepsilon_{AB} - \varepsilon_A) K_1 b + 1/(\varepsilon_{AB} - \varepsilon_A) \; . \qquad (11)$$

When $\epsilon_A = 0$, Eqn. (11) transforms into Eqn. (4), i.e. when the acceptor does not absorb the method reduces to the Benesi–Hildebrand method and differs from the latter by the arrangement of the parameters.

Using Eqns. (1)–(3), Foster and coworkers[74-76] arrived at the expression

$$D/b^n = Kal\varepsilon_{AB_n} - KD \; . \qquad (12)$$

When the relation between L/b^n and L is linear, it is possible to find K and ϵ_{AB_n}. Three cases arise in the application of the method[55,60-69,72,77-85]: (*a*) the slope is negative, i.e. K and ϵ_{AB_n} are positive and non-zero; (*b*) the slope is zero, i.e. $K = 0$ and $\epsilon_{AB_n} = \infty$; (*c*) the slope is positive, i.e. $K < 0$ and $\epsilon_{AB_n} < 0$.

Scott[86] modified the Benesi–Hildebrand method and suggested that $x_B al/D$ be plotted against x_B, where x_B is the mole fraction of the donor. This permits the investigation of the initial slope at very low concentrations since the plot is extrapolated through the region of decreasing concentrations to the intercept[55,87].

Rose and Drago[88,89] demonstrated the applicability of the following relation to systems comprising a Lewis base and molecular iodine:

$$K^{-1} = (D - D_A)/(\varepsilon_{AB} - \varepsilon_A) - a - b + ab(\varepsilon_{AB} - \varepsilon_A)/(D - D_A). \qquad (13)$$

Eqn. (13) is valid for an optical path length of 1 cm. The presence of two unknowns necessitates the calculation of K and ϵ_{AB} for two solutions with different ratios of a and b. If the experimental conditions are such that $(D - D_A)/(\epsilon_{AB} - \epsilon_A) - a$ is negligibly small compared with $ab(\epsilon_{AB} - \epsilon_A)/(L - L_A) - b$, then Eqn. (13) assumes the form of Eqn. (5). When the bands do not overlap at the chosen wavelength, D_A and ϵ_A are zero and Eqn. (13) reduces to

$$K^{-1} = D/\varepsilon_{AB} - a - b + ab \; \varepsilon_{AB}/D \; . \qquad (14)$$

If $L/\epsilon_{AB} - a$ is negligibly small, Eqn. (14) readily transforms into Eqn. (4), i.e. the Benesi–Hildebrand and Ketelaar equations are special cases of Eqn. (13), which is widely used in practice[54,90-94]. Kortüm and Weber[95] introduced the modulus of extinction $m = \epsilon_A C_A + \epsilon_B C_B + \epsilon_{AB} C_{AB}$ for the calculation of the stability. For reaction (1), we have

$$(m - \varepsilon_A a - \varepsilon_B \; b)/a - b = (\varepsilon_{AB} - \varepsilon_A - \varepsilon_B)[K_1 - K_1^2(a + b)] \; , \qquad (15)$$

it is suggested that Eqn. (15) be used for 1 : 1 complexes. The authors propose the following relation for the determination of the parameters of 1 : 1 and 1 : 2 complexes when they are present simultaneously:

$$m/ab = \varepsilon_{AB} \; K_1[1 - K_1(a + b) + K_1^2 ab - 2K_1 K_2 ab - K_1 K_2 b^2] + \\ + \varepsilon_{AB_2} \; K_1 K_2[b - 2K_1 ab - K_2 b] \; .$$

The present author investigated twenty systems by this method[96]. The results differ little from those calculated using the literature data[18,63,74].

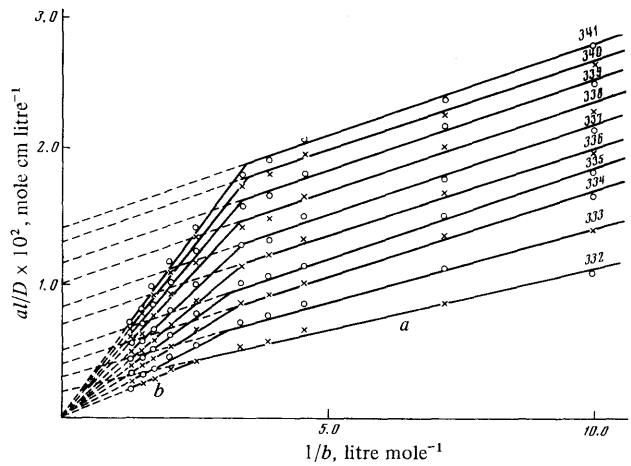

Figure 2. Application of the Benesi–Hildebrand method in the *m*-dinitrobenzene–2-methylnaphthalene system[26] in cyclohexane; the numbers against the plots represent wavelengths (nm).

Liptay[97] was the first to propose a method requiring a computer treatment and applicable for any concentration ratio of the components[98].

Lang[99] and Chandra[100-102] proposed modifications of the Benesi–Hildebrand method. Cilento and Sanioto[103] used a method on dilution. The working equation is

$$V^n = K\varepsilon_{AB} \; l \; m_A m_B^n / VD - K m_B^n \; ,$$

where V is the volume of the solution, D its optical density, and m_A and m_B are the numbers of moles of A and B. The plot of V^n against $1/VD$ should be linear. The intercept is $-Km_B^n$ and the slope is $K\epsilon_{AB} l m_A m_B^n$. Data for different wavelengths should yield the same intercept but different slopes.

Lavrushkin et al.[104] proposed two equations permitting a graphical determination of K and ϵ_{AB} when $b \gg a$:

$$a/(D-D_A) = 1/(\varepsilon_{AB}-\varepsilon_A) + 1/Kab(\varepsilon_{AB}-\varepsilon_A) ,$$
$$(D-D_A)/a = \varepsilon_{AB}-\varepsilon_A-(D-D_A)/Kab \quad .$$

Dewar and Thompson[105] put forward a system of four equations to be used for computer calculations whereby it is possible to find K, ϵ_{AB}, and C_{AB} (l = 1 cm):

$$C_{AB} = \{Ka+Kb+1-\sqrt{[K(a-b)+2Ka+2Kb+1]}\}/2K , \quad (16)$$
$$D_{AB} = \varepsilon_{AB}\ C_{AB} = D-\varepsilon_A(a-C_{AB})-\varepsilon_B(b-C_{AB})\ldots , \quad (17)$$
$$ab/D_{AB} = 1/K\cdot\varepsilon_{AB}+(a+b-C_{AB})/\varepsilon_{AB}\ldots , \quad (18)$$
$$ab/D_{AB}(a+b-C_{AB}) = 1/K\cdot\varepsilon_{AB}(a+b-C_{AB})+1/\varepsilon_{AB}\ldots \quad (19)$$

The method of solution is as follows: using an arbitrary value of K, Eqn.(16) is solved for C_{AB}, D_{AB} is subtracted from Eqn.(17), and $1/\epsilon_{AB}$ and $1/K\epsilon_{AB}$ are found from Eqns.(18) and (19) respectively. The latter two values are used to find a new value of K.

Complex formation is not always accompanied by an increase of the optical density; the reverse process, i.e. an absorption by the reaction mixture less than the additive value, is commonly observed in the spectrum of the mixture of interacting components. Gol'tsev et al.[106] modified the method of Foster et al.[74] K can be obtained by plotting $(D_A-D)/b^n$ against D_A-D. The slope of this relation is numerically equal to K.

Hammond[107,108] simplified the method of Cilento and Sanioto[103] by introducing the dilution coefficient n into the equation and obtained the relation

$$1/nD = n/Ka^2\varepsilon_{AB}+1/\varepsilon_{AB}\cdot a+1/\varepsilon_{AB}\cdot b \quad . \quad (20)$$

Hence we have the working equation

$$d\lg D/d\lg n = -\{1+1/[1+(Ka+Kb)/n]\} \quad . \quad (21)$$

Eqns.(20) and (21) are valid when $a \gg b$ or $b \gg a$, which permits the neglect of $(1/\epsilon_{AB})b$ or $(1/\epsilon_{AB})a$ respectively, or when $a = b$.

Mamedov and Aleskerova[109] proposed a method which hardly differs from Nagakura's procedure[110,111]. Here

$$K = [a(D_0-D_1)+a'(D-D_0)]/a\cdot a'(D_1-D) , \quad (22)$$

where D_0, D, and D_1 are the optical densities of solutions in which the concentrations of the molecules of A are zero, a, and a' respectively. Eqn.(22) can be used when $C_{AB} \ll a$ and when D_A is negligibly small at the wavelengths used to determine the stability constant.

Gol'dshtein and Gur'yanova[112] developed a procedure called the "method for eliminating one of the unknowns" and suitable for the evaluation of K from spectroscopic (ultraviolet, infrared, Raman, and NMR), dielectric, calorimetric, etc. data for complexes of any stoichiometry. The method has been analysed in detail[113] and therefore is not quoted here. We shall only describe the general procedure. One unknown is eliminated from the general equation with two unknowns ϵ and K. This is achieved by taking logarithms in the general equation for K and by subsequent differentiation of the resulting expression. This yields a quadratic equation with one unknown. The method is suitable for a computer treatment and gives good results when not less than ten experimental points are used.

Meallier et al.[114] demonstrated the application of the following relations to the dioxane (A)–aniline (B) complex in hexane:

$$a/(\bar{\varepsilon}-\varepsilon_0) = [1/(\varepsilon_1-\varepsilon_0)]\,1/K+a/(\varepsilon_1-\varepsilon_0)+b(\varepsilon_1-\varepsilon_0)+b(\bar{\varepsilon}-\varepsilon_0)/(\varepsilon_1-\varepsilon_0)^2 , \quad (23)$$

where ϵ_0 and ϵ_1 are the molar extinction coefficients of aniline in hexane and dioxane respectively and $\bar{\epsilon} = D/bl$ is the formal extinction coefficient of aniline in the dioxane–hexane mixture. When $a \gg b$, Eqn.(23) becomes

$$a/(\bar{\varepsilon}-\varepsilon_0) = [1/(\varepsilon_1-\varepsilon_0)]\,1/K+a/(\varepsilon_1-\varepsilon_0) ,$$

whence

$$K = (\bar{\varepsilon}-\varepsilon_0)/a(\varepsilon_1-\bar{\varepsilon}) \quad .$$

An equation describing a hyperbolic curve and suitable for 1 : 1 complexes has been put forward[26,115]:

$$y^2+Kxy-y[Ka(\varepsilon_{AB}-\varepsilon_A-\varepsilon_B^*)+\varepsilon_B^*]-x\varepsilon_B^*K = 0 , \quad (24)$$

where $x = D$, $y = D/b$, and ϵ_B^* is the extinction coefficient of the donor in solution in the acceptor. The plot of D/b against D should yield a hyperbola or one of its branches [cf. Eqn.(12)]:

$$K = -\tan 2\alpha,$$

where α is the angle of rotation of the coordinate axes relative to the axis of the hyperbola. Fig. 3 illustrates the application of the method for a system which cannot be treated by the Benesi–Hildebrand method[18] and the method of Foster et al.[74] (Fig. 1): $K_1 = 0.69$ litre mole^{-1}.

Eqn.(24) can only be used effectively in a computer treatment using the method of least squares, since a manual graphical plot gives errors of the order of 20–30%.

Using the method of differential spectroscopy, Kampar and Neiland[116] put forward the relation

$$cl/\Delta D = 1/\varepsilon_{AB}+[(1-KC_{AB})/2K\ \varepsilon_{AB}]\cdot 1/c , \quad (25)$$

where $c = a = b$ and $\Delta D = \epsilon_{AB}C_{AB}\times 2l$ is the difference between the optical densities of the test and reference systems. Since in the majority of cases $KC_{AB} \ll 1$, it is assumed that $KC_{AB} = 0$ and Eqn.(25) represents the linear correlation between the function $cl/\Delta D$ and the argument $1/c$. When the linearity fails, the authors suggest an expression permitting a more accurate determination of K and ϵ_{AB}:

$$cl/\Delta D = 1/2\varepsilon_{AB}+[(1+\sqrt{4Kc+1})/4K\cdot\varepsilon_{AB}]1/c \quad .$$

The method can be used to determine K and ϵ_{AB} in those cases where both components and the complex absorb in the same region. The authors proposed their method for complexes of the ion–ion type, but it can also be used to investigate complexes of other types. However, it undoubtedly suffers from some of the disadvantages of the Benesi–Hildebrand method.

Apart from the equations discussed above, many expressions have been proposed for the determination of K and ϵ, differing from those quoted mainly by their form or by a different arrangement of the initial parameters[65,98,117–133].

Thus all the expressions employed to calculate K and ϵ were derived by combining the mass action and Bouguer–Beer–Lambert Laws and the majority presupposed the employment of an overwhelming excess of one of the components. For this reason, the fundamental defects of the Benesi–Hildebrand method are characteristic of all spectroscopic methods for determining K and ϵ for weak molecular complexes[134,135].

III. THE DIFFICULTIES ARISING IN THE DETERMINATION OF K AND ϵ

The main difficulties are the inconsistency of K and ϵ for weak molecular complexes, i.e. low values of K and very high values of ϵ are determined experimentally.

Orgel and Mulliken[136] were the first to attempt to elucidate this behaviour. They put forward the concept of contact charge transfer, according to which complexes with zero stability and appreciable absorbance can exist, i.e. the absorption by the complex arises in the course of random collisions. To illustrate their concept, the authors employed complexes of molecular iodine with saturated and aromatic hydrocarbons treated by the Benesi–Hildebrand method. The slight curvature obtained in the plot of $\ln K$ against $1/T$ was used by Orgel and Mulliken as evident proof that several geometrical isomers are present. It was shown that the iodine–n-heptane system forms only contact pairs and this is why the Benesi–Hildebrand line intersects the ordinate at the origin. Taking into account the "contact", Eqn.(4) becomes

$$al/D = 1/Kbe_{\text{eff}} + 1/e_{\text{eff}} ,$$

where $\epsilon_{\text{eff}} = \epsilon_{AB} + \alpha C_{AB}/K$, α being a coefficient characterising the number of molecules of B near the molecules of A.

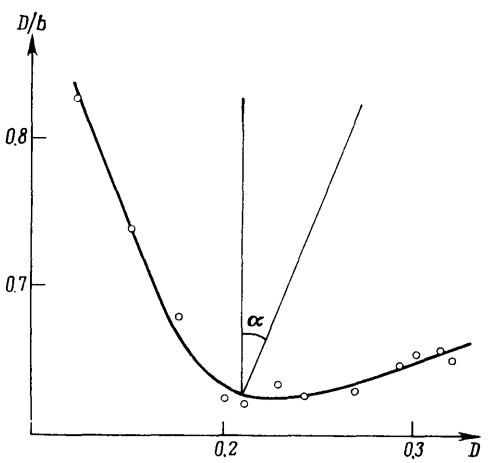

Figure 3. The *m*-dinitrobenzene–*o*-bromoaniline system[26] in methanol; $\lambda = 380$ nm; $l = 1$ cm.

Prue[137] derived an equation for the stability constants of 1 : 1 contact charge-transfer complexes of electron-donating and electron-accepting molecules: $K = 4\pi r^2 \Delta r N$, where r and $r + \Delta r$ are the distances between the centres of the molecules for which the presence of complexes is revealed in the charge-transfer spectra. When $r = 5$ Å and $\Delta r = 0.94$ Å, we have $K \simeq 0.2$ litre mole^{-1}. It was shown that values of K smaller than this and estimated from charge-transfer spectra do not constitute evidence for any kind of attractive forces between the donor and acceptor molecules in the ground state apart from the usual dispersion forces.

It should be noted that the estimation of r and $r + \Delta r$ in real systems is very complicated.

Murrell[138], who considered the inconsistency between K and ϵ, suggested that in a series of related complexes the relative behaviour of the intensity of the charge-transfer band and of the stability of the complex depends on the energy difference between the most stable configuration and the configuration contributing most to the intensity.

Many investigators attribute the inconsistency between K and ϵ to the effect of the solvent[86,124,139–148].

In an analysis of the concept of contact charge transfer, Carter et al.[142] concluded that it is unsatisfactory for two reasons: (a) the small thermodynamic justification of the hypothesis of two types of complexes one of which obeys the law of mass action and the other does not; (b) failure to take into account the role of the solvent in the theory despite the fact that in the case of weak complexes the donor competes with the solvent for a site around the acceptor.

Bearing in mind the competition between complex formation and solvation, there is no need to introduce two types of complexes and the behaviour of weak complexes can be accounted for by the same theory as that of strong complexes[142–144]:

$$AS_n + BS_m \rightleftarrows ABS_p + qS ,$$

where $q = n + m - p$, i.e. the donor, acceptor, and the complex are surrounded by a solvation shell:

$$K = C_{AB} x_S q / C_{AS_n} C_{BS_m} ,$$

where x_S is the mole fraction of the free solvent determined from the total number of moles of A, B, and S (bound and free). K is determined in the same way as in the Benesi–Hildebrand method:

$$al/D = (x_S q/K \cdot \varepsilon_{AB})(1/b) + 1/\varepsilon_{AB} .$$

The authors conclude that the Benesi–Hildebrand analysis underestimates K by an amount $q(m + 1)/G_0$ (G_0 is the total concentration of the solvent and $b = 0$) and overestimates ϵ_{AB} by an amount K/K_{B-H}. For stable complexes, $K \gg q(m + 1)/G_0$ and the Benesi–Hildebrand method gives good results.

The method proposed cannot be widely employed, since it is by no means easy to determine the numbers of solvent molecules with which the donor and acceptor are combined.

Semiempirical methods for the assessment of the influence of solvents have been proposed[124,145]. Hunter et al.[146], who examined four-component systems, demonstrated a method permitting the separation of the role of the solvent for moderately strong complexes of the type of chloranil–hexamethylbenzene (HMB)–n-heptane–carbon tetrachloride. The fundamental equation is

$$1/\varepsilon_A = 1/Y \cdot \varepsilon_{AB} + 1/K_{AB} \cdot Y \varepsilon_{AB} X b . \qquad (26)$$

Eqn.(26) differs from Eqn.(4) only by the presence of the terms X and Y, ϵ_A being the formal extinction coefficient of the acceptor calculated by dividing the total optical density of the solution by a and l.

$$X = 1 - (C_2 + C_3 + \ldots)b, \; Y = 1 - (C_2' + C_3' + \ldots)/a ,$$

where C_2, C_3, etc. are the concentrations of complexes of the solvent with the donor and C_2', C_3', etc. are the concentrations of complexes of the solvent with the acceptor. The method is based on the same postulates as the Benesi–Hildebrand method, i.e. $C_{AB} \ll b$. X and Y are expressed in terms of the concentrations of the four components present in the system:

$$X = (1 + T)^{-1}, \; Y = [1 + S/(1 + K_{AB} \; b \; X)]^{-1} ,$$

where

$$T = \sum_{n=2}^{n} K_n(x) x_l^{n-1}, \; S = \sum_{m=2}^{m} K_m(x) x_h^{m-1} ,$$

in which K_m is the stability constant of the chloranil–(n-heptane)$_{m-1}$ complex, K_n is the stability constant of the hexamethylbenzene–$(CCl_4)_{n-1}$ complex, and x_h and x_l

are the mole fractions of n-heptane and carbon tetrachloride respectively.

In the experimental test of the method, the concentration ratio of n-heptane and carbon tetrachloride was varied but K and ϵ remained constant in all cases. The fact that the K are much higher than for the complexes in pure carbon tetrachloride[149] (although the hexamethylbenzene–carbon tetrachloride complex is very weak) indicates the influence of carbon tetrachloride on the complex formation process.

It has been shown[146] that, even for very strong complexes, the interaction of the components with the solvent is comparable to the complex formation proper. The authors suggest that the formation of competing complexes with the solvent is the most likely explanation of the inconsistency between K and ϵ.

The simultaneous employment of different concentration scales (litre mole^{-1} in the determination of K_{AB} and the reciprocal of the mole fraction in the determination of K_{As} and K_{Bs}) hinders the application of the method[142].

Scott[147] considered the determination of the stability constants of weak complexes from the standpoint of a quasichemical calculation for a cell with donor, acceptor, and inert solvent molecules. Using Guggenheim's theory[150], the author showed that the stability constants calculated by methods of the Benesi–Hildebrand type are imaginary. A disadvantage of the proposed method is that it is based on the concept of contact charge transfer. Moreover, the author considers the possibility of the existence of contact complexes with $\epsilon = 0$ and $K > 0$.

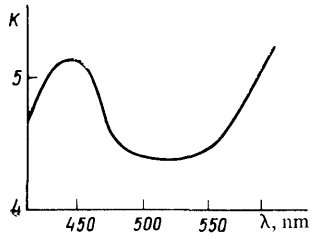

Figure 4. Variation of K with wavelength[32] in the tetracyanoethylene–naphthalene system in carbon tetrachloride at 25°C.

To predict the effect of solvents on the equilibrium, Christian et al.[148] employed a non-polar analogue model (NAM) in which a non-polar analogue of the polar solute is used in the calculation of the properties of the solutions. The chosen NAM molecule must have the same molecular volume and the same energy of interaction with the surrounding solvent as the polar solute. It was shown that NAM can be used under a wide range of conditions.

Kuntz et al.[36] attribute the inconsistency between K and ϵ to an incorrect choice of the concentration scale. They considered reaction (1) in the presence of an inert solvent S, i.e. they assumed that there is no competition between the donor and the solvent. This resulted in relations between different concentration scales:

$$(K_x)_{B-H} = K_c/v_S + (v_B - v_S)/v_S;\ (\epsilon_x)_{B-H} = K_c\epsilon_{AB}/(v_B - v_S + K_c);$$
$$(K_m)_{B-H} = \rho_S(K_c + v_B);\ (\epsilon_m)_{B-H} = \epsilon_{AB}\ K_c/(K_c + v_B)\ ,$$

where x is the concentration expressed in terms of mole fractions, m the molality, c the molarity, ρ the density, and v the molar volume. It is concluded that reasonable values of K_C, v_B, and v_S can give rise to zero or negative values of K_X when the Benesi–Hildebrand method is used. However, the form of the Benesi–Hildebrand linear plot cannot be used to conclude that one or other concentration scale is preferable; an experimental study with the aid of two inert solvents is necessary. For complexes of the aromatic amine–aromatic nitro-compound type, the concentration is best expressed on the molar scale.

General equations for the interaction with solvents relating different concentration scales have been published[143].

The problem of the inconsistency between K and ϵ can also be approached in a different way. On the basis of solvation theory, one should observe constant products $K\epsilon$, obtained by the Benesi–Hildebrand or similar methods, over a wide range of donor and acceptor concentrations. This was in fact done in a study of the *NN*-dimethylaniline–1,3,5-trinitrobenzene (TNB) in chloroform. K varied from 0.62 to 1.18 litre mole^{-1} and ϵ from 1800 to 954. Ross and Labes[151] explained this result by postulating the existence of 1 : 2 and 2 : 1 complexes in the system. Foster and coworkers[152,153] suggested that the observed extinction coefficient is a function of the concentration of the component present in excess, usually the donor: $\epsilon = \epsilon_0(1 + \alpha b)$, where ϵ_0 is the extinction coefficient at infinite dilution. Application of this expression showed that appreciable variation in K_{B-H} and ϵ_{B-H} may occur for very small values of α; ϵ is overestimated and K underestimated. On the other hand, the product $K\epsilon$ remains unchanged. It is nowadays frequently recommended that $K\epsilon$ and not K be used to determine the thermodynamic parameters[12,154].

A remarkable phenomenon has been noted by a number of workers[29,32,34,53,66–69,105,121,144,155–163]—the dependence of K on wavelength. This has been interpreted in different ways. Thus Johnson and Bowen[32] (Fig. 4) believe that this relation cannot be explained by the presence of isomeric 1 : 1 charge-transfer complexes and (or) contact absorption. They postulate the existence of stable charge-transfer complexes with at least two different stoichiometric compositions.

The study of complexes of aromatic nitro-compounds with alkylbenzenes in carbon tetrachlorides[156] demonstrated a dependence of K on the wavelength for all the systems studied. For example, K for the *p*-dinitrobenzene–1,3,5-trinitrobenzene complex decreases from 2.24 to 0.62 litre mole^{-1} when λ is raised from 325 to 390 nm. Jurinski and de Maine[156] suggest that the results cannot be accounted for by the existence of any isomeric 1 : 1 complexes or higher-order complexes.

Carter[144] extended the Benesi–Hildebrand method to the case of the simultaneous presence of 1:1 and 1 : 2 complexes:

$$al/D = (1/K_1 \cdot \epsilon_1)(1/b) + (K_1 - \epsilon_2K_2/\epsilon_1)/K_1\epsilon_1\ .$$

When the condition $b \gg a$ is maintained, the observed $K = K_1 - (\epsilon_2/\epsilon_1)K_2$ and the slope yields $K_1\epsilon_1$, which was in fact observed on the assumption that 1 : 2 complexes exist. Hence follows the conclusion that the presence of 1 : 2 complexes should lead to a dependence of K on λ. Christie and Selinger[160] analysed the experimental data and conclusions of Johnson and Bowen[32] and showed that the dependence of K on λ need not be explained by the presence of isomeric complexes, but could simply be a result of the algebraic addition of the optical densities of the donor, acceptor, and the complex.

A clear example of the dependence of the observed K on λ and on the ratio of the donor and acceptor concentrations is illustrated in Table 1. The method[105] described above was used.

Table 1.

λ, nm	[TCNE] = 1.8×10^{-3} M [HMB] = (1.2–4.1) × 10^{-3} M	[TCNE] = 1.4×10^{-4} M [HMB] = 0.222–0.333 M	λ, nm	[TCNE] = 1.8×10^{-3} M [HMB] = (1.2–4.1) × 10^{-3} M	[TCNE] = 1.4×10^{-4} M [HMB] = 0.222–0.333 M
450	47.4	19.1	560	26.6	19.1
460	46.9	19.4	570	28.8	19.2
470	39.3	20.1	580	27.6	19.1
480	39.0	20.2	590	26.1	19.2
490	36.7	20.4	600	27.2	19.6
500	33.3	20.1	610	28.4	20.1
510	32.0	20.3	620	24.7	21.1
520	27.7	20.2	630	27.5	22.2
530	31.6	19.7	640	25.5	26.5
540	30.7	19.6	650	23.2	28.6
550	29.7	19.3			

Note. TCNE = tetracyanoethylene, HMB = hexamethylbenzene.

It is remarkable that the values of K obtained for more concentrated solutions vary little with the wavelength and the direction of their variation is the opposite to that observed at low concentrations. If the relation between K and λ is due to the appearance of complexes with a higher stoichiometry[32,144], the opposite behaviour should have been observed, i.e. the changes should have been greater at higher concentrations, since there is a greater probability of the formation of higher-order complexes.

The dependence of K and ϵ on the ratio of the donor and acceptor concentrations has been observed and discussed frequently[13,53,56,105,164]. Using the Benesi–Hildebrand method, Inoue and Kato[53] put forward two series of K values for the *NN*-dimethylaniline–nitrobenzene system in cyclohexane. When a donor concentration less than 0.3 M was used, $K_{ev} = 0.22$ litre mole^{-1}; at donor concentration greater than 0.3 M, $K_{ev} = 0.083$ litre mole^{-1}. The nitrobenzene concentration was 0.0162 M. Generally speaking, the Benesi–Hildebrand lines have the form analogous to that illustrated in Figs. 1 and 2 with the sole difference that the intercept is positive for both donor concentration ranges.

All three types of intercept (positive, zero, and negative) in the application of the Benesi–Hildebrand method were demonstrated for real systems by Davis and Farmer[34]. A negative intercept of the Benesi–Hildebrand method [Eqn. (4)] corresponds to a positive slope of Foster's method [Eqn. (12)]. We shall refer to the slope as anomalous, since it yields values of K and ϵ lacking physical significance.

The first attempt to account for the anomaly was undertaken by Fofonova[165] in connection with the interpretation of the results of Syrneva and Fofonova[77]. When the singlet–singlet band of the acceptor, displaced to one side under the influence of intermolecular interaction, is superimposed on the singlet–triplet band of the donor, the following observations may be made. If in the spectral region studied the intensities of both bands are of the same order of magnitude (the singlet–triplet band is located on the wing of the singlet band), then the intensities of both bands increase simultaneously with increase of the concentration of one of the components. Under these conditions, the experimental straight lines of the Benesi–Hildebrand method and the method of Foster et al. will have anomalous slopes and the characteristics of the complex cannot be determined.

It is possible to examine the cause of the anomaly from a different standpoint. Consider the commonest cases arising in the study of the absorption spectra of complex-forming systems (we are considering systems with a positive deviation of the optical density from additivity).

1. The complex AB absorbs in the region where A and B are absolutely transparent. The solvent is put in the reference cuvette, $b \gg a$, and K is calculated from Eqns. (4) or (12). For any numerical values of ϵ_{AB}, the straight lines should have the normal slope.

2. A also absorbs in the region of absorption by the complex, the reference cuvette contains a solution of A at a concentration a, and $b \gg a$. The spectrophotometric data are analysed in terms of Eqns. (5) and (27):

$$D/b^n = -KD + Kal(\varepsilon_{AB} - \varepsilon_A) \quad . \tag{27}$$

Since $\epsilon_{AB} > \epsilon_A$ (positive deviation from additivity), the straight lines described by Eqns. (5) and (27) will always have the normal slope regardless of the value of ϵ_A. Thus the intrinsic absorption by the component A does not alter the form of the straight line, but does affect the value of K. Calculation without allowing for ϵ_A yields values of ϵ_{AB} which are too low by an amount equal to ϵ_A.

3. The deviation from additivity in the mixture of components is observed only in the regions where A and B absorb.

On the basis of the Bouguer–Beer–Lambert law, the optical density of the solution (1 : 1 complex) can be written as follows:

$$D = l[(a - C_{AB})\varepsilon_A + (b - C_{AB})\varepsilon_B^* + C_{AB} \cdot \varepsilon_{AB} - a\varepsilon_A] \quad , \tag{28}$$

where ϵ_B^* is the extinction coefficient of the donor in solution in the acceptor (one must not confuse this with ϵ_B — the extinction coefficient of the donor in the pure solvent).

An expression for the concentration of the complex can be obtained from Eqn. (28).

$$C_{AB} = (D - bl\varepsilon_B^*)/l(\varepsilon_{AB} - \varepsilon_A - \varepsilon_B^*) \quad . \tag{29}$$

Next we have

$$(D - bl\varepsilon_B^*)/l(\varepsilon_{AB} - \varepsilon_A - \varepsilon_B^*) = Kab/(1 + Kb) \quad , \tag{30}$$

where the right-hand side of the equation is an expression obtained from the law of mass action subject to the condition $b \gg a$. The replacement of $(b - c)$ by b does not give rise to a large error.

When $l = 1$, Eqn. (30) can be written as:

$$D - \varepsilon_B^* b + KbD - Kb^2\varepsilon_B^* = Ka'(\varepsilon_{AB} - \varepsilon_A - \varepsilon_B^*) \quad . \tag{31}$$

After elementary transformations, we obtain from Eqn. (31)

$$D/b + KD = Ka(\varepsilon_{AB} - \varepsilon_A - \varepsilon_B^*) + \varepsilon_B^* + Kb\varepsilon_B^* \quad . \tag{32}$$

When the notation $D/b = y$, $D = x$, and $b = x/y$ is introduced, Eqn. (32) can be rewritten in the form of the fundamental equation (24). If $\epsilon_{AB} = \epsilon_A + \epsilon_B^*$, the hyperbola defined by Eqn. (24) splits into two straight lines:

$$\begin{cases} y_1 = \varepsilon_B^* \\ y_2 = -Kx \end{cases} \quad . \tag{33}$$

The coordinates of the focus of the hyperbola are

$$\begin{cases} y = \varepsilon_B^* \\ x = -\varepsilon_B^*/K \end{cases} \quad . \tag{34}$$

When $\epsilon^*_B = 0$, Eqn.(24) becomes

$$y^2 + Kxy - yKa(\varepsilon_{AB} - \varepsilon_A) = 0 \ . \qquad (35)$$

Eqn.(35) describes a degenerate hyperbola, which splits into two intersecting straight lines:

$$\begin{cases} y_1 = 0 \\ y_2 = -Kx + Ka(\varepsilon_{AB} - \varepsilon_A) \ . \end{cases} \qquad (36)$$

Fig. 5 illustrates two limiting cases of Eqn.(24): $\epsilon^*_B = 0$ and $\epsilon_{AB} = \epsilon_A + \epsilon^*_B$. The A'B'C' lines corresponds to two intersecting asymptotic lines defined by Eqns.(33): the section $y_0 = \epsilon^*_B$ and the section $x_0 = -\epsilon^*_B/K$. The ABC line describes two intersecting straight lines defined by Eqn.(36), the line AB representing the linear plot of Foster's method [Eqn.(12)]. When $\epsilon^*_B = 0$, the line BC coincides with the abscissa axis and, when $\epsilon^*_B > 0$, it lies above the axis and is responsible for the appearance of anomalous slopes in the graph.

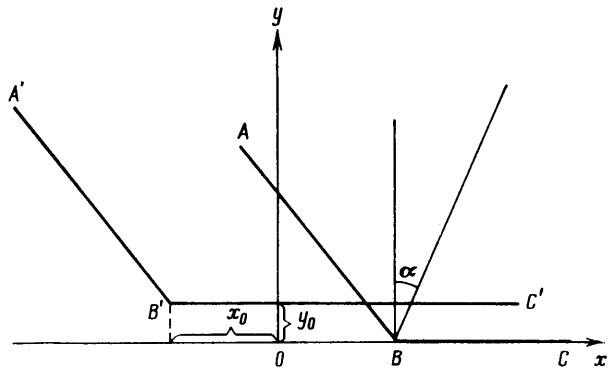

Figure 5. The limiting cases of the equation of the hyperbola [26].

Thus the slopes of the straight lines are influenced by the ratio ϵ^*_B/K. The higher its value (i.e. the higher the value of ϵ^*_B and the lower the value of K) the greater the probability of obtaining lines with an anomalous slope and neither a change in the donor concentration nor in the other experimental conditions yields straight lines with a normal slope. Hence the appearance of anomalous straight lines for weak complexes and the absence of "anomalies" for strong complexes with $K \gg \epsilon^*_B$ becomes understandable. For high values of ϵ^*_B/K, methods taking into account the absorption by the donor [88,112] will not help either, since there is no possibility of an experimental determination of ϵ^*_B. For low values of ϵ^*_B/K and high values of $\epsilon_{AB} - \epsilon_A - \epsilon^*_B$ in a study covering a fairly wide range of donor concentrations, we obtain hyperbolic plots of D/b against D and the stability constant is determined in terms of the tangent of the angle of rotation of the coordinate axes, in accordance with Eqn.(24).

IV. THE RELIABILITY OF THE LITERATURE VALUES OF K AND ϵ

The need to determine K and ϵ, the fundamental characteristics of complex-forming systems, has given rise to publications where the conditions under which the usual methods are applicable are discussed.

Thus Hammond [167,168] examined the influence of experimental errors on K and ϵ obtained when four terms of the Benesi–Hildebrand equation [Eqn.(4)] are used.

$$ab/D = 1/K\varepsilon_{AB} + b/\varepsilon_{AB} \ ; \ (a) \quad b/D = 1/K \cdot \varepsilon_{AB}\ a + b/\varepsilon_{AB}\ a \ ; \ (b)$$
$$a/D = (1/K \cdot \varepsilon_{AB})(1/b) + 1/\varepsilon_{AB} \ ; \ (c) \quad 1/D = (1/K \cdot \varepsilon_{AB}\ a)(1/b) + 1/\varepsilon_{AB}\ a \ (d)$$

The scatter of the points around the straight lines has different effects on K. Thus Eqns.(a) and (b) give rise to a significant scatter for low values of K and Eqn.(c) and (d) give rise to a large scatter for high values of K. This means that, for the same value of a, b, and D, Eqns.(a) and (b) are most suitable when $K < 1$ litre mole^{-1}. Eqn.(d) is suggested for the case where the scatter of the points is caused only by errors in the determination of b and D (a = const.). It has been shown that, when the error in the measurement of D is 1%, the relative error in the determination of K increases from 11% (K = 1 litre mole^{-1}) to 83% (K = 0.10 litre mole^{-1}). The errors in the determination of ϵ are approximately the same; 9 and 81% respectively. The optimal conditions in the determination of K by the Benesi–Hildebrand method are obtained when $5 < K < \epsilon/12$.

In an analysis of the methods described [18,58,86,88], Pearson [163] concluded that reliable stability constants are obtained only when the equilibrium concentration of the complex is of the same order of magnitude as the equilibrium concentration of the dilute component. If the donor and acceptor form 1 : 1 compounds only, then $D_{AB} = \epsilon_{AB} l C_{AB} = \epsilon_{AB} l K C_A C_B$. When $b \gg a$, we have $C_B \simeq b$ and $C_A \simeq a - C_{AB}$.

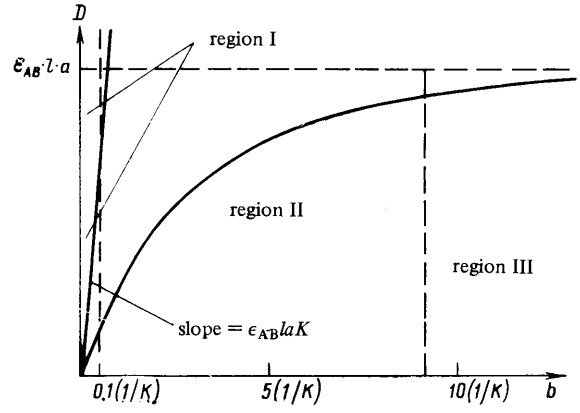

Figure 6. Variation of the absorption of the complex as a function of increasing donor concentration [169].

If a slight excess of the donor is used, the concentration of the complex in solution will be very small, so that $C_A \simeq a$. In this case $D_{AB} = \epsilon_{AB} lKab$ and the absorption by the complex increases linearly with increase of the initial concentration of the donor. On the other hand, in

the presence of a large excess of the donor the entire acceptor is in the complex and the addition of more donor does not alter the optical density.

Fig. 6 shows that the plot of the absorption by the complexes against donor concentration can be divided into three regions. In region I, where the donor concentration is low, the absorption increases linearly. For large values of b, the absorption remains unaltered. Between these two extremes, there is region II where the absorption does not increase linearly with increase of b. It is suggested that measurements should be made in the intermediate concentration range. This range has been determined approximately:

$$0.1a < C_{AB} < 0.9a \text{ or } 0.1(1/K) < b < 9.0(1/K) . \quad (37)$$

From this it follows that a zero slope in the methods of Foster et al.[74] and Scott[86] or a zero Benesi–Hildebrand intercept[18] can be obtained for any complexes, including strong complexes—this depends on the ratio of the donor and acceptor.

Deranleau[168,170] uses the term "saturation fraction" s:

$$s \equiv C_{AB}/a = Kb/(1 + Kb) . \quad (38)$$

The saturation fraction varies in the range $0 \leqslant s \leqslant 1$. For region II (Fig. 6) with $b = 0.1(1/K)$ and $9(1/K)$ the saturation fraction is respectively 0.09 and 0.9; the half-saturation point ($s = 0.5$) occurs when $b = 1/K$. For $b \gg a$, C_{AB} is neglected in Eqn. (38) and an error is introduced into the calculation:

$$(K^1 - K)/K = -sa/b , \quad (39)$$

where K^1 is an approximate value of the constant and K the value calculated from the exact equation.

This error cannot exceed a/b and is always negative[116] whatever the value of s, i.e. K calculated with this approximation is always greater than the correct value. If the errors in a and b are insignificant compared to the error in s, the relative error in K is in practice determined explicitly:

$$\Delta K/K \geqslant \Delta s\,[1/s^2 - 1/(1-s)^2] .$$

The error in ϵ_{AB} is given by the equation

$$\Delta e_{AB}/e_{AB} \geqslant \Delta s \sqrt{2/s} . \quad (40)$$

Eqns. (39)–(40) give the minimum values, but their derivation in a practical experiment is difficult. The relative errors defined by Eqns. (39) and (40) have been plotted as a function of s in Fig. 7. The most accurate values of ϵ_{AB} are obtained when the concentration of the complex is a maximum ($s = 1$), but an adequate accuracy can be achieved above a saturation fraction of 0.2. The correct values of K are obtained when s varies from 0.2 to 0.8. Beyond the limits of this range, the values investigated become indefinite and the error reaches 100% and more.

Deranleau believes that only by measuring 75% of the saturation curve can one asses with certainty the validity of the composition and the parameters of the complex being analysed. Generally speaking, the author reaches this conclusion for weak complexes, but notes that the proposed criterion is suitable for any instance of complex formation.

Table 2 illustrates[134] the employment of the reliability criteria of Pearson[168] and Deranleau[166]. Analysis of the data presented shows that systems with $K > 1$ satisfy Pearson's requirement (37). We shall consider the values of s for the tabulated systems. Complexes of 2-methylnaphthalene with nitro-compounds satisfy Deranleau's criterion, i.e. the measurements are in the region where the errors in K and ϵ_{AB} are minimal. For nitrobenzene–benzene ($K = 0.094$ litre mole^{-1}) and 1,3,5-trinitrobenzene–benzene ($K = 0.184$ litre mole^{-1}) complexes, the optical density measurements do not fall within the region of reliability as defined by Pearson and Deranleau. In measurements on the nitrobenzene–benzene system the donor (benzene) concentration was varied in the range 0.68–1 M, which correspond to the variation of the saturation fraction from 0.06 to 0.09, whereas according to Deranleau's reliability criterion, the benzene concentration should vary in the range from 1.5 to 40 M and according to Pearson's criterion from 1 to 90 M. For complexes with $K < 1$ litre mole^{-1}, it is difficult to reach in practice even the lower limit of reliability, let alone achieve the measurement of 75% of the saturation curve.

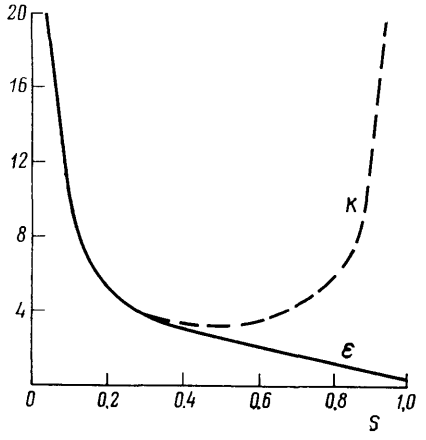

Figure 7. The relative percentage errors 100 $\Delta K/K$ and 100 $\Delta\epsilon/\epsilon$ as a function of s.[166]

The reliability criteria proved to be the most favourable for complexes with stability constants in the range 2–10 litre mole^{-1}. Thus for $K = 2$, 3, 5, and 10 litre mole^{-1}, the concentration ranges are respectively 0.12–2.0, 0.06–1.33, 0.05–0.8, and 0.025–0.40 M. These values are quite realistic for donors and the saturation fraction can be used as a criterion of the reliability of the results for complexes with stability constants in the above range. For complexes with stability constants of the order of 20 litre mole^{-1} and above, other difficulties arise in the choice of concentrations. According to both Pearson and Deranleau, the required donor concentration is so low that it is difficult to select an acceptor concentration satisfying the condition $b \gg a$.

The assessment of the reliability of the results by the Deranleau and Pearson methods is complicated by the fact that, not knowing the stability constant, it is impossible to predict the choice of the concentrations of the component present in excess for a correct determination of the parameters of the complex but, having determined the constant (possibly incorrectly), we will know whether the right concentration range has been used. This uncertainty in the values of K makes it difficult to employ the above reliability criteria.

The criteria have been used[40,54,164], but they have also been criticised. Heric[171] concluded that under certain conditions Pearson's criterion leads to incorrect findings.

Using the principles of mathematical statistics, the author suggests the investigation of groups of points on the Benesi–Hildebrand straight line and not all the points at once. One group includes points differing by not more than two standard deviations from the average Benesi–Hildebrand line fitted by least squares and the other includes the remaining points. Next these groups are divided into subgroups containing points differing along the ordinate by not more than two standard deviations. Similar subgroups are set up also with respect to the abscissae. Next the application of a special statistical table makes it possible, according to the author, to obtain more reliable results than those achieved with the aid of Pearson's criteria.

Table 2. The limits of reliability according to Pearson and Deranleau.

System	$-\Delta K/K$		s		b (after Pearson)	
	min.	max.	min.	max.	min.	max.
m-DNB-2-methylnaphthalene	$0.4\cdot10^{-5}$	$0.22\cdot10^{-3}$	0.08	0.44	$0.37/K$	$0.87/K$
o-DNB-2-methylnaphthalene	$0.5\cdot10^{-4}$	$0.5\cdot10^{-3}$	0.40	0.80	$1.04/K$	$5.2/K$
p-DNB-2-methylnaphthalene	$0.14\cdot10^{-4}$	$0.4\cdot10^{-3}$	0.04	0.32	$0.16/K$	$0.68/K$
1,3,5-TNB-2-methylnaphthalene	$0.25\cdot10^{-4}$	$0.24\cdot10^{-3}$	0.40	0.77	$0.66/K$	$3.32/K$
NB–2-methylnaphthalene	$0.8\cdot10^{-4}$	$0.13\cdot10^{-2}$	0.16	0.52	$0.20/K$	$1.14/K$
NB–benzene	$0.13\cdot10^{-3}$	$0.24\cdot10^{-3}$	0.06	0.09	$0.066/K$	$0.094/K$
1,3,5-TNB–benzene	$0.25\cdot10^{-4}$	$0.21\cdot10^{-3}$	0.05	0.17	$0.062/K$	$0.184/K$

The errors in the determination of K and ϵ have been analysed in studies [172,173] other than those discussed above.

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To summarise, one can point out the causes of the anomalies discussed above (the inconsistency between K and ϵ, zero and negative values of K when the complexes absorb strongly, the dependence of K on wavelength, etc.).

1. The calculated stability constants are concentration constants, since the activity coefficients are in most cases totally unknown. This is probably the reason for the dependence of K on the ratio of the donor and acceptor concentrations. There is no doubt that an incorrectly chosen concentration scale also has an effect.

2. The possible failure of the Bouguer–Beer–Lambert Law for the complexes under investigation. If the law holds, then in the presence of a large excess of the donor a linear relation should be observed between the optical density of the complex and the initial acceptor concentration [174].

3. Effect of the solvent, i.e. competition of the solvent with the components in the formation of association complexes. Absolutely inert solvents are known not to exist; moreover, the choice of the inert solvent is affected by the solubilities of the reactants. If the equilibrium constants for the reactions between A and S and between B and S are negligibly small compared with K for the reaction between A and B, the solvent is assumed to be neutral and can be used in the investigation.

4. The absorption by the donor in the acceptor solution, which is usually assumed in practice to be equal to its absorption in the pure solvent. It was shown above that the higher the value of ϵ^*_B/K the greater the probability of a curvature in the Foster, Benesi–Hildebrand, and other plots.

5. The existence of complexes with a higher stoichiometry. As a rule conclusions concerning the existence of 1 : 2, 1 : 3, etc. complexes are speculative or based on Foster, Benesi–Hildebrand, and other plots. To obtain a linear relation between D/b^n and D (Foster's method) when there is a curvature for $n = 1$, one substitutes $n = 2$, 3, etc. until a straight line is obtained. It was shown in Section III that the deviation of Foster's plot from linearity is due to ϵ^*_B; when this is taken into account, the parameters of the 1 : 1 complex can be calculated. An independent determination of the compositions of weak complexes is extremely difficult, but in many cases the application of Job's and Bent and French's methods [171,175] gives good results.

6. The error of the calculations of K and ϵ_{AB}. The few reports where graphs from which K and ϵ were calculated are published [34,40,41,43,62] show that on average not more than five points are used for 2–3 wavelengths. We may recall the non-equivalence of the points corresponding to high and low donor concentrations when methods of the Benesi–Hildebrand type are used. For example, for six consecutive additions the value for the most dilute solution (the least accurate value) will have a statistical weight approximately equal to the statistical weight for the four values corresponding to more concentrated solutions [166]. Experience shows that in such cases the line is drawn on the basis of the two least accurate values (the most dilute solutions). This reduces the probability of detecting the curvature in the graph. The application of the method of least squares without a preliminary analysis of the relation conceals the error in the determination of K and ϵ. When a small number of experimental points are used, no reliability criteria can be of assistance. In the determination of K it is necessary to employ not less than 10–15 points over the longest possible concentration range and the investigation should be carried out over the entire wavelength range where the complex absorbs. The variation of K with the wavelength can be used for an unambiguous determination of the electron-donating component of the donor–acceptor complex [56]. Thus, in publishing K and ϵ values, it is essential to indicate the concentration ranges, the number of experimental points, and the wavelength range in which the study was made.

The employment of published literature values of K and ϵ requires a certain amount of caution. The values of K obtained for a series of donors with a single acceptor and under identical conditions and conversely are valuable. We then obtain an unambiguous answer to the question of the relative stabilities of the complexes and can infer the structure of the association complexes formed. It is interesting to use the relative stabilities K/K_S, [176,177] where K_S is the stability constant of a reference acceptor for a series of donor or of a reference donor for a series of acceptors.

The objective nature of spectrophotometric results can be confirmed by a comparison with the results of fundamentally different techniques (dielectric constant measurements, calorimetry, NMR spectroscopy, etc.).

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The Application of Certain Physical Methods in the Study of the Properties of Carborane-12† and Its Derivatives

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The review presents the results of the application of various physical methods (X-ray diffraction analysis, electron diffraction, ^{1}H, ^{11}B, and ^{13}C nuclear magnetic resonance, nuclear quadrupoler resonance, nuclear gamma-resonance, and the dipole moment method) in the study of the geometric and electronic structures of the isomers of carborane-12 and a number of its derivatives. The results obtained with the aid of these methods are compared.
The bibliography includes 165 references.

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I. INTRODUCTION

In view of the nature of the bonds in which boron and particularly carbon atoms are involved, which is unusual for classical organic chemistry, and the capacity of carboranes to take part in various chemical reactions such as metallation, electrophilic substitution, and others, their chemistry now constitutes one of the most interesting and vigorously developing fields in the chemistry of organic derivatives of the elements.

However, many problems associated with the reactivity and structure, with the transmission of the influence of substituents via the icosahedral skeleton, with the dynamics of structural rearrangements, etc. are still not entirely clear. The difficulty of solving these problems by the methods of classical chemistry are evident. On the other hand, with the aid of a series of physical methods, it is possible to make a significant approach to an understanding of the phenomena associated with the characteristics of the structure and the nature of the bonds in carborane systems.

Bearing in mind the continuous growth of interest in the chemistry of carboranes (the number of publications has now exceeded 500), the fact that the relevant information is scattered in a wide variety of journals, and also the virtual absence of reviews on the application of physical methods in the study of carboranes, it appeared interesting to compile the available information in a single review. The aim of the present review was to give the fullest possible description of the state of research using a series of familiar physical methods. Since the review deals mainly with the thoroughly investigated *closo*-carborane-12, subsequently the prefix "*closo*" will be omitted.

The numbering of the atoms in the icosahedron differs from that which has been proposed and follows the rule that the 2nd atom is linked to the 7th and 8th atoms, the second carbon atom in the isomers corresponding to the 2nd atom for *ortho*-carborane, the 7th atom for *meta*-carborane, and the 12th atom for *para*-carborane‡.

† Dicarba-*closo*-dodecaborane(12) [Ed. of Translation].

‡ *o*-, *m*-, and *p*-Carboranes are 1,2-, 1,7-, and 1,12-dicarba-*closo*-dodecaboranes(12) [Ed. of Translation].

The following abbreviations have been adopted: NMR = nuclear magnetic resonance; NGR = nuclear gamma-resonance [Mössbauer spectroscopy]; CS = chemical shift in NMR spectra; IS = isomer shift in Mössbauer spectra; QS = quadrupole splitting in Mössbauer and NQR spectra; SSIC = spin–spin interaction constant in NMR spectra; LCAO – MO = method of molecular orbitals with linear combination of atomic orbitals; SCF = self-consistent field method; NEMO = non-empirical molecular orbital method; CNDO/2 = method of complete neglect of differential overlap.

Table 1. The bond lengths (Å) in *o*-, *m*-, and *p*-carboranes (according to X-ray and electron diffraction studies).

o-$B_{10}H_{12}C_2$ [27]		*o*-$B_{10}H_{10}C(CH_2Br)_2$ [3]		*o*-$B_{10}Br_2H_{10}C_2$ [6]		*o*-$B_{10}Br_4H_8C_2$ [7]		*o*-$B_{10}Cl_4H_8C_2$ [1]		*o*-$B_9C_2H_{12}AlEt$ [19]	
C—C (1,2)	1.65	1.64		1.64		1.65		1.67		C—Al	1.561
B—C (2,3)	1.708	1.71	av. 1.72	1.71	av. 1.72	1.73	av. 1.72	1.73	av. 1.715	B—C	1.697
(2,7)		1.73		1.73		1.71		1.70		B—B	1.777 (av.)
B—B (3,7)	1.800	1.78	av. 1.783	1.76	av. 1.773	1.78	av. 1.78	1.81	av. 1.803	Al—B	2.137
(7,11)		1.79		1.80		1.78		1.79		Al—C	2.173
(6,10)		1.76		1.73		1.77		1.75			
(10,11)		1.75		1.74		1.79		1.78			
(11,12)	1.787	1.75	av. 1.761	1.76	av. 1.754	1.76	av. 1.779	1.76	av. 1.781		
(10,12)		1.77		1.78		1.79		1.81			
(9,12)		1.81		1.73		1.78		1.81			

m-$B_{10}H_{12}C_2$ [27]		*m*-$B_{10}Br_2H_{10}C_2$ [14]		*m*-$CH_3CB_{10}H_9Br_2CH$ [16]		*p*-$B_{10}H_{12}C_2$ [26]	
B—C (1,2)	1.719	1.64		B (9)—Br (9)	2.04	1.719	
(1,4)		1.68	av. 1.676	B (10)—Br (10)	1.99		
(1,5)		1.74		B (12)—Br (12)	1.99		
B—B (2,3)	1.828	1.89		B—C av.	1.73	1.792 (in the band of C atoms)	
(2,6)	1.790	1.72	av. 1.775	B—B av.	1.73	1.772	
(4,5)	1.83	1.83				(connecting two pentagonal pyramids)	
(6,11)		1.81					
(5,9)		1.70	av. 1.763				
(6,10)	1.816	1.80					
(9,10)		1.77					

shows that the results obtained by semi-empirical computational methods are of greatest interest for the experimental chemist.

Certain information concerning the charge distribution on the boron atoms was obtained recently[42] by determining the pK_a or of all possible *B*-carboranols (Table 2). Although the introduction of a hydroxy-group at a boron atom in the carboranes-12 can lead to certain deviations from the charge distribution in the unsubstituted molecules, nevertheless the overall sequence and the calculated charges should be correlated with the changes in the pK_a. Table 2 shows that the charges on the boron atoms calculated theoretically are only of qualitative significance.

IV. DIPOLE MOMENTS

X-Ray diffraction studies on carboranes-12 and their *C*- and *B*-derivatives showed that a nearly icosahedral structure is retained in all the compounds.

The dipole moment method in conjunction with microwave spectroscopic methods (NMR and NQR) yields extremely valuable information about the structures of derivatives of carborane-12 isomers and particularly their *B*-halogeno-derivatives. This method, developed by a number of investigators[43-49], proved to be very convenient for the determination of the positions of the halogen atoms in *o*-, *m*-, and *p*-carboranes. It is based on a comparison of experimental and calculated dipole moments of various isomers of carborane-12, the calculated values being obtained as a rule with allowance for the differences between the B–B and the B–C bond lengths and some distortion of the valence angles. This is caused both by the infringement of the ideal symmetry of the icosahedral skeleton and by some steric hindrance between the hydrogen atoms attached to neighbouring boron atoms (the B–B–Hal angle is 122° instead of the ideal value of 120°). The calculations were based on the following dipole moments of the B–Hal bond: 1.67 D for *o*-carborane and 1.61 D for *m*-carborane. When the molecules of the halogeno-derivatives of *o*- and *m*-carboranes are regarded as ideal icosahedra, the B–Hal dipole moments are 1.59 D for *o*-carborane and 1.58 D for *m*-carborane. Since the dipole moment of *p*-carborane is zero, that of 2-chloro-*p*-carborane should in fact be equal to the B–Cl bond moment. It has been found[47] that the dipole moment of 2-chloro-*p*-carborane is 1.47 D.

Table 3 lists the experimental dipole moments of various carboranes and heterocarboranes-12 and Table 4 gives a compilation of the experimental and calculated dipole moments of a series of *B*-halogenocarboranes. It is interesting to note that, in the presence of boron–halogen and carbon–halogen bonds respectively, the dipole moment is higher and lower than that of unsubstituted carboranes[43]. This is evidence that the carbon and boron atoms form the positive and negative poles of the dipole respectively. All these considerations apply equally to *o*-, *m*-, and *p*-carbaphosphaboranes and carba-arsaboranes[58,59].

In a series of chemical and structural studies[50-53] it has been shown that, in the electrophilic halogenation of *o*-carborane, four halogen atoms enter the boron skeleton. The first and second halogen atoms enter preferentially the 10- and 12-positions, involving to some extent, depending on the halogenation conditions, also the boron atoms in the 9- and 11-positions of the *o*-carborane nucleus[54]. The third and fourth halogen atoms enter the 9- and 11-positions. In electrophilic halogenation two halogen atoms enter the *m*-carborane nucleus in the presence of $Fe(FeX_3)$ and four and more atoms in the presence of $AlCl_3$.[52,54,55] The first and second atoms enter mainly the 9- and 10-positions. The sites of the third and particularly the fourth halogen atoms could not be determined in this case from the number of the isomers formed (the principle first applied to carboranes by Wiesboeck and Hawthorne[56]). This was done with the aid of the dipole moment method and it was shown that one of the isomers has the 3(5, 8, 11), 9, 10-structure and the other the 4(12), 9, 10-structure[44,57].

Table 3. The dipole moments of the isomeric carboranes-12 and their derivatives.

Compound	μ_{exp}, D			
	in benzene	references	in cyclohexane	references
m-Carborane	2.76	44,45	2.78	43
	2.85	48		
9(10)-Chloro-*m*-carborane	4.22	44,45		
9(10)-Bromo-*m*-carborane	4.24	44,45		
9(10)-Iodo-*m*-carborane	4.20	44,45		
9,10-Dichloro-*m*-carborane	5.37	44,45		
9,10-Dibromo-*m*-carborane	5.40	44,45	5.14	43
9,10-Di-iodo-*m*-carborane	5.43	44,45		
3,4,9,10-Tetrachloro-*m*-carborane	5.86	44,45		
3,4,9,10-Tetrabromo-*m*-carborane	6.26	44,45		
B-Decachloro-*m*-carborane	6.29	44,45		
	4.39	44,45	4.31	
o-Carborane	4.45	44,45	4.49	43
	4.53	48		46
10(12)-Chloro-*o*-carborane	5.93	44,45		
3-Bromo-*o*-carborane	3.69	60		
4-Bromo-*o*-carborane	4.47	60		
9-Bromo-*o*-carborane	5.48	60		
10(12)-Bromo-*o*-carborane	5.90	44,45		
	5.98	60		
10(12)-Iodo-*o*-carborane	5.96	44,45		
10,12-Dichloro-*o*-carborane	6.98	44,45		
10,12-Dibromo-*o*-carborane	7.18	44,45	7.21	43
10,12-Di-iodo-*o*-carborane	7.02	44,45		
B-Decachloro-*o*-carborane	6.36	44,45		
1-Methyl-*o*-carborane	4.75	46		
1-Chloro-*o*-carborane	3.45	46	3.10	46
1-Bromo-*o*-carborane	3.34	60	3.36	46
2-Chloro-1-methyl-*o*-carborane	3.57	46	3.65	46
2-Bromo-1-methyl-*o*-carborane	3.80	46	3.80	46
p-Carborane	0.00	47,48		
2-Chloro-*p*-carborane	1.47	47		
1,2-Dibromo-*o*-carborane			2.82	43
1,7-Dibromo-*m*-carborane			1.64	43
Bis(chloro-*o*-phosphacarborane)			0.73	49
o-Phosphacarborane	3.87	58		
m-Phosphacarborane	2.39	58		
p-Phosphacarborane	0.68	58		
o-Arsacarborane	4.83	59		
m-Arsacarborane	2.76	59		
p-Arsacarborane	0.5	59		

Thus owing to the geometry of carborane-12, the dipole moment method is an effective procedure for the determination of the site of the substituent in the icosahedral skeleton of the molecule.

V. NMR SPECTROSCOPY

There are two main aspects to the application of nuclear magnetic resonance in the study of carboranes-12: in the study of the electronic properties of the carborane system and in the determination of the structures of newly synthesised compounds.

The elucidation of the electronic properties of carborane systems behaving as substituents and the transmission effects in carboranes are important for the determination of the nature of the bond in polyhedral molecules. Hawthorne et al.[61] investigated the electronic properties of 1,2- and 1,7-dicarbadodecaboranes and determined the σ constants by Taft's method[62] from the ^{19}F chemical shifts of the *m*- and *p*-fluorophenyl derivatives of *o*- and *m*-carboranes. They showed that the negative inductive effect ($-I$) of the *C*-substituted *o*-carbonyl group is close to that for halogens and that its resonance effect in the ground state is close to zero. A smaller inductive effect and a very small resonance (electron-donating) effect are characteristic of the *C*-substituted *m*-carbonyl group. It was found that in cyclohexane $\sigma_I = +0.375 \pm 0.010$ and $+0.194 \pm 0.010$ and $\sigma_R = +0.003 \pm 0.005$ and -0.039 ± 0.05 for the 1,2- and 1,7-carboranyl groups respectively.

Table 4. Comparison of the calculated and experimental dipole moments[44,46,47] of halogeno-derivatives of *o*-, *m*-, and *p*-carboranes.

Compound	μ_{exp}, D	Possible positions of halogen atoms in ring	μ_{calc}, D
10,12-Dichloro-*o*-carborane	6.98	9,10	6.27
10,12-Dibromo-*o*-carborane	7.18 cp. 7.08	10,12	7.28
10,12-Di-iodo-*o*-carborane	7.02	9,11	6.07
B-Decachloro-*o*-carborane	6.36	3,4,5,6,7,8,9, 10,11,12	6.23
9,10-Dichloro-*m*-carborane	5.37	9,10	5.50
9,10-Dibromo-*m*-carborane	5.40 cp. 5.40	4,12	4.41
9,10-Di-iodo-*m*-carborane	5.43	9(10), 4(12) 3,9	5.21 4.83
B-Decachloro-*m*-carborane	4.39	2,3,4,5,6,7,8, 9,10,11,12	4.41

The difference between the electronic properties of the carborane system depending on the atom involved in the formation of a bond with the fluorophenyl substituent was demonstrated for 1-substituted and 3-substituted *o*-carborane derivatives[63]. It was shown that the chemical shifts of the fluorine atoms relative to fluorobenzene in chloroform are $\delta_p^F = -2.51$ and -2.22 p.p.m. and $\delta_m^F = -2.22$ and -0.35 p.p.m. Hence $\sigma_I = +0.40$ and $+0.13$ and $\sigma_R = +0.01$ and $+0.06$ were calculated for 1-substituted and 3-substituted *o*-carboranes respectively.

The dependence of electronic properties on the type of solvent was also investigated by Taft's method on the basis of the ^{19}F chemical shifts of the 1-*o*-, 3-*o*-, and 1-substituted *m*-carborane derivatives with *m*- and *p*-fluorophenyl substituents[64].

The study of the influence of substituents at the carbon atoms in *o*- and *m*-carborane systems on their electronic properties[65] demonstrated that Taft's method cannot be used to estimate the properties of *C*-substituted *o*-carboranyl groups. This is in all probability due to the specific "cisoid" disposition of the substituent X and the fluorophenyl ring, which leads to a marked dependence of the ^{19}F chemical shifts on the magnetic anisotropy of the substituent. The influence of the unusual "*ortho*-effect" was also noted in the ^{35}Cl NQR spectra of 1-CH_2Cl-2-X-*o*-carboranes[66].

The most complete investigation of the electronic properties of carborane systems, their anions, and metallocarboranes was made by Adler and Hawthorne[67]. They give a kind of compilation of the available data on the electronic properties of carborane molecules. They note that the $-I$ effect for *C*-substituted *o*-carboranes is greater than for *m*-carboranes. The decrease of σ_I for 3-substituted *o*-carboranes (almost to zero) confirms that the transmission of the electrostatic Coulombic effect of carbon atoms diminishes fairly rapidly with distance. Carboranes with substituents at the boron atoms furthest away from the carbon atoms should have an appreciable $+I$ effect.

A second important problem involved in the understanding of the nature of the bond in carboranes is that of the transmission of the electronic influence of substituents via the carborane nucleus. An attempt was made to solve it[68] by investigating methylmercuri-derivatives of *o*- and *m*-carboranes, namely 1,7-R-$CB_{10}H_{10}$.CHgMe and 1,2-R-$CB_{10}H_{10}$CHgMe. The HgMe group served in this case as an indicator of the influence of the substituent characterised by the spin–spin interaction constant $J_{^{199}Hg-C-^1H}$. It was shown that, depending on R, $J_{^{199}Hg-C-^1H}$ in *o*-carborane varies very significantly (137.2–149.0 Hz in CCl_4). In *m*-carboranes the influence of R is greatly reduced: in weakly solvating solvents $J_{^{199}Hg-C-^1H}$ remains constant within the limits of the error of the measurements (135.9–136.3 Hz in CCl_4). For *o*-carboranes in highly solvating solvents (dioxane, pyridine, dimethyl sulphoxide) and CH_2Cl_2, a satisfactory correlation

$$J^R_{Hg-Me} = J^0_{Hg-Me} + m\sigma^*$$

was found for all R, except R = $PhCH_2$, $MeOCH_2$, or H. For these substituents R, the authors[68] suggest an intramolecular coordination. The above relations indicate a change in the shape of the electron cloud in the Hg–Me bond as a function of the inductive properties of the substituent R. Unfortunately the transmission of effects by the *o*-carborane nucleus ($C_2B_{10}H_{10}$) is difficult to assess from these results, since they reflect the transmission through the *o*-R–C–$B_{10}H_{10}$–C–Hg–Me system only.

Table 5. The ^1H chemical shifts in the spectra of *C*-monosubstituted *o*-, *m*-, and *p*-carboranes in carbon tetrachloride relative to HMDS*.[69,70]

R(C)	σ_I	σ_R	σ^*	Carboranes		
				o-	*m*-	*p*-
CH_2Cl	0.14	−0.03	1.05	3.93		
CH_2Br	—	—	1.00	3.96		
CH_2I	—	—	0.85	3.88		
Cl	0.40	−0.18	2.9	3.91	2.91 (2.93)	2.55
Br	0.44	−0.16	2.8	3.85	2.87 (2.91)	2.71
I	0.44	−0.14	2.36	3.72	2.87 (2.85)	2.91
Et_3Sn	—	—		3.26	2.88	2.62
Me_3Sn	—	—		3.06	2.89	2.67
H	0.0	0.0	0.49	3.50	2.85	2.68
Me	−0.08	−0.15	0.00	3.68	2.80	2.45

* Possibly hexamethyldisiloxane [Ed. of Translation].

Evidently direct information about the transmission of effects through carborane nuclei can be obtained in studies on the chemical shifts of the protons in the C–H bond with different R at the second carbon atom[69] (Table 5). The introduction of a halogen atom at one of the carbon atoms in *o*-carborane causes a shift of the signal due to the proton in the C–H bond involving the second atom to a lower field,

the chemical shifts varying in parallel with the σ* constants of the halogens (Table 5), which reflect the variation of their electron-accepting properties. In *C*-halogeno-substituted *p*-carboranes, whose carbon atoms are located at the opposite corners of the icosahedron, the C–H proton chemical shifts and the σ* constants of the halogen atoms were found to vary in opposition.

The transmission of effects through icosahedral molecules containing three-centre bonds is difficult to describe in terms which are at present generally accepted; nevertheless the variation of the chemical shifts of the C–H protons in *C*-monohalogeno-substituted *o*- and *p*-carboranes indicates two opposed effects of the halogen atoms on the electron density at the second carbon atom. For *C*-halogeno-substituted *m*-carboranes, these effects cancel out to such an extent that the chemical shift of the C–H proton hardly changes regardless of the nature of the halogen.

The introduction of substituents into the carborane ring at the boron atoms alters the chemical shifts of the C–H protons and the form of the ^{1}H NMR spectra[70]. Thus a doublet structure associated with the non-equivalence of the C–H bonds is observed in the spectra of *10*-monosubstituted *o*-carboranes and also of the spectra of *B*-substituted *m*- and *p*-carboranes permits conclusions concerning the symmetry of the molecules of these compounds. The appreciable change in the C–H proton chemical shifts is evidence for a ready transmission of the effect of the substituent in carborane nuclei (Table 6).

Table 6. The chemical shifts of the protons in the C–H bonds of *B*-substituted *o*-, *m*-, and *p*-carboranes[69,70].

Compound	δ relative to TMS*	Compound	δ relative to TMS*
o-Carborane	3.50	10-Iodo-*m*-carborane	3.03
10-Chloro-*o*-carborane	3.40; 3.54	9,10-Dichloro-*m*-carborane	2.85
10-Bromo-*o*-carborane	3.42; 3.53	9,10-Dibromo-*m*-carborane	2.98
10-Iodo-*o*-carborane	3.67; 3.87	9,10-Di-iodo-*m*-carborane	3.14
10,12-Dichloro-*o*-carborane	3.42	4,9,10-Trichloro-*m*-carborane	2.78; 3.19
10,12-Dibromo-*o*-carborane	3.63	3,4,9,10-Tetrachloro-*m*-carborane	3.07
10,12-Di-iodo-*o*-carborane	3.94	*p*-Carborane	2.68
m-Carborane	2.85	2-Chloro-*p*-carborane	2.79; 3.15
10-Chloro-*m*-carborane	2.87	2-Bromo-*p*-carborane	2.76; 3.13
10-Bromo-*m*-carborane	2.94	2-Iodo-*p*-carborane	2.74; 3.09

* Tetramethylsilane [Ed. of Translation].

Hitherto all that has been said referred to the ^{1}H NMR of the protons linked to the carbon atoms in the carborane system. Fairly numerous studies have been made on ^{11}B NMR and ^{1}H NMR of the protons linked to the boron atoms[14,36,69,71-79]. In most of these investigations the second aspect of the problem was solved—the determination of the structure of newly synthesised compounds.

The ^{1}H NMR spectra of the protons linked to boron atoms are always greatly complicated both by quadrupole broadening (owing to the nuclear quadrupole moment of ^{11}B) and by the ^{1}H–^{11}B spin–spin interaction. The ^{1}H NMR spectra are greatly simplified when ^{1}H–{^{11}B} heteronuclear resonance is employed with the application of the frequency at the resonance value for ^{11}B. The chemical shifts of the protons at the boron atoms and also the spin–spin interaction constants $J_{^{11}B-^1H}$ for *o*-, *m*-, and *p*-carboranes and their organotin derivatives have been determined[69] (Table 7).

The difficulties associated with the employment of ^{11}B NMR spectroscopy are due mainly to two causes: (1) the broadening of the NMR line owing to the quadrupole moment of the ^{11}B nucleus and (2) due to the fact that in the usually employed NMR spectrometers (frequencies of 19, 124, and 32.08 MHz) the spin–spin interaction constants $J_{^{11}B-^1H}$ are of the same order of magnitude as the ^{11}B chemical shift. This hinders the assignment of the ^{11}B frequencies to the structurally non-equivalent boron atoms in the complex molecules of carboranes and their derivatives. The method of ^{11}B–{^{1}H} heteroresonance has been used recently in the study of the ^{11}B NMR spectra in conjunction with a noise generator to suppress the ^{11}B–^{1}H spin–spin interaction.

Table 7. The chemical shifts of the protons at the boron and carbon atoms in certain carboranes[69].

Compound	Equivalent protons	^{1}H chemical shift δ relative to TMS*, p.p.m.
o-Carborane	1,2	3.50
	3,6	2.12
	4,5,7,8	2.12
	9,11	2.09
	10,12	2.09
m-Carborane	1,7	2.85
	2,6	2.65
	3,5,8,11	2.20
	4,12	2.20
	9,10	2.20
p-Carborane	1,12	2.68
	2—11	2.16
o-Triethylstannylcarborane	2	3.26
	3,6	2.29
	4,5	2.29
	7,8	2.29
	9,10	2.08
	10,12	2.08
m-Triethylstannylcarborane	7	2.88
	2,6	2.52
	3,5	2.21
	4	2.21
	8,11	2.21
	9,10	2.21
	12	2.21
p-Triethylstannylcarborane	12	2.63
	2,3,4,5,6	2.30
	7,8,9,10,11	2.21

* Tetramethylsilane (Ed. of Translation).

Some of the results of the authors of the review (see Refs. 71 and 79) for ^{11}B NMR of carborane-12 isomers and a number of its derivatives are presented in Table 8. On the basis of the structure of the carborane-12 isomers, it is possible to postulate the number of equal-intensity lines which should comprise the ^{11}B–{^{1}H} NMR spectrum of the given compound. Thus in the spectra of unsubstituted *o*- and *m*-carboranes there are four types of structurally non-equivalent boron atoms and in the ^{11}B–{^{1}H} NMR spectra of each of these compounds there should be four lines with the intensity ratios 2 : 4 : 2 : 2, which is in fact observed experimentally. Since all the boron atoms in *p*-carborane are equivalent, the ^{11}B–{^{1}H} spectrum of this compound consists of one line. The ^{11}B–{^{1}H} spectra of 2-halogeno-*p*-carboranes and 10-halogeno-*o*-carboranes should consist of six lines with the intensity ratios 2 : 2 : 2 : 2 : 1 : 1 and the spectra of 9-halogeno-*m*-carboranes should consist of seven lines with the intensity ratios 2 : 2 : 2 : 1 : 1 : 1 : 1. Although Table 8 shows that the

Table 8. The parameters of the $^{11}B-\{^1H\}$ NMR spectra of the isomeric carboranes-12 and their *B*-monohalogeno- and *BB*-dihalogeno-derivatives [in tetrahydrofuran and carbon tetrachloride solutions; $(MeO)_3B$ standard].

Unsubstituted carboranes				Chlorocarboranes				Bromocarboranes				Iodocarboranes			
Atom	δ, p.p.m.	$J_{^{11}B-^1H}$, Hz	rel. int.	Atom	δ, p.p.m.	$J_{^{11}B-^1H}$, Hz	rel. int.	Atom	δ, p.p.m.	$J_{^{11}B-^1H}$, Hz	rel. int.	Atom	δ, p.p.m.	$J_{^{11}B-^1H}$, Hz	rel. int.
o-carborane				10-chloro-*o*-carborane				10 bromo-*o*-carborane				10-iodo-*o*-carborane			
B(10, 12)	21.4	150	2	B(10)	11.5	0	1	B(10)	16.7	0	1	B(12)	20.1	160	1
B(9, 11)	28.5	160	2	B(12)	20.6	140	1	B(12)	20.0	190	1	B(9, 11)	26.5	165	2
B(3, 4, 5, 6, 7, 8)	32.8	170	6	B(9, 11)	26.9	165	2	B(9, 11)	27.4	185	2	B(3, 4, 5, 6, 7, 8)	32.5	140	6
				B(3, 4, 5, 6, 7, 8)	32.7	170	6	B(3, 4, 5, 6, 7, 8)	33.2	150	6	B(10)	36.1	0	1
				10,12-dichloro-*o*-carborane				10,12-dibromo-*o*-carborane				10,12-di-iodo-*o*-carborane			
				B(10, 12)	11.4		2	B(10, 12)	18.2		2	B(9, 11)	24.0		2
				B(9, 11)	26.5		2	B(9, 11)	25.6		2	B(3, 4, 5, 6, 7, 8, 10, 12)	31.8		8
				B(4, 5, 7, 8)	33.4		4	B(4, 5, 7, 8)	32.6		4				
				B(3, 6)	36.0		2	B(3, 6)	35.0		2				
m-carborane				9-chloro-*m*-carborane				9-bromo-*m*-carborane				9-iodo-*m*-carborane			
B(9, 10)	25.5	150	2	B(9)	17.0	0	1	B(4, 10, 12)	24.3	155	3	B(4, 12)	24.3	185	2
B(4,12)	29.3	170	2	B(4, 12)	24.2	120	2	B(9)	27.0	0	1	B(10)	26.7	150	1
B(3; 5, 8,11)	31.5	160	4	B(10)	27.2	180	1	B(5, 11)	30.0	170	2	B(3, 5, 8, 11)	31.0	165	4
B(2, 6)	35.5	180	2	B(5, 11)*	30.6	160	2	B(3, 8)*	31.7	165	2	B(2)*	35.1	186	1
				B(3, 8)*	31.6	120	2	B(12)*	35.5	155	1	B(6)*	37.4	180	1
				B(2)*	35.3	150	1	B(6)*	38.9	165	1	B(9)	42.5	0	1
				B(6)*	39.1	170	1								
				9,10-dichloro-*m*-carborane				9,10-dibromo-*m*-carborane H				9,10-di-iodo-*m*-carborane			
				B(9, 10)	17.8		2	B(4, 9, 10, 12)	24.0		4	B(4, 12)	22.4		4
				B(4, 12)	24.1		2	B(3, 5, 8, 11)	31.4		4	B(3, 5, 8, 11)	29.9		4
				B(3, 5, 8, 11)	32.3		4	B(2, 6)	39.6		2	B(2, 6)	36.9		2
				B(2, 6)	41.4		2					B(9, 10)	38.4		2
p-carborane				2-chloro-*p*-carborane				2-bromo-*p*-carborane				2-iodo-*p*-carborane			
B(2, 3, 4, 5, 6, 7, 8, 9, 10, 11)	33.2	165	1	B(2)	22.9	0	1	B(2)	30.5	0	1	B(3, 4, 5, 6, 7, 8, 9, 11)	32.0	165	8
				B(3, 4, 5, 6, 7, 8, 9, 11)	34.0	170	8	B(3, 4, 5, 6, 7, 8, 9, 11)	33.4	165	8	B(10)	36.2	150	1
				B(10)	39.0	130	1	B(10)	39.5	120	1	B(2)	46.4	0	1

* Assignment not determined. For explanation, see text.

experimental spectra differ from the theoretical spectra both as regards the number of lines and their intensities (owing to the overlapping of lines with close chemical shifts), nevertheless the results[79] permit the assignment of the lines in the ^{11}B NMR spectrum of each compound. This assignment is unambiguous for *B*-monohalogeno-derivatives of *o*- and *p*-carboranes, although there are certain difficulties for the analogous *m*-carborane derivatives. Thus the assignment of the lines in the spectra of 9-halogeno-*m*-carboranes for the B(5, 11) and B(3, 8) atoms and also for B(2) and B(6) is fairly difficult without additional data and the ^{11}B chemical shifts quoted in Table 8 for these groups may have to be interchanged.

The application of ^{13}C NMR in the study of carboranes is so far extremely limited. There have been only two communications[80,81] on the ^{13}C NMR chemical shifts of carborane isomers and some of their analogues (Table 9). Presumably the ^{11}B and ^{13}C chemical shifts in similar chemical environments are influenced by the same factors. It was noted that on substitution the change in the chemical shifts of these nuclei in carboranes is in the same direction.

The observation of ^{31}P NMR spectra of carbaphospha-dodecaborane derivatives[82] has been only mentioned.

Hitherto we have spoken of high-resolution NMR spectra for the nuclei of various atoms forming the carborane skeleton. The application of broad-line NMR and the spin–echo method, which permit the investigation of the geometry of relative positions, molecular mobility, exchange processes, and the dynamics of the motions in solids, are extremely promising. Only one study has been published[83] in which broad-line NMR was used in conjunction with calorimetric and X-ray diffraction data in the study of molecular mobility in crystalline *o*- and *m*-carboranes. All the results support the view that the reorientational disorder in crystalline carboranes has a kinetic basis. A phase transition was observed in the *o*-isomer at 4.0° ± 3.0°C. The measurement of the second moments of the proton lines in the NMR spectra of carborane isomers as a function of temperature showed that molecular reorientational motions occur down to −130°C. It is difficult to overestimate the value of these first experimental data, which lead to new fields in the study of the characteristics of the crystal structures of carboranes and to the understanding of the dynamics of the molecular motions in solids.

VI. NQR SPECTROSCOPY

NQR data constitute a completely new type of information about molecular structures and permit the determination of the type of electron distribution in space near the nucleus of the given atom.

Although the nuclei of the boron atoms forming the carborane skeleton do have quadrupole moments, purely NQR studies have been made not on boron nuclei (owing to experimental difficulties) but on halogen nuclei (^{35}Cl, ^{79}Br, and ^{127}I) in various derivatives of *o*-, *m*-, and *p*-carboranes[53,84-92] (Table 10). ^{35}Cl and ^{79}Br NQR spectroscopy was applied to halogenocarboranes for the first time[84] in 1965 to elucidate the nature of the carborane nucleus as a substituent in the systems *o*-

$HCB_{10}H_{10}C-C_6H_4-Y$ and *o*-$HCB_{10}H_{10}C-(CH_2)_nCl$ (I), where

$n = 1, 2, 3, 4 \ldots$ (series I) and to investigate the transmission of effects via the carborane nucleus in the system *o*-$Y-CH_2C_2B_{10}H_{10}CH_2-Y$ (II) (series II, Y = Cl or Br).

Table 9. ^{13}C chemical shifts of certain carboranes in acetone[80,81].

Compound	^{13}C chemical shifts relative to CS_2, p.p.m.	Compound	^{13}C chemical shifts relative to CS_2, p.p.m.
1,2-$B_{10}C_2H_{12}$	137.3	1,7-$Me_3SiCB_{10}H_{10}CSiMe_3$	125.4
1,7-$B_{10}C_2H_{12}$	137.4	1,7-$MeSCB_{10}H_{10}CSMe$	120.1
1,7-$B_{10}C_2Br_2H_{10}$—9,10-dibromo	139.7	1,12-$B_{10}C_2H_{12}$	129.3

It was found that the *o*-carborane system exhibits powerful electron-accepting properties, occupying an intermediate place between the NO_2 and COOH groups. The Hammett σ constant for the *o*-carboranyl substituent was estimated from the NQR frequencies as 0.4 ± 0.2, which agrees well with the estimates of the σ_I and σ_R constants from NMR spectra. The decay coefficient for the transmission of the effect of a substituent X in a chain consisting of methylene groups in series I (see above) has also been determined[84] and found to be 0.44 ± 0.01. The study of the transmission of effects through the carborane nucleus itself by comparing the ^{35}Cl NQR frequencies in series II for Y = Cl and in series I for $n = 1$ with the frequencies for $ClCH_2-C\equiv C-CH_2Cl$ and $HC\equiv C-CH_2Cl$ showed that the carbon atoms in the carborane ring do transmit effects. The powerful electron-accepting properties of the $CH_2-C_2B_{10}H_{11}$ and $Ph-C_2B_{10}H_{10}$ substituents follow also from the investigation of the 79Br and ^{81}Br NQR of the corresponding halogen-containing organomercury compounds[88]. Comparison of the ^{35}Cl and ^{127}I frequencies of 2-halogeno-*p*-carboranes, 9-halogeno-*m*-carboranes, and 10-halogeno-*o*-carboranes[86,87] showed that the polarity of the boron–halogen bond decreases in the series *o*-carborane > *m*-carborane > *p*-carborane, which is consistent with the variation of the reactivity of these isomers.

A number of studies have been made[66,90-93] on the ^{35}Cl NQR spectra of the *o*-$XC-B_{10}H_{10}-C-CH_2Cl$ system, where X = H, $ClCH_2$, Et, Me, SMe, HS, $SiMe_3$, MeOOC, NH_2CO, MeHg, Cl, Br, I, Ph, ClCO, or COOEt.

To elucidate the transmission of the effects of substituents in this system, the entire set of ^{35}Cl NQR data were examined[66]. Problems of this kind are usually solved by establishing a correlation between the changes in the characteristics investigated in the given method (NQR frequency, chemical shift, or the spin–spin interaction constant for NMR, etc.) and the Taft–Hammett constants of the substituents in the given series of molecules. It has been shown[66] that in the *o*-$X-C-B_{10}H_{10}C-CH_2Cl$ system the two-parameter correlation of the ^{35}Cl NQR frequencies with the σ constants of the substituents is absent as well as the one-parameter correlation. This is probably evidence for the important role of the steric factors due to the specific disposition of the substituent and the CH_2Cl group, which are in the cisoid positions relative to one another in the *o*-carborane system (a kind of *"ortho"* effect). It appears evident that in the study of the transmission of the electronic influence of substituents in the *o*-carborane series there is no point in subdividing the substituents in accordance with the type of the electronic effect (this was attempted, for example, by Voronkov et al.[91]), since steric interactions are of decisive importance in the behaviour of both NQR frequencies and the NMR chemical shifts in these systems.

NQR spectroscopy is one of the physical methods for the determination of the structural characteristics, identification, and determination of the purity[53,85,86] of the *B*-halogenocarboranes-12 which have been synthesised. Thus it has been shown by ^{35}Cl NMR spectroscopy that the monochloro-derivatives of *o*-, *m*-, and *p*-carboranes are individual compounds and not mixtures of structural isomers, i.e. they are respectively 10-chloro-*o*-carborane, 9-chloro-*m*-carborane, and 2-chloro-*p*-carborane. Similar conclusions concerning the structures of the isomers have been reached[85] for di-, tetra-, octa-, and decachloro-derivatives of *o*- and *m*-carboranes. It is interesting to note that the ^{35}Cl NQR spectrum of 9, 10, 11, 12-tetrachloro-*o*-carborane consists of two doublets, the difference between the average frequencies of which gives a clear idea about the differences between the electron densities in the 10, 12- and 9, 11-positions. The higher frequency is due to the chlorine atoms in the 9- and 11-positions. This finding agrees with the postulated sequence of the electrophilic halogenation of *o*-carborane. The complex structure of the ^{35}Cl NQR spectra of the decachloro-derivatives of *o*- and *m*-carboranes suggests that the molecules of these substances do not have the ideal icosahedral structure[85,89,90]. Broad ^{35}Cl NQR lines are characteristic of decachloro-*o*-carborane, while in the ^{35}Cl NQR spectrum of decachloro-*m*-carborane there are narrow lines, which suggest a high degree of order in its crystals. The presence of an asymmetric broad line[85] in the ^{35}Cl NQR spectrum of 4(12), 9, 10-trichloro-*m*-carborane is evidence for a slight difference between the ^{35}Cl NQR frequencies of the chlorine atoms in the 9- and 10-positions on the one hand and in the 4(12)-position on the other and may be caused by a statistical disorder in the distribution of molecules in the crystals of this substance.

VII. MÖSSBAUER SPECTROSCOPY

Like NQR spectroscopy, the nuclear gamma-resonance method, based on the Mössbauer effect[94,95] and widely used in studies on properties of various compounds[96,97], has been applied to the study of the nature of the bonds between carbon and elements having Mössbauer nuclei. Studies on the ^{119}Sn Mössbauer spectra of organotin derivatives of carboranes[93,98] (Table 11) showed that the *o*-, *m*-, and *p*-carboranyl groups have a greater electron-accepting effect in relation to the tin atom than all the organic substituents investigated hitherto by this procedure. Comparison of the ^{119}Sn Mössbauer parameters of the Et_3Sn derivatives of *o*-, *m*-, and *p*-carboranes as well as other organotin

Table 10. The parameters of the ^{35}Cl, ^{79}Br, and ^{127}I NQR spectra of halogenocarboranes at 78°K.

Compound	Frequency ν, MHz	Type of bond	References
2-Chloromethyl-*o*-carborane	36,044	C—Cl	84,91
1-Chloroethyl-*o*-carborane	31,41 (calc.)	C—Cl	84
1-(1′-Chloropropyl)-*o*-carborane	33,654	C—Cl	84
1,2-Bis(chloromethyl-*o*-carborane	36,664	C—Cl	84,91
	37,009		
	37,342		
	37,405		
1-(1′-Chloropropyl)-*o*-carborane	33.273	C—Cl	84
1-(*p*-Chlorophenyl)-*o*-carborane	35.442	C—Cl	84
1-Chloro-2-phenyl-*o*-carborane	41.64	C—Cl	85
1,2-Bis(bromoethyl)-*o*-carborane	286.344	C—Br	84
1-(*p*-Bromophenyl)-*o*-carborane	274.404	C—Br	84
	273.945		
1-Chloro-2-chloromethyl-*o*-carborane	37.092	C—Cl	66
1-Bromo-2-chloromethyl-*o*-carborane	37.140	C—Cl	66
2-Chloromethyl-1-iodo-*o*-carborane	36.526	C—Cl	66
1-Chloromethyl-2-phenyl-*o*-carborane	36.33	C—Cl	91
	36.85		
1-Chloromethyl-*o*-carboranecarboxylic acid chloride	36.768	C—Cl	66
1-Chloromethyl-2-ethoxycarbonyl-*o*-carborane	37.488	C—Cl	66
1-Chloromethylcarboranecarboxylic acid	36.788	C—Cl	66
	36.855		
	37.072		
	37.758		
1-Chloromethyl-2-methyl-*o*-carborane	37.02	C—Cl	91
1-Chloromethyl-2-ethyl-*o*-carborane	37.026	C—Cl	91
1-Chloromethyl-2-methylthio-*o*-carborane	36.881	C—Cl	91
1-Chloromethyl-2-mercapto-*o*-carborane	36.874	C—Cl	91
1-Chloromethyl-2-trimethylsilyl-*o*-carborane	36.349	C—Cl	91
1-Chloromethyl-2-methoxycarbonyl-*o*-carborane	36.232	C—Cl	91
1-Chloromethyl-*o*-carboranecarboxylic acid amide	36.207	C—Cl	91
1-Chloromethyl-2-methylmercuri-*o*-carborane	35.565	C—Cl	91
10-Chloro-*o*-carborane	23.06	B—Cl	52,85
10,12-Dichloro-*o*-carborane	23.43	C—Cl	85
10,12-Dichloro-1-methyl-*o*-carborane	23.44	B—Cl	85
	23.48	B—Cl	
10,12-Dichloro-1-chloromethyl-*o*-carborane	37.044	C—Cl	85
	23.34	B—Cl	
	23.52	B—Cl	
10,12-Dichloro-1-vinyl-*o*-carborane	23.61	B—Cl	85
	23.39	B—Cl	
9,10,11,12-Tetrachloro-*o*-carborane	23.74	B—Cl	85
	23.91	B—Cl	
	24.39	B—Cl	
9,10,11,12-Tetrachloro-1-methyl-*o*-carborane	24.495	B—Cl	85
	24.204	B—Cl	
	24.040	B—Cl	
9,10,11,12-Tetrachloro-1-chloromethyl-*o*-carborane	37.20	C—Cl	85
	36.87	C—Cl	
	group of lines 23.8—24.4	B—Cl	
4,5,7,8,9,10,11,12-Octachloro-*o*-carborane	24.440	B—Cl	
	24.784	B—Cl	
	24.968	B—Cl	
	25.128	B—Cl	85
	25.560	B—Cl	
	25.660	B—Cl	
(3-12)-Decachloro-*o*-carborane	25.720	B—Cl	
	25.125	B—Cl	85
	24.950	B—Cl	
	24.695	B—Cl	
[^{79}Br]-2-Bromomercuri-1-methyl-*o*-carborane	137.43	Hg—Br	88
[^{81}Br]-2-Bromomercuri-1-methyl-*o*-carborane	135,64		
[^{79}Br]-2-Bromomercuri-1-phenyl-*o*-carborane	142.54	Hg—Br	88
Bipyridylyl-[^{79}Br]-2-bromomercuri-1-methyl-*o*-carborane	138.72	Hg—Br	88
Bipyridylyl-[^{81}Br]-2-bromomercuri-1-methyl-*o*-carborane	115.88	Hg—Br	88
Bipyridylyl-[^{79}Br]-2-bromomercuri-1-phenyl-*o*-carborane	131.70	Hg—Br	88
Bipyridylyl-[^{81}Br]-2-bromomercuri-1-phenyl-*o*-carborane	127.38	Hg—Br	
9-Chloro-*m*-carborane	23.42	B—Cl	85
	23.62	B—Cl	
9,10-Dichloro-*m*-carborane	23.66	B—Cl	85
9,10-Dichloro-1-methyl-*m*-carborane	23.61	B—Cl	85
4,9,10-Trichloro-*m*-carborane	23.86	B—Cl	85
7-(*m*-Chlorophenyl)-1-phenyl-*m*-carborane	35.41	C—Cl	
	35.11		

Table 10 (Continued...).

Compound	Frequency ν, MHz	Type of bond	References
B-Decachloro-*m*-carborane	24.660	B—Cl	
	25.050	B—Cl	
	25.195	B—Cl	
	25.315	B—Cl	
	25,540	B—Cl	85
	25,605	B—Cl	
	25,640	B—Cl	
	25,965	B—Cl	
	26,060		
B-Decachloro-*m*-carborane*	24.659	B—Cl	
	25.043	B—Cl	
	25.050	B—Cl	
	25.194	B—Cl	89
	25.312	B—Cl	
	25.535	B—Cl	
	25.604	B—Cl	
	25.639	B—Cl	
	25.969	B—Cl	
	26.061		
	(273° K)	B—Cl	
	24.354	B—Cl	
	24.689	B—Cl	
	24.790	B—Cl	
	24.822	B—Cl	89,90
	24.977	B—Cl	
	25.177	B—Cl	
	25.257	B—Cl	
	25.297	B—Cl	
	25.590	B—Cl	
	25.723	B—Cl	
2-Chloro-*p*-carborane	23.94	B—Cl	86
10-Iodo-*o*-carborane	$\nu(\pm^1/_2 \rightleftarrows \pm^3/_2)$192.92; $\nu(^3/_2 \rightleftarrows \pm^5/_2)$ 384.8 η=4.5±0.5%; eQq_{zz}=1283.2	B—I	87
9-Iodo-*m*-carborane	$\nu(\pm^1/_2 \rightleftarrows \pm^3/_2)$ 197.78; $\nu(\pm^3/_2 \rightleftarrows \pm^5/_2)$ 395.5 η=1±1% eQq_{zz}=1318.4	B—I	87
2-Iodo-*p*-carborane	$\nu(\pm^1/_2 \rightleftarrows \pm^3/_2)$204.76; $\nu(\pm^3/_2 \rightleftarrows \pm^5/_2)$405.4 η= 8.9±0.2% eQq_{zz}=1353.6	B—I	87
10,12-Di-iodo-*o*-carborane	$\nu(\pm^1/_2 \rightleftarrows \pm^3/_2)$ 195.72 196.14	B—I B—I	87
		204.22	B—I	
9,10-Di-iodo-*m*-carborane	$\nu(\pm^1/_2 \rightleftarrows \pm^3/_2)$	202.88	B—I	87
		198.36	B—I	
		196.63	B—I	
1,12-Di-iodo-*p*-carborane	$\nu(\pm^1/_2 \rightleftarrows \pm^3/_2)$333.2; $\nu(\pm^3/_2 \rightleftarrows \pm^5/_2)$666.1 η=1.9±0.6 eQq_{zz}=2220.6	C—I	87

* The difference between the spectra quoted by Bryukhova et al.[85] and Smith and Tong[89] is that the signal obtained by the former investigators[85] at 25 050 MHz was resolved by Smith and Tong[89] into two lines at 25 043 and 25 050 MHz.

derivatives shows[93] that in the tin compounds the electron-accepting properties of *o*- and *m*-carboranes exceed those of the C_6F_5, C_6Cl_5, CF_3, C≡CH, and C≡CMe groups and are close to those of the C≡C–Cl, C≡C–Br, and C≡C–Ph groups, while the electronegativity of *p*-carborane is close to that of the C≡C–Me group. In turn, the electron-accepting properties of the carborane isomers vary in the sequence *ortho* > *meta* > *para*, which is consistent with the reactivities of these carborane isomers and with the NQR data (see above).

It is interesting to note a significant difference between the spectra of phenyl-*o*-carboranyltriphenyltin and *o*-carboranyltriphenyltin[98] (Table 11). The difference between the Mössbauer parameters of these compounds cannot be explained from the standpoint of the usual concept of the inductive effect. It is difficult to suppose that the higher electron-accepting capacity of the phenyl-*o*-carboranyl residue compared with the *o*-carboranyl residue is due to the electron-accepting effect of the phenyl group, which

cannot be so large. Possibly the reason for the difference is a specific interaction of the electron systems of the *o*-carborane and benzene rings.

Mössbauer spectroscopy has been used to identify and investigate the electronic structures of new carboranyl derivatives of the elements. Thus it has been shown[98] that ^{119}Sn Mössbauer spectroscopic data provide direct evidence that bis(phenyl-*o*-carboranyl)tin (Ph–$C_2B_{10}H_{10}$)$_2$Sn contains bivalent tin and is the first example of true organic derivatives of bivalent tin. By measuring the Mössbauer spectra of this substance as a function of time and the presence of oxygen, it is possible, in principle, to investigate the kinetics and mechanism of the polymerisation and oxidation of compounds of this kind. A study of the *B*-iodocarborane derivatives labelled with the ^{125}I radioactive isotope by ^{125}I Mössbauer emission spectroscopy showed[99] that the radioactive breakdown of ^{125}I results in the formation of carboranyl derivatives of tellurium which are isoelectronic with the corresponding iodine compounds. The linear relation[100] between e^2Qq derived from ^{127}I NQR and ^{125}Te Mössbauer spectra: $e^2Qq_{^{125}Te} = 0.60e^2Qq_{^{127}I} - 492.3$ M Hz (with a correlation coefficient of 0.983) confirms the hypothesis that the radioactive breakdown of ^{125}I in the matrices of *B*-iodo-derivatives of *o*-, *m*-, and *p*-carboranes does indeed result in the formation of tellurium derivatives[99,100].

Table 11. The parameters of the ^{119}Sn Mössbauer spectra of certain organotin derivatives of carboranes[93,98].

Compound	Quadrupole splitting in the Mössbauer spectrum, mm s^{-1}	Isomeric shift in the Mössbauer spectrum relative to α-tin, mm s^{-1}
1-(Trimethylstannyl)-*o*-carborane	1.55	−0.97
1-(Triethylstannyl)-*o*-carborane	1.75	−0.63
1-(Tri-n-propylstannyl)-*o*-carborane	1.65	−0.65
1-(Triphenylstannyl)-*o*-carborane	0.95	−0.05
2-Phenyl-1-(triphenylstannyl)-*o*-carborane	1.20	−0.80
1,2-Bis(tri-n-propylstannyl)-*o*-carborane	1.50	−0.65
Bis-(2,3,5,6-*o*-carborano)-1,4-distannacyclohexane	1.60	−0.90
Tri-(1-phenyl-*o*-carboranyl)tin chloride	0.40	−0.90
Bis-(1-phenyl-*o*-carboranyl)tin dichloride	0.90	−0.65
Bis-(1-phenyl-*o*-carboranyl)tin dibromide	0.80	−1.20
Dibutylbis-(1-phenyl-*o*-carboranyl)tin	1.70	−0.90
Bis-(1,2-triphenylstannyl)-*o*-carborane	0.70	−1.15
1-Phenyl-2-(triphenylstannyl)-*o*-carborane	1.50	−0.75
Bis-(1-phenyl-*o*-carboranyl)tin	1.90	0.85
1-(trimethylstannyl)-*m*-carborane	1.37	−0.82
1-(Triethylstannyl)-*m*-carborane	1.50	−0.68
9-Chloro-1-(triethylstannyl)-*m*-carborane	1.44	−0.64
1-(Trimethylstannyl)-*p*-carborane	1.18	−0.73
1-(Triethylstannyl)-*p*-carborane	1.23	−0.75
2-Chloro-1-(trimethylstannyl)-*p*-carborane	1.57	−0.74

VIII. COMPARISON OF THE RESULTS OF VARIOUS PHYSICAL METHODS

It is quite evident that, for a detailed investigation of the electronic properties of carborane systems, it is necessary to adduce and compare the results obtained with the aid of different methods. Consideration of the entire set of different physical methods (NMR, NQR, and Mössbauer spectroscopy) already permits an assessment of the electron-accepting properties of carborane isomers, which vary in the sequence

ortho > *meta* > *para*.

It is interesting to note that the spin–spin interaction constant $J_{^{119}Sn\text{-}Me}$ (from the NMR spectra) and the isomeric shifts and quadrupole splittings in the ^{119}Sn Mössbauer spectra of organotin derivatives of carboranes also vary consistently in the same sequence.

If it is supposed that the Grant–Litchman model[101] proposed for the spin–spin interaction constant $J_{^{13}C\text{-}H}$ is valid also for $J_{^{119}Sn\text{-}Me}$, then the expression for $J_{^{119}Sn\text{-}Me}$ may be written in the form

$$J_{(k)} = \frac{\Delta_{ref}}{\Delta_k}\left(\frac{N_k}{N_{ref}}\right)^2\left(\frac{\alpha_k}{\alpha_{ref}}\right)^2\left(\frac{Z_k}{Z_{ref}}\right)^3 J_{ref.}\ , \qquad (1)$$

where $J_{(k)}$ is the constant $J_{^{119}Sn\text{-}Me}$ for the kth Sn–Me bond, $J_{(ref)}$ is the constant $J_{^{119}Sn\text{-}Me}$ for the compound chosen as the standard, Δ is the average excitation energy, N are normalised coupling constants, α is a quantity proportional to the amount of s character of the bond, and Z is the effective nuclear charge, which can be written in the following form for the 5s orbital of the tin atom:

$$(Z_k/a_0)^{3/2} = (A + Bzr + Cz^2r^2 + Dz^3r^3 + Ez^4r^4)e^{z\cdot r/5}\ , \qquad (2)$$

where α_0 is the first Bohr radius and r the radius of the 5s orbital of the tin atom. The ratios Δ_{ref}/Δ_k and $(\alpha_k/\alpha_{ref})^2$ may be assumed to be unity[102]. On the other hand, the isomer shift for the tin compound is defined by the relation

$$IS = A\cdot\frac{\Delta R}{R}\{|\psi_{5s}(0)|^2_{abs} - |\psi_{5s}(0)|^2_{source}\}\ , \qquad (3)$$

where A and $\Delta R/R$ are constants and the $|\psi_{5S}(0)|^2$ are the 5s-electron densities for the absorber and source of the resonance γ-quanta.

The isomer shift as well as Z^3 (see chapter I of the monograph of Goldanskii and Herber[102]) are proportional to $|\psi_{5S}(0)|^2$, i.e. the isomer shift can be substituted for Z^3 in Eqn. (1) and we obtain

$$J_{(k)} = \frac{\Delta_{ref}}{\Delta_k}\left(\frac{N_k}{N_{ref}}\right)^2\left(\frac{\alpha_k}{\alpha_{ref}}\right)^2\left(\frac{IS_k}{IS_{ref}}\right) J_{(ref)}. \qquad (4)$$

Thus, when there is a linear relation between $J_{^{119}Sn\text{-}Me}$ and the isomer shift for a series of organotin compounds, one can assume that the effective nuclear charge model is valid in this case. Such a relation has been observed[69].

The increase of $J_{^{119}Sn\text{-}Me}$ for a given class of compounds on passing from triethylstannyl derivatives of *p*-carborane to those of *o*- and *m*-carboranes is probably associated with the increase of the 5s-electron density at the tin atom in this series. A similar behaviour obtains also in the trimethylstannyl derivatives of the carborane-12 isomers.

The quadrupole splittings by ^{119}Sn in the spectra of organotin derivatives of carboranes vary in the sequence of the *ortho*-, *meta*-, and *para*-compounds in parallel with the reactivity and the values of $J_{^{119}Sn\text{-}Me}$ and pKa.[63,93] This finding can be explained by a change in the electron populations of the 5p orbitals of tin owing to interaction with the many-centre orbitals of the bonds in the C_2B_{10} icosahedron. In this case the decrease of the screening of the 5s electrons by 5p electrons[103], leading to an increase of the 5s-electron density at the ^{119}Sn nucleus, reflects the electron-accepting properties of the carborane nuclei. Linear relations are observed also between the parameters of organotin derivatives of carboranes, namely between $J_{^{119}Sn\text{-}Me}$ and the isomer shift, between the quadrupole splitting and the isomer shift, and between the

quadrupole splitting and pK_a; there is also a linear relation between ^{127}I eQq_{zz} and the ^{35}Cl NQR frequency for *B*-halogeno-derivatives of *o*-, *m*-, and *p*-carboranes [87]. The latter can be written in the form

$$eQq_{zz}(^{127}\mathrm{I}) = \{-638.7 + 83.3\nu(^{35}\mathrm{Cl})\}\ \mathrm{MHz}. \quad (5)$$

This suggests that the asymmetry parameters of *o*-, *m*-, and *p*-*B*-monochlorocarboranes are small as for *B*-monoiodocarboranes. On the other hand, comparison of the electric field gradients along the axis of the B–Hal bond in monohalogenocarboranes showed [87] that the gradients along the bond involving the iodine atom are somewhat higher than for the chlorine atom. This is probably due to certain differences between the polarisations of the boron–iodine and boron–chlorine bonds in carboranes.

It follows from the ^{11}B NMR spectra of monohalogeno-substituted isomers of carborane-12 [79] that the chemical shifts of the boron atoms to which the halogen (chlorine, bromine, and iodine) is attached vary in the sequence *para* > *meta* > *ortho* (Table 8). Whereas the ^{11}B NMR data for the isomeric monochloro- and monobromo-carboranes suggest the descreening of the boron atom to which the halogen is attached, in the spectra of the isomeric iodo-derivatives of carborane-12 the signal of the same boron atom undergoes a shift to a higher field (relative to the chemical shifts of the unsubstituted carborane-12 isomers).

On the basis of the general theory of chemical shifts, the screening of nuclei (for which NMR is observed) depends on the ratios of three contributions:

$$\sigma = \sigma_{dia} + \sigma_{para} + \sigma', \quad (6)$$

where σ_{dia} is the diamagnetic screening of the given nucleus, σ_{para} is the paramagnetic contribution to the screening, and σ' is a term which includes the screening due to the other atoms in the given molecule.

The contribution of σ' depends on the anisotropy of the magnetic susceptibilities of the groups of atoms in the molecule remote from the nucleus under consideration. It has been shown [104] that for heavy nuclei, including ^{11}B, σ' amounts in most cases to only several per cent of the observed shift. Therefore in the consideration of the ^{11}B chemical shifts the σ' contribution may be neglected. Moreover a number of investigators have shown [104-106] for ^{13}C and other heavy atoms that the diamagnetic contribution σ_{dia} is usually small and also can be neglected in the interpretation of the chemical shift. For this reason, the paramagnetic term gives the main contribution to the chemical shifts of heavy atoms. In this connection mention should be made of the study by Lipscomb and coworkers [75], who estimated the extent of the diamagnetic and paramagnetic screening for *o*-, *m*-, and *p*-carboranes. The estimates were carried out under the following conditions. The constancy of the average energy for the entire series was assumed. The electrons in the 2*p* orbitals of both the nucleus under consideration and in the bonds involving all other atoms were taken into account. The diamagnetic screening, averaged over all orientations, was calculated from the formula [105]

$$\sigma_{dia} = \alpha/3 \sum_{n=1}^{m} \sum_{b=1}^{m} P_{ab} \langle r^{-1} \rangle_{ab}, \quad (7)$$

where P_{ab} are the elements of the usual charge matrix with respect to all the orbitals *a* and *b* of the centre *A*. The corresponding expression for the paramagnetic screening is

$$\sigma_{para} = -\frac{\alpha^2}{2\Delta E} \langle r^{-3} \rangle_{2p} \left(Q_{AA} + \sum_{A \neq B} Q_{AB} \right) = -\frac{19{,}5}{\Delta E} \left(Q_{AA} + \sum_{A \neq B} Q_{AB} \right). \quad (8)$$

where

$$Q_{AA} = 4/3 [(P_{X_A X_A} + P_{Y_A Y_A} + P_{Z_A Z_A}) - 1/2 (P_{X_A X_A} P_{Y_A Y_A} + P_{Z_A Z_A} P_{Y_A Y_A} + P_{Z_A Z_A} P_{X_A X_A}) + 1/2 (P^2_{X_A Y_A} + P^2_{Y_A Z_A} + P^2_{Z_A X_A})], \quad (9)$$

$$Q_{AB} = 2/3 [-(P_{X_A X_B} P_{Y_A Y_B} + P_{Y_A Y_B} P_{Z_A Z_B} + P_{Z_A Z_B} P_{X_A X_B}) + (P_{X_A Y_B} P_{Y_A X_B} + P_{Y_A Z_B} P_{Z_A Y_B} + P_{Z_A X_B} P_{X_A Z_B})], \quad (10)$$

α is the fine structure constant and $\langle r^{-3} \rangle_{2p} = K^3/3$ is the one-centre integral, K being the Slater 2*p* exponent of the boron atom.

Using the diborane and ethane data [107] obtained by the SCF method for the calculation of the borohydride wave functions, Lipscomb and coworkers [75] calculated Q_{AA}, ΣQ_{AB}, and σ_{dia} for the non-equivalent atoms in all three carborane isomers. It was found that the observed chemical shifts, corrected for the diamagnetic shift ($\delta = \delta_{obs} - \delta_{dia}$), are satisfactorily correlated with the sum $Q_{AA} + \Sigma Q_{AB}$. The changes in σ_{dia} on passing from one atom to another are small (Table 12).

Table 12.

Carborane		Q_{AA}	Q_{AB}	σ_{dia}	δ, p.p.m.	
					obs.	calc.
ortho-	B3 3*	1.211	0.123	187.8	15.2	16.7
	B4 4	1.250	0.128	188.8	13.9	12.5
	B9 8	1.300	0.131	190.0	9.9	7.4
	B10 9	1.300	0.136	190.0	2.7	6.8
meta-	B2 2	1.197	0.123	187.6	17 3	18.2
	B3 4	1.251	0.127	188.8	13.6	12.5
	B4 5	1.252	0.131	188.8	11.0	11.9
	B9 9	1.301	0.132	190.0	7.0	7.2
para-	B2	1.251	0.128	188.8	15.2	12.5

* The numbering is based on the data of Lipscomb and coworkers [75] and the ^{11}B shifts are quoted relative to $Et_2O.BF_3$.

The calculation reflects satisfactorily the effects of the nearest adjacent carbon atom but the influence of the carbon atom is inadequately reflected in calculations on remote boron atoms [cf. B(9) and B(10) in *o*-carborane]. Thus the chemical shifts of the boron atoms in icosahedral carboranes vary mainly owing to the variation of the paramagnetic screening of the boron atoms in different chemical environments. LCAO-MO calculations have shown [108] that the paramagnetic screening can also be formulated by the expression

$$\sigma_{para} = -2/3 (e^2h^2/m^2c^2)(1/\Delta E) \langle 1/r^3 \rangle_{2p} \cdot P_u, \quad (11)$$

where ΔE is the average electronic excitation energy for the molecule or ion, r the radius of the 2*p*-electron orbital (in ^{11}B), and P_u a quantity which reflects the electron populations of the 2*p* orbitals, and is proportional to the number of unbalanced *p* electrons.

Thus the degree of descreening of ^{11}B nuclei must depend on the number of unbalanced *p* electrons. It is also known that the NQR frequencies ν and the electric field gradients eQq_{zz} at the halogen nuclei are directly proportional to the number U_p of unbalanced *p* electrons. According to the Townes–Dailey theory [108], under these

conditions the number of unbalanced p electrons responsible for the electric field gradient at the halogen nuclei is defined by the expression

$$U_P = \frac{N_x + N_y}{2} - N_z, \qquad (12)$$

where N_x, N_y, and N_z are the electron populations of the P_x, P_y, and P_z orbitals of the halogens.

Hence it is reasonable to compare the ^{11}B chemical shift data for the atoms involved in the boron–halogen bond[79] with ^{35}Cl and ^{127}I NQR spectroscopic data for a series of B-halogeno-derivatives of o-, m-, and p-carboranes[86,87]. Since atoms involved in the same bond are considered, the change in U_p for halogen atoms will reflect the change in the number of the unbalanced $2p$ electrons of the corresponding boron atoms.

Comparison of ^{11}B NMR and ^{35}Cl and ^{127}I NQR data shows[79] that, with increase of the number of unbalanced p electrons in the halogen atoms, i.e. with decrease of the number of unbalanced $2p$ electrons in boron, the chemical shifts in the ^{11}B spectra increase. The results confirm that the main contribution to changes in the chemical shifts of the ^{11}B nuclei comes from the paramagnetic term. On the basis of a comparison of ^{11}B NMR and ^{35}Cl and ^{127}I NQR data, Babushkina et al.[79] also postulated that the ^{11}B chemical shifts for the boron atom in carborane-12 linked to halogens should be greatly influenced by the effect of the lone electron pair of the halogen, which causes a high-field shift of the NMR signal due to the boron atom linked to iodine, relative to those of the atom linked to bromine and chlorine.

We shall restrict to these examples the comparison of the results of various physical methods used in the study of the isomers of carborane and its derivatives, assuming that an increase in the number of correlations of this kind will not only make it possible to estimate certain quantities from the results of different investigations but will also allow a new approach to the study of the electronic properties of carborane-12 isomers.

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Organoarsenic Compounds of the Acetylene Series

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The review gives a systematic account of the literature on the methods of preparation and certain physical and chemical properties of acetylene derivatives of arsenic.
The bibliography includes 46 references.

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I. INTRODUCTION

Although the syntheses of acetylene derivatives of arsenic were first mentioned in 1921 [1] and 1923, [2] the main studies in this field were made in the last 10–15 years. Fairly complete reviews have now been published [3,4], but these are concerned only with α-ethynyl derivatives of arsenic and cover the literature up to 1967.

The methods of synthesis of acetylene derivatives of Group III–V elements are discussed by Davidson and Henry [3], who also examine the chemical properties of organoarsenic acetylene derivatives and compare them with other organic derivatives of the elements.

Apart from a brief discussion of the chemical properties, Cadiot and Chodkiewicz [4] quote infrared, NMR, and ultraviolet frequencies for certain organoarsenic acetylene derivatives.

In the present review, the first published in the USSR on this subject, an attempt is made to give a systematic account of the methods of synthesis of ethynyl organoarsenic compounds and of the types of their chemical reactions. Data published up to November 1973 and embracing organoarsenic acetylene derivatives in which the ethynyl groups are in the α- and other positions [5-10] relative to the arsenic atom were used.

Continuing the traditional review format [3,4], the authors have presented data on the methods of synthesis and certain physical properties of these compounds (including infrared, ultraviolet and NMR spectroscopic data), in the form of compilations in Tables.

II. METHODS OF SYNTHESIS

Direct and Indirect Ethynylation of Organosilicon Compounds

The commonest method of synthesising organoarsenic acetylene derivatives (OAAD) involves the interaction of organoarsenic halides with ethynyl derivatives of Group I, II, and IV metals.

In contrast to the syntheses in the series of carbochain and organophosphorus acetylenes, sodium and lithium acetylides have not found an extensive application in the OAAD synthesis. It was discovered that the reactions carried out in liquid ammonia (method 1a, Table 1) are much less effective than in oxygen-containing solvate-forming solvents (method 1b)—tetrahydrofuran (THF), [10,11] ether [12], and a 2:1 THF–benzene mixture [13] for sodium acetylides, ether [14,15] and THF [16] for lithium acetylides, and a 2:1 benzene–THF mixture for the reaction of silver acetylides with $AsCl_3$. [17] As a rule, the synthesis of OAAD by method 1b proceeds smoothly in the cold, although in certain cases heating is required to complete the reaction [12].

Carty et al. [15] obtained from ethynyldiphenylphosphine a disubstituted acetylene containing phosphorus and arsenic atoms:

$$Ph_2PC{\equiv}CH \xrightarrow[N_2;\ -78°]{n\text{-BuLi; } Ph_2AsCl} Ph_2PC{\equiv}CAsPh_2\ (50\%)\ .$$

The main bulk of OAAD have been synthesised using the Iotsich reagent (method 2). This procedure proved to be the most convenient on a preparative scale.

Compounds with the general formula $R_2AsC{\equiv}CR'$ [10,11,18,19] have been obtained in THF solution by adding a disubstituted halogenoarsine to an Iotsich reagent at room temperature. For R ranging from C_2H_5 to n-C_6H_{13} and R' = H, subsequent heating is required [18]. For R = C_6H_5 or α-$C_{10}H_7$ and R' = H, [10,11] the reaction reaches completion in several minutes. Dialkynyl compounds [10] $PhAs(C{\equiv}CR)_2$, where R = Me or Ph, and trisethynylarsines $As(C{\equiv}CR)_3$, where R = H, [20] Me, [10] or Ph, [13] are formed in high yields under similar conditions.

Polyacetylene derivatives of the type $R_2As(C{\equiv}C)_mR'$ have been synthesised [10]:

$$R_2AsX + R'(C{\equiv}C)_mMgX \xrightarrow[48-83\%]{THF} R_2As(C{\equiv}C)_mR'\ .$$

For compounds with $m = 2$, the reactions were carried out at −5°C but for $m = 3$ the reaction temperature had to be reduced to −20°C.

Diacetylene diarsenic compounds $R_2AsC{\equiv}C-C{\equiv}C-AsR_2$ (R = Et, Pr, i-Pr, n-Bu, or i-Bu) have been obtained by the reaction of dialkyliodoarsines with a diacetylene Iotsich reagent in ether [21]. OAAD with the general formula $R_2AsC{\equiv}CAsR_2$, where R = Pr, n-Bu, i-Bu, n-C_5H_{11}, or n-C_6H_{13}, were synthesised similarly [8] using $BrMgC{\equiv}CMgBr$ as the acetylenic component [17,22]. It has been shown for R=Et, C_6H_{11}, and α-$C_{10}H_7$ that the replacement of ether by chloroform promotes a greater degree of completion of the reaction [23].

Fluorine-containing OAAD $CF_3C{\equiv}CAsMe_2$ and $(CF_3C{\equiv}C)_2AsMe$ have been obtained [24] in low yields via the mechanism (n = 1, 2)

$$n\,CF_3C{\equiv}CMgI + Me_{3-n}AsI_n \xrightarrow{ether} (CF_3C{\equiv}C)_nAsMe_{3-n}\ .$$

Ethynylarsenic acids $C_6H_{11}C{\equiv}CAs(O)(OH)_2$ and $(C_6H_{13}C{\equiv}C)_2As(O)(OH)$ have been synthesised by a general method [25] using the corresponding aminohalogenoarsines:

$$n\,RC{\equiv}CMgBr \xrightarrow[3.ether,\ 30\%\ H_2O_2]{\substack{1.Cl_nAs(NEt_2)_{3-n},\ ether\\ 2.hydrolysis\ with\ dil.HCl}} (RC{\equiv}C)_nAs(O)(OH)_{3-n}\ .$$

Table 1. Acetylenic organoarsenic compounds.

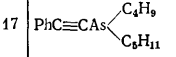
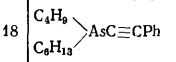
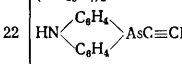
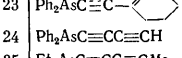
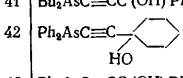
No.	Compound	Yield, %	M.p., degC	B.p., °C/mmHg	n_D^{20}	d_4^{20}	$[AR_D]_{As}$	ν, cm^{-1} C≡C	ν, cm^{-1} C≡CH	Method of preparation	Refs.
	$R_2As(C{\equiv}C)_nR'$										
1	$Et_2AsC{\equiv}CH$	32.7	—	133—133.5	1.4940	1.1430	11.19	2026 w[a]	3280, 3300 s.	2	18,34
2	$(n\text{-}Pr)_2AsC{\equiv}CH$	40.8	—	66.5—67.5 (17)	1.4884	1.0850	11.15	2024 w.	3275, 3290 s.	—	
								2030 w.[b]	3302[b]	2	18,34
3	$(n\text{-}Bu)_2AsC{\equiv}CH$	41.1	—	87—88 (11)	1.4865	1.0470	11.34	2030	3300	2	18
4	$(n\text{-}C_5H_{11})_2AsC{\equiv}CH$	12.7	—	125—127 (16)	1.4826	1.0180	11.45	2029	3282 3300 s.	2	18,34
5	$(n\text{-}C_6H_{13})_2AsC{\equiv}CH$	26.7	—	107—108 (2)	1.4827	0.9949	11.54	2026 w.	3280	2	18,34
6	$Ph_2AsC{\equiv}CH$	85	23	140 (1.5)	—	—	—	2030	3270	2	10
7	$(\alpha\text{-}C_{10}H_7)_2AsC{\equiv}CH$	—	123	—	—	—	—	—	—	1b, 2	11
8	$Ph_2AsC{\equiv}CMe$	86	—	128 (1)	—	—	—	2180	—	2	10
9	$Ph_2AsC{\equiv}CEt$	92	—	110 (0.01)	—	—	—	2180	—	2	10
10	$Bu_2AsC{\equiv}CBu$	—	—	—	—	—	—	2170 m.	—	—	34
11	$Et_2AsC{\equiv}CC_6H_{11}$	—	—	—	—	—	—	2170 m.	—	—	34
12	$Bu_2AsC{\equiv}CC_6H_{11}$	—	—	—	—	—	—	2168 s.	—	—	34
13	$Et_2AsC{\equiv}CPh$	31.2	—	104—105 (0.8)	1.5906	1.1676	13.27	2150	—	4	19
14	$Pr_2AsC{\equiv}CPh$	36.0	—	120 (0.8)	1.5710	1.1206	13.19	2150	—	4	19
15		25.9	—	141—143 (1)	1.5648	1.1043	13.09	2150	—	4	19
16	$Bu_2AsC{\equiv}CPh$	40.6	—	145—147 (1)	1.5611	1.0904	13.24	2150	—	4a, 4b, 2	19,29
17		34.2	—	164—165 (1)	1.5541	1.0730	13.34	2150	—	4a	19
18		31.5	—	151—152 (0.8)	1.5480	1.0601	13.15	2150	—	4a	19
19	$(C_5H_{11})_2AsC{\equiv}CPh$	25.2	—	164—167 (1)	1.5480	1.0598	13.18	2135	—	4b	29
20	$Ph_2AsC{\equiv}CPh$	—	43	168 (3)	—	—	—	—	—	1b, 2	8,11
21	$(\alpha\text{-}C_{10}H_7)_2AsC{\equiv}CPh$	—	142	—	—	—	—	—	—	1b, 2	11
22		—	172	—	—	—	—	—	—	1b	12
23		70	42	—	—	—	—	2120	—	2	10
24	$Ph_2AsC{\equiv}CC{\equiv}CH$	48	55	—	—	—	—	2030	3300	1a, 2	10
25	$Et_2AsC{\equiv}CC{\equiv}CMe$	83	—	70 (0.5)	—	—	—	2040, 2100	—	2	10
26	$Ph_2AsC{\equiv}CC{\equiv}CMe$	76	60	—	—	—	—	2080, 2190	—	2	10
27	$Ph_2AsC{\equiv}CC{\equiv}CPr$	75	40	—	—	—	—	2090, 2200	—	2	10
28	$Ph_2AsC{\equiv}CC{\equiv}CPh$	55	63	—	—	—	—	2100, 2200	—	2	10
29	$Ph_2AsC{\equiv}CC{\equiv}CC{\equiv}CMe$	60	125	—	—	—	—	2040, 2195	—	2	10
30	$Bu_2AsC{\equiv}CCH(OH)Me$	65.3	—	104—105 (1.5)	1.5024	1.0818	12.25	2135, 2140	—	A	31
31	$Bu_2AsC{\equiv}CCH(OH)Et$	51.5	—	115—117 (2.5)	1.5006	1.0681	12.11	2135 w	—	A	31,34
32	$Bu_2AsC{\equiv}CCH(OH)Pr$	57.5	—	119.5—120.5 (2)	1.4980	1.0450	12.71	2135, 2140	—	A	31
33	$Bu_2AsC{\equiv}CCH(OH)(i\text{-}Pr)$	48.0	—	117—118 (2)	1.4982	1.0450	12.75	2135 w.	—	A	31,34
34	$Bu_2AsC{\equiv}CCH(OH)Bu$	55.0	—	129.5—130 (2.5)	1.4942	1.0340	12.30	2135, 2140	—	A	31
35	$Bu_2AsC{\equiv}CCH(OH)Ph$	46.5	—	158—160 (2)	1.5489	1.1276	13.62	2135—2140	—	A	31
36	$Bu_2AsC{\equiv}CC(OH)Me_2$	44.9	—	98.5—100 (1,5)	1.4952	1.0550	12.32	—	—	A	18
37	$Bu_2AsC{\equiv}CC(OH)MeEt$	48.6	—	107—108 (1,5)	1.4951	1.0430	12.34	2165 w.	—	A	31,34
38	$Bu_2AsC{\equiv}CC(OH)Et_2$	48.5	—	112.5—113 (1,5)	1.4949	1.0360	12.34	2160—2170	—	A	31
39	$Bu_2AsC{\equiv}CC(OH)MeBu$	41.4	—	120—121 (1,5)	1.4909	1.0120	12.59	2160—2170	—	A	31
40	$Bu_2AsC{\equiv}CC(OH)Me(i\text{-}Bu)$	42.6	—	116.5—117.5 (2)	1.4901	1.0170	12.54	2165 w.	—	A	31,34
41	$Bu_2AsC{\equiv}CC(OH)Pr_2$	36.7	—	129—131 (2)	1.4865	1.0080	12.36	2160—2170	—	A	31
42		87	57	—	—	—	—	—	—	A	10
43	$Ph_2AsC{\equiv}CC(OH)Ph_2$	87	136	—	—	—	—	—	—	A	10
44	$Et_2AsC{\equiv}CC(O)Me$	45.2	—	72.5—73 (3)	1.5210	1.1870	13.05	2138	—	A	32,34
45	$Et_2AsC{\equiv}CC(O)Et$	53.6	—	84—84.5 (2,5)	1.5162	1.1543	13.20	2135 s.	—	A	32,34
46	$Pr_2AsC{\equiv}CC(O)Me$	24.5	—	82—83 (2,5)	1.5080	1.1190	13.24	2136 v.s.	—	A	32,34
47	$Pr_2AsC{\equiv}CC(O)Et$	46.0	—	108—109 (2,5)	1.5065	1.1001	13.32	2135 v.s.	—	A	32,34
48	$Bu_2AsC{\equiv}CC(O)Me$	42.6	—	107—108 (2,5)	1.5058	1.0864	13.18	2137 v.s.	—	A	32,34
49	$Et_2AsC{\equiv}CC(O)OH$	45.5	—	—	1.5389	1.3105	13.12	2165 s.	—	A	34,35
50	$Pr_2AsC{\equiv}CC(O)OH$	62.5	—	—	1.5270	1.2232	13.38	2165 s.	—	A	34,35

Table 1 (continued).

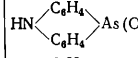
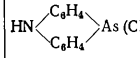
No.	Compound	Yield, %	M.p., degC	B.p., °C/mmHg	n_D^{20}	d_4^{20}	$[AR_D]_{As}$	ν, cm⁻¹ C≡C	ν, cm⁻¹ C≡CH	Method of preparation	Refs.
51	$Bu_2AsC{\equiv}CC(O)OH$	60.5	—	—	1.5192	1.1674	13.45	2165 s.	—	A	34,35
52	$Ph_2AsC{\equiv}CC(O)OH$	58	130	—	—	—	—	—	—	A	10
53	$Et_2AsC{\equiv}CC(O)OEt$	24.0	—	89—90 (2)	1.5080	1.1989	12.68	2165 s.	—	A	34,35
54	$Pr_2AsC{\equiv}CC(O)OEt$	21.6	—	103—103.5 (2)	1.5010	1.3990	12.96	2165 s.	—	A	34,35
55	$Bu_2AsC{\equiv}CC(O)OEt$	19.4	—	128—131 (3)	1.5000	1.0988	13.37	2165 s.	—	A	34,35
56	$Et_2AsC{\equiv}CCH_2NEt_2$	—	—	—	—	—	—	2150 w.	—	A	34
57	$Pr_2AsC{\equiv}CCH_2NEt_2$	—	—	—	—	—	—	2160 w.	—	A	34
58	$n\text{-}Bu_2AsC{\equiv}CCH_2NEt_2$	18	—	142.5—144 (11)	1.4889	0.9908	12.73	2157 w.	—	A	18,34
59	$Me_2AsC{\equiv}CCF_3$	35	98[c]	—	—	—	—	2210	—	2	24
60	$Ph_2AsC{\equiv}CCF_3$	65	—	79—80 (0,1)	—	—	—	—	—	1b	15
61	$Ph_2AsC{\equiv}CCl$	82	—	130 (0.03)	—	—	—	2128	—	6	30
62	$Ph_2AsC{\equiv}CPPh_2$	50	86—87	—	—	—	—	2092[d]	—	1b	15
	$R_2As(X_2)C{\equiv}CR'$										
63	$Ph_2As(O)C{\equiv}CMe$	95	105	—	—	—	—	2190	—	A	10
64	$Ph_2As(OH)_2C{\equiv}CMe$	95	68	—	—	—	—	2190	—	A	10
65	$Ph_2As(O)C{\equiv}CEt$	95	130	—	—	—	—	2190	—	A	10
66	$Ph_2As(OH)_2C{\equiv}CEt$	95	80	—	—	—	—	2190	—	A	10
67	$Ph_2As(O)C{\equiv}CC(OH)(CH_2)_4CH_2$	90	205	—	—	—	—	2180	—	A	10
68	$Ph_2As(O)C{\equiv}CC(OH)Ph_2$	90	260 (decomp.)	—	—	—	—	2200	—	A	10
69		—	150 (decomp.)	—	—	—	—	—	—	A	12
70		—	148	—	—	—	—	—	—	A	12
71	$C_6H_{11}C{\equiv}CAs(O)(OH)_2$	21	unpurified	—	—	—	—	2195	—	2	25
	$[R''R_2As(C{\equiv}C)_nR']^+X^-$										
72	$[Ph_2(Me)AsC{\equiv}CH]^+OTs^-$	10	159	—	—	—	—	2050	3280[e] 3095[f]	A	10
73	$[Ph_2(Me)AsC{\equiv}CMe]^+OTs^-$	30	170	—	—	—	—	—	—	A	10
74	$[Ph_2(Me)AsC{\equiv}CPhOH]^+I^-$	10	260	—	—	—	—	—	—	A	10
75	$[Et_2(Me)AsC{\equiv}CC{\equiv}CMe)^+I^-$	92	137 (decomp.)	—	—	—	—	—	—	A	10
76	$[Et_3AsC{\equiv}CC{\equiv}CMe]^+Br^-$	98	160	—	—	—	—	—	—	5	10
77	$[Et_3AsC{\equiv}CC{\equiv}CPh]^+Br^-$	95	170—180 (decomp.)	—	—	—	—	—	—	5	10
	$RAs(C{\equiv}CR')_2$										
78	$PhAs(C{\equiv}CMe)_2$	85	—	75 (0,01)	—	—	—	2180	—	2	10
79	$PhAs(C{\equiv}CPh)_2$	63	63	—	—	—	—	2150	—	2	10
80	$MeAs(C{\equiv}CCF_3)_2$	15	—	122—124/760	—	—	—	2210	—	2	24
81	$(C_6H_{13}C{\equiv}C)_2As(O)(OH)$	34	unpurified	—	—	—	—	2195	—	2	25
	$As(C{\equiv}CR')_3$										
82	$As(C{\equiv}CH)_3$	62,6	49—50	—	—	—	—	2054	3291	2	20
83	$As(C{\equiv}CMe)_3$	92	131	—	—	—	—	2160	—	2	10
84	$As(C{\equiv}CPh)_3$	75	127	—	—	—	—	2160	—	1b, 2	13,17
85	$As(C{\equiv}CCMe_3)_3$	99	62—63	—	—	—	—	2155,2189	—	1b	16
86	$As(O)[C{\equiv}CCMe_3]_3$	95	141—2	—	—	—	—	—	—	A	16
87	$As(S)[C{\equiv}CCMe_3]_3$	88	112—3	—	—	—	—	—	—	A	16
	Diarsenic ethynyl derivatives of various types										
88	$Me_2AsC{\equiv}CAsMe_2$	50	—	84.5	—	—	—	—	—	2	2,38
89	$Et_2AsC{\equiv}CAsEt_2$	72	—	139 (8)	—	—	—	—	—	2	23
90	$Pr_2AsC{\equiv}CAsPr_2$	42.5	—	118.5—119.5 (2)	1.5268	1.1570	12.42	—	—	2	22
91	$Bu_2AsC{\equiv}CAsBu_2$	43	—	159—160 (1.5)	1.5168	1.1154	12.46	—	—	2	22
92	$(i\text{-}Bu)_2AsC{\equiv}CAs(Bu\text{-}i)_2$	30.1	—	134—136 (2)	1.5122	1.0986	12.24	—	—	2	22
93	$(C_5H_{11})_2AsC{\equiv}CAs(C_5H_{11})_2$	17	—	196—198 (3)	1.5103	1.0600	12.77	—	—	2	22
94	$(C_6H_{13})_2AsC{\equiv}CAs(C_6H_{13})_2$	16	—	199—201 (1.5)	1.4963[g]	1.0222[h]	12.26	1960 v.w.	—	2	22
95	$(C_6H_{11})_2AsC{\equiv}CAs(C_6H_{11})_2$	70	72	—	—	—	—	—	—	2	23
96	$Ph_2AsC{\equiv}CAsPh_2$	74	105	—	—	—	—	—	—	1a, 2, 3	23, 26, 37
97	$(\alpha\text{-}C_{10}H_7)_2AsC{\equiv}CAs(C_{10}H_7\text{-}\alpha)_2$	61	232	—	—	—	—	—	—	1a, 2	23
98	$(\alpha\text{-}C_{10}H_7)_2As(O)C{\equiv}C(O)As(C_{10}H_7\text{-}\alpha)_2$	—	—	—	—	—	—	—	—	A	23
99	$Et_2AsC{\equiv}CC{\equiv}CAsEt_2$	49.3	—	125.5—126 (0.7)	1.6039	1.2736	13.86	2060	—	2	21
100	$Pr_2AsC{\equiv}CC{\equiv}CAsPr_2$	40.9	—	141.5 (0.3)	1.5740	1.1766	14.78	2060	—	2	21
101	$(i\text{-}Pr)_2AsC{\equiv}CC{\equiv}CAs(Pr\text{-}i)_2$	37.6	—	133.5—134 (0.3)	1.5740	1.1717	14.32	2060	—	2	21

Table 1 (continued).

No.	Compound	Yield, %	M.p., degC	B.p., °C/mmHg	n_D^{20}	d_4^{20}	$[AR_D]_{As}$	ν, cm⁻¹ C≡C	ν, cm⁻¹ C≡CH	Method of preparation	Refs.
102	$Bu_2AsC{\equiv}CC{\equiv}CAsBu_2$	13.15	—	182—185 (0.6)	1.5440	1.1092	13.71	2060	—	2	21
103	$(i\text{-}Bu)_2As(C{\equiv}C)_2As(Bu\text{-}i)_2$	27.7	—	172—174 (0.6)	1.5407	1.1082	13.45	2060	—	2	21
104	$Ph_2AsC{\equiv}CC{\equiv}CAsPh_2$	40	115 (decomp.)	—	—	—	—	2060	—	1a, 3	10, 27, 28
105	$(\alpha\text{-}C_{10}H_7)_2As(C{\equiv}C)_2As(C_{10}H_7\text{-}\alpha)_2$	50	218 (decomp.)	—	—	—	—	2070	—	3	27, 28
106	$[Et_2(Me)AsC{\equiv}CAsEt_2]^+I^-$	—	68	—	—	—	—	—	—	A	23
107	$[(C_6H_{11})_2AsC{\equiv}CAs(C_6H_{11})_2]^+I^-$ (Me)	—	133	—	—	—	—	—	—	A	23
	Various organoarsenic compounds containing the acetylene group										
108	$Et_2AsCH_2C{\equiv}CH$	46.7	—	56 (14)	—	—	—	—	—	2	8
109	$Et_2AsCH(Me)C{\equiv}CH$	12	—	64 (14)	—	—	—	—	—	2	8
110	$Ph_2AsCH_2C{\equiv}CH$	67.5	—	110 (0.01)	—	—	—	—	—	2	8
111	$Ph_2AsCH(Me)C{\equiv}CH$	65	—	120 (0.01)	—	—	—	—	—	2	8
112	$Et_2AsCH_2C{\equiv}CMe$	15	—	62 (14)	—	—	—	—	—	2	8
113	$Et_2AsCH(Me)C{\equiv}CMe$	48	—	72 (14)	—	—	—	—	—	2	8
114	$Ph_2AsCH_2C{\equiv}CMe$	57.7	—	120 (0.01)	—	—	—	—	—	2	8
115	$Ph_2AsCH(Me)C{\equiv}CMe$	70	—	125 (0.01)	—	—	—	—	—	2	8
116	$(p\text{—}PhC{\equiv}C)C_6H_4As(O)(OH)_2$	92	>300	—	—	—	—	—	—	6	9
117	$[Ph_2(Et)AsCH_2C{\equiv}CH]^+Br^-$	—	—	—	—	—	—	—	—	A	8
118	$[Ph(Et)AsCH_2C{\equiv}CMe]^+Br^-$	—	—	—	—	—	—	—	—	A	8
119	$[Ph_2(Et)AsCH_2C{\equiv}CPh]^+Br^-$	—	—	—	—	—	—	—	—	A	8
120	$[Ph_2(Et)AsCH_2C{\equiv}CH]^+Br^-$	99	194 (decomp.)	—	—	—	—	—	3305 3180	5	10
121	$[Ph_2(Et)AsCH_2C{\equiv}CH]^+I^-$	98	178	—	—	—	—	—	3305 3195	5	10
122	$[Ph_2(Et)AsCH_2C{\equiv}CH]^+OTs^-$	78	129 144	—	—	—	—	—	3305 3205 3200	5	10
123	$[Ph_3AsCH_2C{\equiv}CH]^+Br^-$	97	246 (decomp.)	—	—	—	—	—	3300 3150	5	10
124	$[Ph_3AsCH_2C{\equiv}CH]^+I^-$	98	196 (decomp.)	—	—	—	—	—	3300 3165	5	10
125	$[Ph_3AsCH_2C{\equiv}CH]^+OTs^-$	92	215 (decomp.)	—	—	—	—	—	3300 3190	5	10
126	$Bu_2AsC{\equiv}CCu$	—	—	—	—	—	—	—	—	A	39
127	$Ph_2AsC{\equiv}CCu$	60	—	—	—	—	—	1950 w.	—	A	36
128	$H[-(C{\equiv}CC_6H_4C{\equiv}CAs)_m(Ph)\text{—}C{\equiv}CC_6H_4C{\equiv}C]_nH$		—	—	—	—	—	—	—	1b	14

Note. a) v.s. = very strong, s. = strong, m. = medium, w. = weak, and v.w. = very weak; b) in n-hexane; c) middle fraction in distillation; d) intense band in the Raman spectrum; e) in chloroform solutions; f) in the solid state; g) n_D^{40}; h) d_4^{40}.

Compounds in which the arsenic atom is in the α-position relative to the triple bond have been examined so far. Benaim [8] synthesised a large series of propargyl derivatives of arsenic with the general formula $R_2AsCH(R')C{\equiv}CR''$ via the mechanism

$$R_2AsX + R'CH(MgBr)C{\equiv}CR'' \xrightarrow[12-70\%]{20°;\ \text{ether}} R_2AsCH(R')C{\equiv}CR'' + MgBrX \quad .$$

It was established the the yield of the required product increases when the disubstituted halogenoarsine is taken in excess. The synthesis of propargyl arsines by the reaction of sodium derivatives of disubstituted arsines with propargyl bromides is not useful, since the yield is low [8]. Thus, for R = Ph, R′ = Me, and R″ = H, one obtains a 65% yield of the product via the first scheme and only 18% via the second.

$$Ph_2AsNa + Me\text{—}\underset{Br}{CH}\text{—}C{\equiv}CH \xrightarrow[18\%]{\text{liq. } NH_3;\ -40°} Ph_2AsCH(Me)\text{—}C{\equiv}CH \quad .$$

The exchange reaction between diarylchloroarsines and acetylene and diacetylene dizinc and ditin derivatives, leading to the formation of diarsenic acetylene derivatives (method 3), is of theoretical interest:

$$Ar_2AsCl + Y(C{\equiv}C)_nY \xrightarrow{t°} Ar_2As(C{\equiv}C)_nAsAr_2 \quad .$$

For Ar = Ph, Y = $SnMe_3$, and $n = 1$, Borisov et al. [26] used an alcoholic medium. For Ar = Ph or naphthyl, $n = 2$, and Y = ZnMe [27] or $ZnMe_3$, [28] the reaction was carried out in absolute toluene and benzene.

In 1968 Kuz'min and Panfilovich [19] proposed a novel method for the synthesis of OAAD having the general formula $\begin{matrix}R_1\\R_1\end{matrix}\!\!>\!AsC{\equiv}CPh$, based on the use of the nucleophilic properties of phenylacetylene:

$$\begin{matrix}R_1\\R_2\end{matrix}\!\!>\!As\text{—}OH + HC{\equiv}CPh \rightarrow \begin{matrix}R_1\\R_2\end{matrix}\!\!>\!As\text{—}C{\equiv}CPh \xrightarrow{\text{thermal isomerisation}}$$

$$\rightarrow \begin{matrix}R_1\\R_2\end{matrix}\!\!>\!AsOC{\equiv}CPh \xrightarrow{PhC{\equiv}CH} \begin{matrix}R_1\\R_2\end{matrix}\!\!>\!AsC{\equiv}CPh \quad .$$

By heating dialkylarsinic acids and phenylacetylene in molar proportions of 1 : 2 in benzene or toluene with azeotropic distillation of water, OAAD with different R were obtained: $R_1 = R_2 = C_2H_5$; $R_1 = R_2 = C_3H_7$; $R_1 = C_3H_7$, $R_2 = C_4H_9$; $R_1 = R_2 = C_4H_9$; $R_1 = C_4H_9$, $R_2 = C_5H_{11}$; $R_1 = C_4H_9$, $R_2 = C_6H_{13}$.

Subsequently this method was extended to arsenic(III) derivatives (method 4b) [29]:

$$PhC{\equiv}CH + \begin{cases} R_2AsI \\ R_2AsOC\,(O)\,Me \\ R_2AsOR\ (\text{где } R = Alk) \end{cases} \rightarrow R_2AsC{\equiv}CPh \quad .$$

Quaternary arsonium salts with the general formula $[Ph_2As(R)CH_2C{\equiv}CH]^+X^-$, where R = Ph or Et and X = Br, I, or OTs, are formed in high yields [10] when tertiary arsines are refluxed in acetonitrile with the corresponding propargyl derivatives (method 5). Diacetylene compounds $[Et_3AsC{\equiv}C-C{\equiv}CR]^+Br^-$, where R = Me or Ph, were obtained similarly in ether.

The method of indirect ethynylation of organoarsenic compounds is not of particular importance in the synthesis of OAAD (method 6). Here, mention should be made of the synthesis in high yield of the acid (p-$PhC{\equiv}C)C_6H_4As(O).(OH)_2$ from its styryl analogue (bromination of the olefin and dehydrobromination by KOH in butanol) [9] and also of chlorodiphenylarsinoacetylene via the mechanism [30]

$$Ph_2AsBr + ClCH = CHCl + 2Na \xrightarrow[82\%]{\text{liq. } NH_3,\ -60^\circ} Ph_2AsC{\equiv}CCl \quad .$$

2. Synthesis Based on Organoarsenic Acetylene Derivatives

Many OAAD have been obtained using ethynylarsenic(III) derivatives, described in the preceding section, with a terminal $-C{\equiv}CH$ group (method A).

Thus, secondary and tertiary ethynyl alcohols with the general formula $R_2AsC{\equiv}C-C(OH)R'R''$ have been synthesised by the carbonylation of OAAD via the Favorskii reaction [10] and by the reaction of organomagnesium derivatives of the type $R_2AsC{\equiv}CMgBr$ with compounds containing carbonyl groups [18,31]. The condensation of diphenylethynylarsine with benzophenone and cyclohexanone proceeds smoothly in the presence of KOH in THF solution [10].

Iotsich reagents obtained from dialkylarsinoacetylenes react with aldehydes and acetone with evolution of heat, while the reactions involving other aliphatic ketones (ethyl methyl, diethyl, butyl methyl, and dipropyl ketones) require heating.

The ketones $R_2AsC{\equiv}C-\underset{\underset{O}{\|}}{C}-R'$ were obtained by the reaction [32]

$$2\,R_2AsC{\equiv}CMgBr + 2\,(R'CO)_2O \rightarrow 2R_2AsC{\equiv}\underset{\underset{O}{\|}}{C}C-R' + MgBr_2 + (R'COO)_2Mg \quad .$$

When an excess of the anhydride is taken and the synthesis is carried out at a temperature not exceeding $-60^\circ C$, adding the organomagnesium derivative of the dialkylethynylarsine to an ethereal solution of the anhydride, the reaction stops at the ketone formation stage.

Dialkyl arsino-α-ethynyl ketones are slightly coloured liquids, which distil without decomposition but are unstable in air.

Diphenylarsinoacetylenecarboxylic acid $Ph_2AsC{\equiv}CCOOH$ is formed when ethynyldiphenyl arsine reacts with carbon dioxide in THF solution (using magnesium as the condensing agent) [10]. The corresponding dialkyl derivatives have been synthesised via the magnesium derivatives of the dialkylethynylarsine by adding solid carbon dioxide to its ethereal solution [33]:

$$R_2AsC{\equiv}CMgBr + CO_2 \rightarrow R_2AsC{\equiv}CCOOH \quad .$$

Ethyl esters of dialkylarsinoacetylenecarboxylic acids $R_2AsC{\equiv}CCOOEt$ were obtained [33] in low yields by the reaction of the organomagnesium derivative of dialkylethynylarsine and ethyl chlorocarbonate:

$$R_2AsC{\equiv}CMgBr + ClCOOEt \xrightarrow[-15^\circ]{\text{ether}} R_2AsC{\equiv}CCOOEt \quad .$$

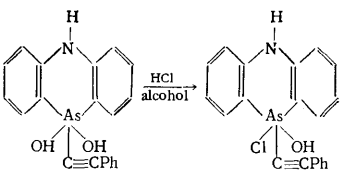
In contrast to dialkylethynylphosphines [33,34] dialkylethynylarsines enter into the Mannich reaction. The compound $Bu_2AsC{\equiv}C-CH_2-NEt_2$ is formed in low yield on heating for 24 h a reaction mixture consisting of paraformaldehyde, diethylamine, and dibutylethynylarsine in the presence of copper acetate as the catalyst [18,34,35].

The reaction of terminal OAAD with copper(I) salts in aqueous ammonia does not lead to the formation of acetylides. Copper diphenylarsinoacetylide was obtained [36] only by the decomposition with a dilute ammonia solution of the ternary complex of CuCl, the ethynyl compound, and dimethyl sulphoxide (DMSO), which had been prepared beforehand.

Oxidative addition and arsenic(III) quaternisation reactions have been used to synthesise a series of ethynyl derivatives of tetracoordinate and quinquevalent arsenic.

Owing to the reduced (compared with tervalent phosphorus) nucleophilicity of arsenic(III), the quaternisation of ethynylarsines proceeds with greater difficulty than that of the corresponding phosphines. It was established that dialkylethynylarsines are more reactive in this process than their aromatic analogues [16,19]. The quaternisation of polyacetylenic arsines with the general formula $R_{3-n}As.[(C{\equiv}C)_mR']_n$ is hardly observed in ether, but is markedly facilitated in acetonitrile [10]. Diarsenic compounds $R_2AsC{\equiv}CAsR_2$ react with methyl iodide in ether in the cold only for R = Et and C_6H_{11}. For R = Ph or α-$C_{10}H_7$, the formation of salts was not observed even after prolonged heating [23].

Ethynylarsine oxides and hydroxides have been obtained by the oxidation of OAAD with hydrogen peroxide in acetone or acetic acid. The OAAD employed were ethynyldiphenylarsines $Ph_2AsC{\equiv}C-R$, [10] tris-(t-butylethynyl)arsine [16], bis(di-α-naphthylarsino)acetylene [23], and 10-phenylethynyl-9,10-dihydrophenarsazine [12]. In the last case it was shown that one hydroxy-group in the oxidised product is readily substituted by chlorine via the reaction



Tris-(t-butylethynyl)arsine forms the sulphide [24] $(Me_3C-C{\equiv}C)_3As{=}S$ on refluxing with sulphur in CS_2.

III. CHEMICAL PROPERTIES

OAAD contain in their structure several reactive centres (As^{III}, $\equiv C-H$, $C{\equiv}C$, $As-C{\equiv}C-$), which is the reason for the wide variety of the chemical properties of compounds of this class. These properties have already been partly considered in the second part of the previous

section. Below we shall consider problems of the thermal and hydrolytic stability and light resistance of OAAD, the effect of the tetracoordination of arsenic on the properties of OAAD, and certain spectroscopic data.

1. Thermal Stability and Light Resistance of OAAD

In Davidson and Henry's review [3] OAAD are classified as potentially explosive substances. However, judging from the latest data, in the vast majority of cases no special precautions are necessary in handling OAAD.

Trisalkylethynyl derivatives of Group VB elements are known [3,4] to be unstable under the usual conditions and compounds of the type $(HC{\equiv}C)_3E$ (E = element) explode in air. As for polyethynyl derivatives of the elements in other Groups, the arsenic(III) compound with t-butylethynyl substituents $(Me_3C-C{\equiv}C)_3As$ proved to be thermally stable and insensitive to light [16].

The monoethynylarsine $Me_2AsC{\equiv}CCF_3$ is hardly coloured by ultraviolet light, but darkens on heating to 160–180°C. However, according to infrared and NMR spectroscopic data, these visual changes are not accompanied by the decomposition of the initial OAAD. [24] The diethynylarsine $MeAs(C{\equiv}CCF_3)_2$ is less stable: thus marked charring was observed after heating the specimen at 140°C; the specimen, which was colourless at the end of ultraviolet irradiation, soon became black [24].

It has been reported [16] that the compound $Ph_2AsC{\equiv}CCF_3$ may be stored for a long time at room temperature without decomposition. Dialkylethynylarsines remain unchanged after oxidative condensation [40] in the absence of a catalyst. The triethynylarsine $(MeC{\equiv}C)_3As$ is resistant to the action of oxygen and atmospheric moisture at −20°C in the course of many months [20]. Bis(dialkylarsino)acetylenes $R_2AsC{\equiv}CAsR_2$ (R = Pr, n-Bu, i-Bu, or C_5H_{11}) are stable in air indefinitely [22].

In contrast to the corresponding arsines, the acids $(C_6H_{13}C{\equiv}C)_nAs(O)(OH)_{3-n}$ (n = 1, 2) proved to be fairly unstable [9].

2. The Cleavage of OAAD at the ≡C–As Bond

As a rule ethynylarsines are fairly inert with respect to water. Thus the compound $Me_2AsC{\equiv}CCF_3$ withstands contact with water without decomposition over a period of four months at 20°C and for five days at 110°C. [24] The resistance to hydrolysis persists in diethynylarsines [for example $MeAs(C{\equiv}CCF_3)_2$] [24] and triethynylarsines [$(HC{\equiv}C)_3As$], [20] while the diarsenic alkyl derivatives $R_2AsC{\equiv}CAsR_2$ are slowly cleaved by water even in the cold [23].

Among all the OAAD whose behaviour in relation to alkalis was investigated, only 10-phenylethynyl-9,10-dihydrophenarsazine is not decomposed by aqueous solutions of alkali, but hydrochloric acid cleaves its ≡C–As bond [12].

Strong alkalis decompose the ethynylarsines $Ph_2AsC{\equiv}CPh$, $(\alpha\text{-}C_{10}H_7)_2AsC{\equiv}CPh$, and $(\alpha\text{-}C_{10}H_7)_2AsC{\equiv}CH$ with evolution of $PhC{\equiv}CH$ and acetylene respectively [11]. The cleavage of the bisarsines $R_2AsC{\equiv}CAsR_2$ by alkalis takes place readily and more so for R = C_6H_{11} than for R = Ph. [23]

The arsenic(III) derivatives of trifluoromethylacetylene $Me_nAs(C{\equiv}CCF_3)_{3-n}$ (n = 1, 2) evolve the initial acetylene in low yield (36% for n = 1 and 29% for n = 2) on treatment with 10% aqueous sodium hydroxide [24]. Triethynylarsine $As(C{\equiv}CH)_3$ is decomposed by alkalis with evolution of acetylene [20].

Bis(di-α-naphthylarsino)acetylene oxide remains unchanged when treated with alkalis, decomposing partly on refluxing with aqueous silver nitrate [23].

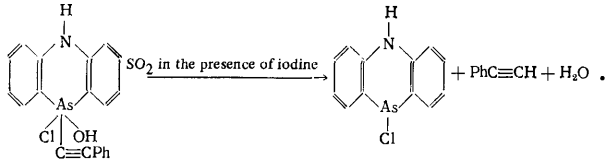
Acetylene and diacetylene derivatives of arsenic [40] are unstable on treatment with dry hydrogen chloride. Apart from hydrochlorination, the As–C≡ bond is broken.

Shpanskii [12] showed that, on treatment with iodine in the cold, 10-phenylethynyl-9,10-dihydrophenarsazine is cleaved with formation of 9-iodo-9,10-dihydrophenarsazine and iodophenylacetylene.

3. Tetracoordination of Arsenic

Although the resistance to oxidation of the acetylene derivatives of Group VB elements decreases from phosphorus to bismuth [4], OAAD do not obey this rule. In the general case the formation of ethynylarsine oxides and hydroxides under the influence of atmospheric oxygen or other oxidants (for example H_2O_2) proceeds with greater difficulty than for the corresponding ethynylphosphines [10,23]. For compounds of the type $R_2AsC{\equiv}CAsR_2$, the oxide was obtained only with R = $\alpha\text{-}C_{10}H_7$; for R = Ph or C_6H_{13}, only the cleavage of the As–C≡ bond was observed under the same conditions [23].

On passing from tervalent to quinquevalent arsenic, the properties of OAAD change significantly, in particular the resistance of the As–C≡ bond to the action of electrophilic agents increases. Thus 10-phenylethynyl-9,10-dihydrophenarsazine hydroxide no longer reacts with iodine, hydrochloric acid does not split off phenylacetylene, and on treatment with alcoholic hydrogen chloride the product of the substitution of one hydroxy-group by chlorine is formed. Its reduction proceeds via the mechanism



It has been noted [23] that bis-(di-α-naphthylarsino)-acetylene oxide is not hydrolysed by alkali, in contrast to the initial compound.

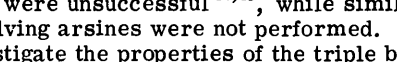
The arsenic(III) OAAD are converted into sulphides, like phosphines, on refluxing with sulphur in carbon disulphide [41–44], but they lose sulphur on isolation.

The quaternisation of ethynylarsines is difficult [10,23].

4. Addition to the Triple Bond

All attempts at the catalytic hydrogenation of ethynylphosphines were unsuccessful [44,45], while similar experiments involving arsines were not performed.

To investigate the properties of the triple bond in OAAD, Kuz'min et al. [40] hydrochlorinated certain acetylene and diacetylene derivatives of arsenic by passing hydrogen chloride through a chloroform solution of the compound:



The polarisation of the triple bond is responsible for the addition of a proton to the α-carbon atom. The chloride ion is directed to the *trans*-position, which is characteristic of disubstituted acetylene derivatives. Hydrogen chloride adds to one of the triple bonds of the diyne group of bis(diethylarsino)diacetylene.

The hydrochlorination of OAAD is accompanied by the dissociation of the As–C≡ bond with formation of the corresponding chloroarsines and monosubstituted acetylenes and diacetylenes. The increase of the polarity of the As–C≡ bond probably facilitates the nucleophilic attack on the arsenic atom and the electrophilic attack on the carbon atom. It has been shown [40] that the rate of formation of products of nucleophilic substitution at the arsenic atom is much higher than the rate of addition of hydrogen chloride to the triple bond.

The behaviour of OAAD in relation to halogens has been hardly investigated. It has been suggested that chlorine and bromine add to the triple bond in 10-phenylethynyl-9,10-dihydrophenarsazine and not to the arsenic atom [12].

Benain [4] reported the addition of diazomethane to acetylenic arsenic-containing compounds.

Cullen and Leeder [24] obtained a cyclopropane derivative, stable at 20°C and even on heating, by the reaction of an organotin trifluoromethyl derivative with a fluorine-containing ethynylarsine:

$$Me_2AsC{\equiv}CCF_3 + Me_3SnCF_3 \rightarrow Me_2As{-}C(CF_2){=}C{-}CF_3 + Me_3SnF$$

Table 2. NMR and ultraviolet spectroscopic data for certain acetylenic organoarsenic derivatives

No.	Compound	Chemical shift[a] δ, p.p.m.	λ_{max} in u.v. absorption, nm ($10^{-3}\epsilon$)	Refs.
1	$(\underline{H}C{\equiv}C)_3As$	2.62	—	20
2	$Ph_2AsC{\equiv}\underline{C}H$	2.82	225 (13.5), 235 (11), 270 (9)	10
3	$[Ph_2As(\underline{Me})C{\equiv}CH]^+OTs^-$	4.50	—	10
4	$Ph_2AsC{\equiv}C{-}C{\equiv}\underline{C}H$	2.12	225 (24), 257 (5.8), 270 (3.6)	10
5	$(\underline{C}H_3)_2AsC{\equiv}C\underline{C}F_3$	(H) 1.08 (F) 27.9	—	24
6	$(\underline{C}H_3)As(C{\equiv}C\underline{C}F_3)_2$	(H) 1.44 (F) 26.4	—	24
7	$Ph_2AsC{\equiv}C\underline{C}H_3$	2.05	—	10
8	$Ph_2As(O)C{\equiv}C\underline{C}H_3$	2.10	—	10
9	$[Ph_2As(Me)C{\equiv}C\underline{C}H_3]^+OTs^-$	2.28	—	10
10	$Ph_2AsC{\equiv}CC{\equiv}C\underline{C}H_3$	1.97	258 (4.3), 271 (2.6)	10
11	$[Et_2As(Me)C{\equiv}CC{\equiv}C\underline{C}H_3]J^-$	2.08	—	10
12	$Ph_2AsC{\equiv}CC{\equiv}CC{\equiv}C\underline{C}H_3$	1.97	226 (80), 240 (48)	10
13	$(CH_3C{\equiv}C)_3As$	1.96	228 (4.2)	10
14	$[(\underline{C}H_3)_3C{-}C{\equiv}C]_3As$	1.26	—	16

[a] For the isolated atom.

5. Reactions of the Acetylenic Hydrogen

Ethynyl derivatives of Group VB elements can be metallated by Grignard reagents [10,18] or by lithium alkyls [33].

The condensations of Iotsich reagents obtained from OAAD with a terminal ≡C–H group [18,31–33,35],

$$R_2AsC{\equiv}CMgBr + \begin{cases} R'R''C{=}O \rightarrow R_2AsC{\equiv}CC(OH)R'R'' \\ (R'(CO_2)O \rightarrow R_2AsC{\equiv}CC(=O){-}R' \\ CO_2 \rightarrow R_2AsC{\equiv}CCOOH \\ ClCOOEt \rightarrow R_2AsC{\equiv}CCOOEt \end{cases}$$

and also the involvement of such acetylene derivatives in the Favorskii [10] and Mannich [33] reactions were examined previously (see Section II, 2). In these reactions the introduction of an arsenic atom in the α-position relative to the triple bond does not alter the type of reactivity of the ethynyl hydrogen atom. However, when an attempt was made to carry out oxidative condensation [40] to obtain organoarsenic derivatives of diacetylene,

$$2R_2AsC{\equiv}CH \xrightarrow[CuCl]{O_2} R_2AsC{\equiv}C{-}C{\equiv}CAsR_2 + 2H$$

bis(dialkylarsino)acetylenes were obtained in all the experiments instead of the expected diacetylene derivatives. Under oxidative condensation conditions, a more complex reaction probably takes place and its overall course can be represented by the equation

$$2\,R_2AsC{\equiv}CH \underset{70\%}{\rightarrow} R_2AsC{\equiv}CAsR_2 + HC{\equiv}CH$$

6. Certain Spectroscopic Data

By comparing the infrared spectra of dialkylarsinoacetylenes, dialkylarsinoacetylenic alcohols, and also dialkylarsinoacetylenic acids and their esters, Kuz'min and Pavlova [35] showed that the vibration frequency of the acetylenic bond changes only slightly as a function of the nature of the group substituting the ethynyl hydrogen atom while the intensity of the band due to the acetylenic linkage depends significantly on the substituent.

Continuing the study of the spectra of dialkylethynylarsines, dialkylarsinoalkynes, bisdialkylarsinoacetylenes, and bisdialkylarsinodiacetylenes, Shagidullin et al. [34] established that the introduction of an arsenic atom in the α-position relative to the acetylene and diacetylene groups greatly reduces the C≡C vibration frequency, which may be due both to a specific interaction of the p_π–d_π type and to the effect of the mass of the arsenic atom.

Table 3.

Compound	*m/e* for parent ion	*m/e* for fragment			
		$-CH_3$	$-(CH_3)_2$	$-(CH_3)_3$	$-(CH_3)_3C$
$^{75}As(C{\equiv}CCMe_3)_3$	318	303	288	273	261

Monosubstituted dialkylethynylarsines are capable of self-association with formation of hydrogen-bonded complexes.

The absorption and photoconduction spectra of copper acetylides having the general formula $R_2AsC{\equiv}CCu$, where R = Ph or Bu, have been investigated in detail [39]. The stretching vibration frequencies of the C≡C and ≡C–H groups are presented in Table 1. Certain NMR and ultraviolet spectroscopic data are in Table 2.

Reiff and Pant[16] reported mass-spectrometric data for tris-(t-butylethynyl)arsine (Table 3).

Organosilicon compounds containing one or several ethynyl groups in the molecule are nowadays attracting increasing attention. Such compounds are of definite theoretical and practical interest as models for the study of the transmission of conjugation via the arsenic atom and also, for example, as potential physiologically active substances.

A more vigorous investigation of the properties of organosilicon compounds of the acetylene series has been made in recent years. Thus it has been established that copper acetylides exhibit photosemiconducting properties[36].

Hay and coworkers[14] reported the synthesis of an interesting group of highly stable arsenic-containing phenylethynyl polymers.

A search is being made for new ligands among organoarsenic compounds[15]. Ethynylarsinic acid synthesised recently may find application in the extraction of heavy lanthanide ions[25].

An important practical factor is the availability of an industrial source of arsenic raw materials (the waste from non-ferrous metallurgy), which leads to the expectation of a further expansion of studies on this interesting class of compounds.

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Ring-Chain Isomeric Transformations of Hydroxy-, Amino-, and Mercapto-Derivatives of Carbonyl Compounds and Their Heteroanalogues

R.Valters

The ring-chain isomeric (including tautomeric) transformations of hydroxy-, amino- and mercapto-derivatives of aldehydes, ketones, other carbonyl compounds, imines, hydrazones, and nitriles are examined. The effect of molecular structure and the structure of substituents at the interaction functional groups and also of external factors on the relative stabilities of the isomers and on the nature of the equilibrium has been analysed.
The bibliography includes 246 references.

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I. INTRODUCTION

Since the appearance of the first review[1] dealing with ring–chain tautomerism, numerous experimental studies in this field based on modern spectroscopic techniques have been published. The ring–chain isomerism of carboxylic acids with formyl and oxo-groups and their derivatives formed by the modification of the carboxy-group were discussed in a recently published review[2].

This review considers the advances during the last decade in the field of ring–chain isomeric (including tautomeric) transformations[3-6] of hydroxy-, amino-, and mercapto-derivatives of aldehydes, ketones, other carbonyl compounds†, imines, hydrazones, and nitriles. In the above series of compounds the formation of a cyclic isomer takes place via the intramolecular addition of a nucleophilic centre (OH, NH, SH) to the electrophilic carbon atom of the polar bond C=O, C=N, or C≡N (see Scheme 1).

It is possible to distinguish three fundamental types of ring–chain isomeric transformations[2,4].

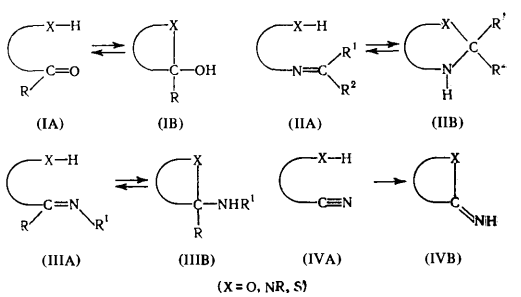
1. Tautomerism

Only one or, more rarely, both isomers are isolated in a pure form. With the aid of spectroscopic methods, it is possible to demonstrate a dynamic equilibrium between the open-chain (A) and cyclic (B) forms in solution at room temperature.

The case where only one isomer (for example A) is isolated in a pure form and its stability in solution has been demonstrated requires special consideration. One cannot then rule out the possibility of an equilibrium $A \rightleftharpoons B$ displaced so much towards A that the concentration of the isomer B is below the limit of sensitivity of the identification procedure employed. Such a possibility can be rigorously excluded only by the isolation of both isomers in a pure form, provided that their stability in solution has been proved.

†With the exception of monosaccharides.

Scheme 1



2. Reversible Isomerism

Both isomers are obtained in a pure form. They are stable in solution at room temperature and equilibrium mixtures are not formed. The isomerisation processes A → B and B → A take place under the influence of specific reagents, acid or alkaline catalysts, or on heating.

3. Irreversible Isomerism

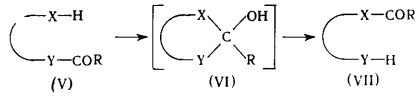
The isomerisation can take place in only one direction (A → B).

We shall also consider cases where either open-chain (A) or cyclic (B) isomers are formed, depending on the structure of the substituents at the interacting functional groups, but for a given set of substituents the isomeric interconversions cannot be achieved.

This review deals only with the results of studies where the structure of the isomers and the presence of a tautomeric equilibrium has been reliably established by spectroscopic methods (infrared, ^{1}H NMR, and ultraviolet spectroscopy). The formation of derivatives of both forms (A and B) in chemical reactions does not as a rule constitute a rigorous proof of a tautomeric equilibrium[1,7].

The electronic and steric effects of the substituents at the interacting functional groups and the effect of the structure of their connecting link on the relative stabilities of isomers and on the equilibrium are of greatest interest. It has been demonstrated in many instances that all the structural changes resulting in an enhancement of the nucleophilic properties of the oxygen, nitrogen, or sulphur atoms (OH, NH, SH) or the electrophilic properties of the carbon atoms in the C=O, C=N and C≡N bonds stabilise the ring form and displace the equilibrium towards it. The steric approach of the interacting groups is even more important. The open-chain form is stabilised by electronic effects acting in the opposite direction (the diminution of the nucleophilic properties of the XH groups or of the electrophilic properties of the carbon atom) and by the steric screening of the interacting groups by bulky substituents.

We are unable to discuss studies in which the isomers were not isolated or the ring–chain equilibrium was not demonstrated by spectroscopic methods and its occurrence in an intermediate stage is merely postulated to account for the mechanism of the formation of the final reaction products. However, such an equilibrium frequently constitutes the only possible explanation of the occurrence of the reaction in question. For example, the intramolecular rearrangement (V) → (VII), involving the migration of the acyl residue between two nucleophilic groups (OH, NH, SH), proceeds via the intermediate cyclic isomer (VI):

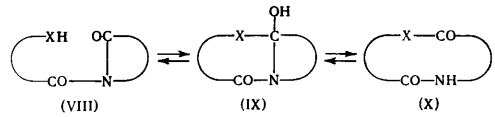


(V) (VI) (VII)

(X, Y = O, NR', S)

In view of its low stability, it is rarely possible to isolate this compound in a pure form or to demonstrate rigorously its presence in solution[4,8].

An interesting example of intramolecular transacylation is also provided by the reaction involving the inclusion of the residues of hydroxy- or amino-acids in lactam, peptide, or depsipeptide rings. This reaction proceeds via the intermediate formation of the so called cyclols [IX, X = O (oxacyclols) or X = NR (azacyclols)] and leads to cyclic peptides (X, X = NR) or depsipeptides (X, X = O):[9-16]



(VIII) (IX) (X)

(X = O, NR, S)

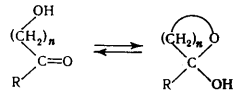
Studies on *N*-hydroxyacyl-lactams (VIII, X = O) showed that[9,14,17-21], depending on ring size and the structure of the hydroxyacyl group, either spontaneous isomerisation (VIII) → (X) takes place or it is possible to isolate the oxacyclols (IX, X = O), which are incapable of isomerisation to macrocyclic derivatives (X). In certain cases (*N*-glycolylvalerolactam[14], *N*-glycolylcaprolactam[20], *N*-hydroxyacyldioxopiperazines[22] and others[9,23]) the presence of the tautomeric equilibrium (VIII) ⇌ (IX) in solution was confirmed spectroscopically. *N*-Hydroxyacylbutyrolactams do not form cyclols.

The isomeric transformations (VIII) → (IX) → (X) have been observed also in the series of azacyclols. However, the azacyclols themselves (IX, X = NR) are relatively unstable and cannot be isolated[9,24-32]. The azacyclol formed from *N*-(2-methylaminobenzoyl)butyrolactam has been isolated in a pure form[33]. The tautomeric equilibrium (VIII) ⇌ (IX) ⇌ (X) occurs in solutions of thiacyclols (IX, X = S) formed from *N*-(thiosalicyloyl)-lactams[34,35]. With increase in the lactam ring size and also with increase of the dielectric constant of the solvent, the equilibrium shifts towards the macroring (X).

II. CARBONYL COMPOUNDS

Hydroxy-derivatives (IA ⇌ IB, X = O)

The simplest examples of hydroxycarbonyl compounds which can give rise to a cyclic form are hydroxyketones and hydroxyaldehydes[1,4,6,36]. The equilibrium (XIA) ⇌ (XIB) is rapidly established[36-38] in solutions of 5-hydroxy-2-pentanone (XIa) and 6-hydroxy-2-hexanone (XIb), with the open-chain form predominating slightly:



(XIA) (XIB)

a) R = Me, *n* = 3; b) R = Me, *n* = 4;
c) R = H, *n* = 3; d) R = H, *n* = 4

The contents of the tautomeric forms were determined[38] from the intensities of the proton signals of the methyl groups of both tautomers (the tautomeric transformations are slow on the ^{1}H NMR time scale) and also by measuring the intensities of the 265–280 nm bands observed in the ultraviolet spectra of the open-chain isomers (XIA).

Table 1. The tautomeric equilibrium constants in solutions of 5-hydroxy-2-pentanone (XIa) and 6-hydroxy-2-hexanone (XIb) determined[38] by ^{1}H NMR and ultraviolet spectroscopic methods.

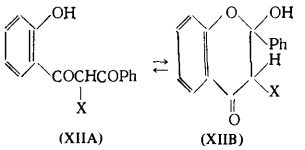
Solvent	K_T = [B]/[A]			
	^{1}H NMR at 37°C		u.v.spectra at 25.1°C	
	(XIa)	(XIb)	(XIa)	(XIb)
Pure liquid	0.83	0.85	—	—
Cyclohexane*	0.81	0.95	0.78	0.87
Dioxane	—	—	0.83	0.74
Carbon tetrachloride	0.73	0.95	0.75	0.96
Chloroform	0.82	0.85	0.75	0.81
Acetone*	0.82	0.82	—	—
Ethanol*	0.83	0.62	0.80	0.54
Methanol	—	—	0.81	0.51
Acetonitrile*	0.82	0.79	0.79	0.61
Dimethyl sulphoxide*	0.64	0.81	0.56	0.77
Water*	0	0	0	0

*The ^{1}H NMR spectra were recorded in deuteriated solvents.

An increase of temperature[38,39] and of solvent polarity[38] displaces the equilibrium towards the open-chain form, although the equilibrium constants in various solvents, with the exception of water, differ insignificantly (Table 1). The cyclic form predominates in aqueous solution. The addition of water to solutions of hydroxyketones in dioxane, ethanol, or dimethyl sulphoxide rapidly displaces the equilibrium towards the open-chain form. The thermodynamic properties (ΔH° and ΔS°) of the (XIA) ⇌ (XIB) transformation in various solvents have been determined[38].

Compared with hydroxyketones, in solutions of hydroxyaldehydes (XIc and XId) the equilibrium is displaced appreciably towards the cyclic form [in 75% aqueous dioxane at 25°C K_T = 7.8 for (XIc) and K_T = 15.4 for (XId)].[40]

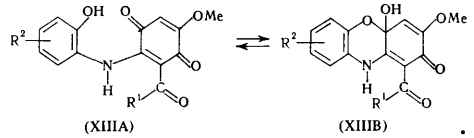
The formation of the cyclic form via the intramolecular addition of the phenolic hydroxyl to the formyl or keto-group has been observed in *o*-hydroxyphenylglyoxal[41], 2-(*o*-hydroxybenzyl)cyclohexanone[42], and in a series of substituted benzoyl(*o*-hydroxybenzoyl)methanes (XII, a–c).[43,44] In the crystalline state, the compounds (XII, a–c) have a cyclic structure, while in chloroform solution the equilibrium (XIIA) ⇌ (XIIB) is established rapidly [K_T = 3.7 for (XIIa) and K_T = 0.5 for (XIIb)]. The substitution of the hydroxy-group by bromine enhances the electrophilic properties of the carbon atom of the keto-group and shifts the equilibrium towards the cyclic form:



(XIIA) (XIIB)

a) X=Br; b) X=OH; c) X=OOCPh)

As a result of the intramolecular addition of the phenolic hydroxyl to the C=O group of the quinone, (XIIIA) ⇌ XIIIB) equilibrium mixtures are formed in solutions of substituted 2-(*o*-hydroxyphenylamino)-1,4-benzoquinones[45–47]. A similar tautomeric equilibrium was observed previously[48] in solutions of 2-(*o*-hydroxyphenylamino)-1,4-naphthoquinones. The amounts of the tautomers were determined by ultraviolet spectroscopy[48]:

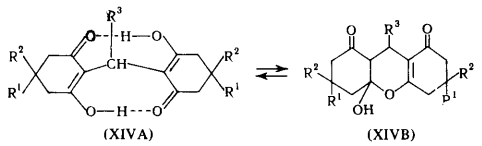


(XIIIA) (XIIIB)

a) R^1 = Me, and R^2 = 3' – Ac.

The long-wavelength band is at 470 and 394 nm respectively in the spectra of model compounds with fixed open-chain and cyclic structures[45,46]. In ethanol solution of 3-acetyl-2-(3'-acetylphenylamino-2'-hydroxy-)-5-methoxy-1,4-benzoquinone (XIIIa) the cyclic form predominates, while in non-polar solvents the equilibrium is displaced towards the open-chain form (XIIIA). The authors assume that[46] the open-chain form is stabilised by the intramolecular hydrogen bond O–H...O=C (3'-acetyl). Both isomers were isolated in a pure form: (XIIIa – A) as a black powder on crystallisation from benzene and (XIIIa – B) as yellow crystals on crystallisation from methanol. The ultraviolet spectra of solutions of both isomers are identical, i.e. after dissolution identical equilibrium mixtures are formed regardless of which isomer is used to prepare the solution.

Lielbriedis and Gudriniece[49–52] observed an interesting type of tautomerism in which the cyclic form is produced as a result of the intramolecular addition of the enolic hydroxyl to the keto-group:

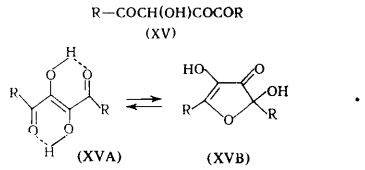


(XIVA) (XIVB)

a) $R^1 = R^2$ = Me; b) $R^1 = R^2$ = H;
c) R^1 = Ph, R^2 = H; d) R^1 = Me, R^2 = H

Bisdimedonylmethanes (XIVa), obtained by the condensation of dimedone with aliphatic aldehydes and also with *m*- and *p*-substituted benzaldehydes, have the open-chain structure (XIVa – A) in the crystalline state. This structure is stabilised by two intramolecular hydrogen bonds. The products of the condensation of dimedone with *o*-substituted benzaldehyde have the cyclic structure (XIVa – B). Both isomers of *p*-[*NN*-bis(β-chloroethyl)amino]phenyl bisdimedonylmethane [XIVa, R^3 = *p*-$(ClCH_2CH_2)_2NC_6H_4$] were isolated in a pure state. Isomerisations in both directions were achieved: (XIVA) → (XIVB) on refluxing in alcohol or on recrystallisation from acetic acid and (XIVB) → (XIVA) on slow crystallisation from dioxane. The products of the condensation of cyclohexane-1,3-dione and its 5-phenyl- and 5-methyl-substituted derivatives with aldehydes (XIV, b – d) were isolated either in the open-chain (XIVA) or cyclic (XIVB) forms, but no clear relation between the structure of the substituents and the preferential formation of one of these isomers could be traced in this instance.

As a result of the intramolecular addition of the enediol hydroxyl to the keto-group, the cyclic form of acetylformoins is produced[53–60]. The enolisation of acetylformoins (XV) can proceed to two direction. The symmetrical enediol has the open-chain structure (XVA) with two intramolecular hydrogen bonds, while the asymmetric enediol has the cyclic structure (XVB). Both forms can be readily identified from their infrared spectra [ν(C=O) = 1620 – 1630 cm^{-1} for (XVA) and ν(C=O) = 1695 – 1705 cm^{-1} for (XVB)] and ultraviolet spectra [λ = 355–360 nm for (XVA) with R = alkyl, λ = 390–410 nm for (XVA) with R = aryl, λ = 305–310 nm for (XVB) with R = alkyl, and λ = 355–360 nm for (XVB) with R = aryl][58]:



R–COCH(OH)COCR
(XV)

(XVA) (XVB)

Here R = Me(A)‡, i-Pr(B), t-Bu(B), *p*-XC_6H_4 [X = H(B), Me(B), MeO(A), t-Bu(B), Me_2N(A), Cl(A and B), Br(A and B), or NO_2(B)], 2,4,6-$Me_3C_6H_2$(A), α-naphthyl (A), or β-naphthyl (A and B).

The introduction of electron-donating substituents (MeO, Me_2N) into the aromatic ring of aroylbenzoins diminishes the electrophilic properties of the carbon atom of the keto-group and stabilises the open-chain form, while electron-accepting substituents act in the opposite direction[59]. Both isomers of *p*-bromo- and *p*-chlorobenzoylformoins[58] and β-naphthoylformoins[60] were isolated in a pure form: (XVB) crystallises as yellow crystals from ethanol and (XVA) as red crystals from benzene after prolonged heating of the solution. When the cyclic isomers are fused, the isomerisation (XVB) → (XVA) takes place[54,58].

In proton-accepting solvents (ethanol, tetrahydrofuran) acylformoins exist exclusively in the cyclic form (XVB). This form is stabilised by the hydrogen bonds (OH...O<) between the hydroxyl of the cyclic form and the solvent molecule[56]. Mesitoylformoin, which does not give rise to a cyclic form, evidently due to the steric screening of the carbonyl group by the bulky substituent, constitutes

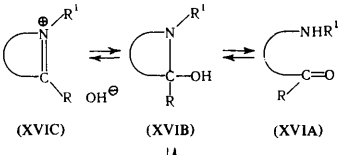
‡ The structure of the crystalline substance is indicated in brackets.

an exception (cf. Refs. 2, 61–63). In solvents which are not proton-acceptors the open-chain form (XVA) predominates[58,59].

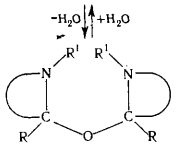
In polar proton-accepting solvents the equilibrium involving the above examples of the ring-chain tautomerism of compounds (XIIIa), (XIV), and (XV), where the open-chain is stabilised by one or two intramolecular hydrogen bonds, is displaced towards the cyclic form. The formation of the latter as a result of the intramolecular addition to the C=O group of the hydroxy-group at a nitrogen atom (NHOH, =NOH) has also been observed[64,65].

Amino-derivatives (IA ⇌ IB, X = NR)

The aminoaldehyde or aminoketone ⇌ hydroxyalkylamine ring–chain tautomeric systems (XVIA) ⇌ (XVIB) can be formed on covalent hydration[66-69] of heterocycles containing an immonium nitrogen atom. The equilibrium (XVIC) ⇌ (XVIB) has been most frequently investigated. In a study of the hydroxyalkylamines obtained from isoquinoline or 3,4-dihydroisoquinoline bases, Beke[70,71] established that the less basic the nitrogen atom in the (XVIB) molecule the greater the probability of the formation of the open chain form (XVIA):



(XVIC) (XVIB) (XVIA)



(XVII)

Four cases are considered[70].

1. Strong bases. In the crystalline state and in non-polar solvents they exist as the hydroxyalkylamines (XVIB), while in polar solvents they exist in the ionic form (XVIC). The presence of the open-chain form (XVIA) cannot be demonstrated by either chemical or physical methods.

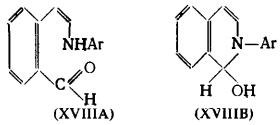
2. Moderately strong bases. In the crystalline state they have the structure (XVIB). The equilibrium (XVIC) ⇌ (XVIB) ⇌ (XVII) is observed in aqueous solution. The open-chain form (XVIA) is absent.

3. Hydroxyalkylamines incapable of giving rise to the ionic form (XVIC) isomerise to the open-chain form (XVIA). The existence of both forms can be demonstrated in solution or they can be actually isolated in a pure state[71].

4. Compounds showing no pseudobasic properties exist only in the open-chain form (XVIA). The hydroxyalkylamine (XVIB), formed when the solution of a quaternary salt of the nitrogen-containing heterocycle is made alkaline, is unstable and isomerises spontaneously to (XVIA).

It is clear from the foregoing that the equilibria (XVIC) ⇌ (XVIB) and (XVIB) ⇌ (XVIA) are not observed simultaneously. Hydroxyalkylamines capable of giving rise to the ionic form (XVIC) are not converted into the open-chain form (XVIA) and conversely.

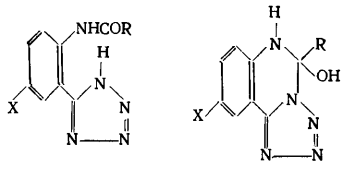
The products of the covalent hydration of *N*-arylpyridinium compounds[72] have an open-chain structure. On hydration of *N*-(2,4-dintrophenyl)isoquinolinium[71], both isomers, (XVIIIA) and (XVIIIB), were obtained and their interconversions were achieved. By investigating the esterification kinetics, it was established that under the reaction conditions the equilibrium (XVIIIA) ⇌ (XVIIIB) obtains. The absence of the open-chain form in the crystalline state and in solutions of covalent quinazoline hydrates has been demonstrated by infrared spectroscopy[66,73,74].



(XVIIIA) (XVIIIB)

[Ar-2,4-$(NO_2)_2C_6H_3$]

Postovskii[75-79] showed that the covalent hydrates of 5-R-9-X-tetrazolo[1,5-c]quinazolines have the structures (XIXA) or (XIXB) depending on the structure of the substituents R and X:

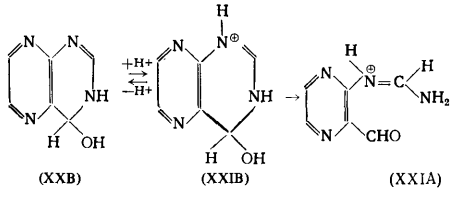


(XIXA) (XIXB)

Here X = R = H (A and B),[76] X = H and R = Me (B),[75] X = COOH and R = Ph (B),[78] X = Br and R = Me (A), and X = Br and R = Ph (A).[77,79]

Both isomers of the unsubstituted compound (XIX, X = R = H) were isolated in a pure state[76]. It has been shown for the methyl derivative (XIX, X = H, R = Me) that an acid medium stabilises the cyclic form and on dissolution in pyridine the isomerisation (XIXB) → (XIXA) takes place[75].

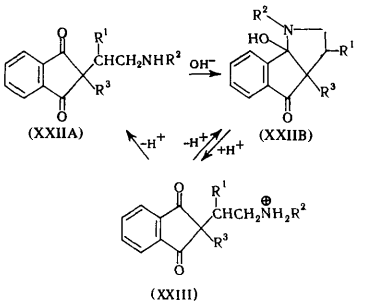
The covalent hydrates of pteridines[66,67,80,81] (XXB) and of 1,3,6-triazanaphthalenes[82] are rapidly converted in an acid medium into the open-chain isomers (XXIA). The opposite process takes place on neutralisation. Evidently the isomerisation (XXIB) ⇌ (XXIA) can be accounted for by the fact that the basicity of the nitrogen atom is sharply reduced by protonation:



(XXB) (XXIB) (XXIA)

Depending on the molecular structure, the protonation of aminocarbonyl compounds can stabilise either the cyclic or the open-chain form. Vanags and Dregeris obtained[83] both isomers of 2-β-(*N*-cyclohexyl)aminoethyl-2-phenylindan-1,3-dione—(XXIIa – A) and (XXIIa – B). The isomerisation (XXIIa – A) → (XXIIa – B) takes place in the

presence of bases. Such base-catalysed isomerisation has also been observed for a series of γ-ketoacid amides[2,84-86] and other aminocarbonyl compounds[87,88].



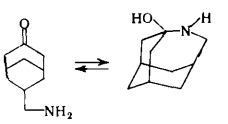
(XXIIA) (XXIIB)

(XXIII)

a) R^1 = H, R^2 = cyclo-C_6H_{11}, and R^3 = Ph.

The protonation of the cyclic isomer entails ring opening, (XXIIB) → (XXIII), while deprotonation is accompanied by the reverse process[83,89].

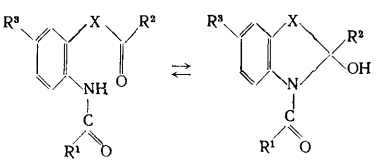
In solution 7-aminobicyclo]3, 3, 1]nonan-3-one gives rise to the equilibrium mixture (XXIVA) ⇌ (XXIVB).[90]



(XXIVA) (XXIVB).

The total absence of the C=O absorption from the spectrum of the hydrochloride suggests that the protonated form has a cyclic structure.

In the crystalline state, *o*-acetamidobenzil (XXV, R^1 = Me, R^2 = Ph, R^3 = H, X = CO) has the cyclic structure (XXVB), while in solution an equilibrium is established slowly[91]. A similar equilibrium has been observed[92-95] for a series of *N*-acyl-2-(2′-oxoalkyl)anilines (XXV, X = CH_2 or CHMe), the cyclic form predominating for the formyl derivatives (R^2 = H) and the open-chain form for the keto-derivatives (R^2 = Me). Analysis of the mass spectra established[96] that in the gas phase the equilibrium is completely displaced towards the open-chain form (XXVA):

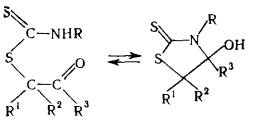


(XXVA) (XXVB)

(X = >CO, >CH_2, >CHMe)

There are many examples of ring–chain tautomerism in the series of aminocarbonyl compounds of more complex structure, where the cyclic isomer is a heterocycle with two or more heteroatoms.

The contents of the tautomers in solutions of S-(2-oxoalkyl)dithiocarbamates (XXVI) have been determined by infrared spectroscopy[97]. The open-chain isomer (XXVIa – A) and the cyclic isomer (XXVIa – B) were isolated on crystallisation from methylenechloride and from a methanol–water mixture respectively:



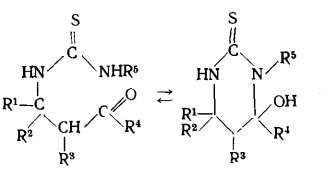
(XXVIA) (XXVIB)

a) R = Ph, R^1 = R^2 = H, and R^3 = *t*-Bu.

The introduction of the alkyl substituents R^1 and R^2 displaces the equilibrium towards the cyclic form (the *gem*-dimethyl effect[3,98]). The enhancement of the electron-donating properties of the substituent R^3 and the increase of the steric bulk of the substituents R and R^3 stabilise the open-chain form[97,99].

S-(3-Oxoalkyl)dithiocarbamates[100,101] exhibit a smaller tendency towards the formation of the cyclic form. However, compounds of this series, containing the *gem*-dimethyl fragment, have the cyclic structure in the crystalline state and in solution the equilibrium is displaced towards the open-chain form[101].

Unkovskii and coworkers[102-104] showed that *N*-(3-oxoalkyl)-*N*′-substituted thioureas have the cyclic structure in the crystalline state, with one exception[103], and in solution they give rise to the equilibrium mixtures (XXVIIA) ⇌ (XXVIIB), the equilibrium being established slowly (over a period of 6–15 days):



(XXVIIA) (XXVIIB)

The equilibrium concentrations of the tautomers were determined[104] from the intensities of the C=O band in the infrared spectra of the solutions. The introduction of methyl groups as the substituents R^1, R^2 and R^3 (R^4 = Me throughout) stabilises the cyclic form in the following sequence (the arrow indicates the direction of the increase of stability of the cyclic form):

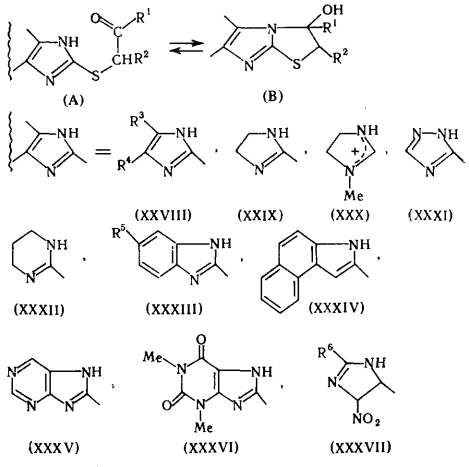
R^1	H	H	Me	Me	Me
R^2	H	H	H	H	Me
R^3	Me	H	Me	H	H

An increase of the effective bulk of the substituent R^5 is accompanied by an increase of the rate of ring opening and a shift of the equilibrium towards the open-chain form (XXVIIA). One cannot agree with the assertion[104] that the enhancement of the electron-donating properties of the substituent R^5 acts in the same direction. In contrast to keto-derivatives, the aldehydes (XXVII, R^4 = H) exist in solution entirely in the cyclic form.

A similar situation, where the crystalline compounds have the cyclic structure and equilibrium mixtures are produced in solution, has been described for a series of *S*-methyl-*N*-(3-oxoalkyl)isothioureas[105,106].

2-Ureido-,[107,108] 2-thioureido-,[109,110] and 2-guanidinoindan-1,3-diones[108] and 2-ureido- and 2-thioureidobenzophenones[111-113] have cyclic structures and there is no evidence for the occurrence of the ring–chain equilibrium in solution.

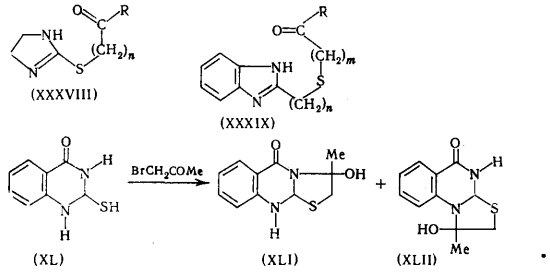
The ring–chain tautomerism of *S*-acylalkyl-substituted 2-mercaptoimidazole (XXVIII),[114-119] 2-mercaptoimidazoline (XXIX),[114,117,119-121] 2-mercapto-1-methylimidazolinium (XXX),[122] 3-mercapto-1,2,4-triazole (XXXI),[119] 2-mercapto-3,4,5,6-tetrahydropyrimidine (XXXII),[119] 2-mercaptobenzimidazole (XXXIII),[114,120,121,123-129] 2-mercaptonaphtho[1,2-*d*]imidazole (XXXIV),[114,130,131] 8-mercaptopurine (XXXV),[114,132] 8-mercaptotheophylline (XXXVI),[114,132] and 5-mercapto-4-nitroimidazole (XXXVII,[133,134] which were isolated in most cases as intermediates in the synthesis of imidazo[2,1-*b*]thiazoles and their condensed derivatives, was investigated by infrared and ^{1}H NMR spectroscopy. In a study of the effect of the structure and the state of aggregation on the stability of the tautomers and on the equilibrium, it was established[114,127] that 2-formylmethylmercaptoimidazoles and their condensed derivatives have cyclic structures both in the crystalline state and in solution. On passing from aldehydes to ketones of the aliphatic (R^1 = Me) and aromatic (R^1 = Ph) series, the stability of the open-chain form increases.



It has been shown[127] that in the series of 2-acylmethylmercaptobenzimidazoles (XXXIII, $R^2 = R^5 = H$) with a wide range of substituents R^1, the open-chain form is stabilised by bulky substituents R^1 and also by the conjugation of the carbonyl group with the aromatic ring and the ethoxycarbonyl or cyclopropyl group. The compounds (XXXIII, R^1 = *p*-XC_6H_4, COOEt, cyclo-C_3H_5, $R^2 = R^5 = H$) exist exclusively in the open-chain form (A) in the crystalline state and in solution. It is remarkable that the stability of the open-chain form is unaffected[125] by the introduction of electron-accepting substituents in the *para*-position of the aromatic ring (R^1 = *p*-$NO_2C_6H_4$), although it has been shown for the trifluoromethyl derivative (XXXIII, $R^1 = CF_3$, $R^2 = R^5 = H$) [126,127] that the presence of a powerful *I*-effect in the substituent R^1 completely displaces the equilibrium towards the cyclic form. The introduction of the nitro-group into the benzimidazole ring to give (XXXIII, R^1 = Me, $R^2 = H$, $R^5 = NO_2$) diminishes the nucleophilic properties of the nitrogen atom and displaces the equilibrium towards the open-chain form relative to the unsubstituted compound (XXXIII, $R^5 = H$).

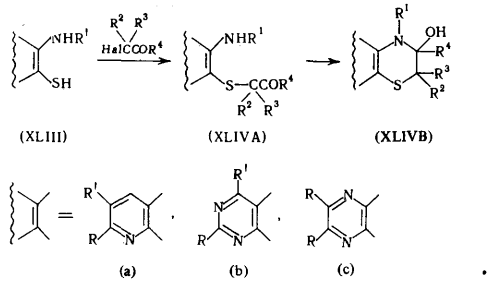
The crystalline state stabilises the cyclic form[114]. While the compound has the open-chain structure (A) in the crystalline state, in solution the equilibrium is completely displaced towards (A). Crystalline cyclic isomers (B) have either the cyclic structure also in solution or (A) ⇌ (B) equilibrium mixtures are produced[127].

A study of the effect of the size of the ring formed on the stability of the cyclic isomer in a series of hydroxyderivatives of imidazoline (XXXVIII, n = 1 or 2) and benzimidazole (XXXIX, n = 0 or 1 and m = 1 or 2) established[120,121] that the cyclic form is produced only on closure of a five-membered ring (XXXVIII, n = 1; XXXIX, n = 0, m = 1).



The reaction of 2-mercapto-4-oxotetrahydroquinazoline (XL) with bromoacetone results in the formation[135] of a mixture of products (XLI) and (XLII) in proportions of **9**:1. On this basis, the authors conclude that the formation of the cyclic form involves preferentially the sterically less hindered nitrogen atoms even if the competing nitrogen atom is more basic.

In reactions of *o*-aminomercapto-derivatives of pyridine (XLIIIa),[136-140] pyrimidine (XLIIIb),[88,141-144] and pyrazine (XLIIIc)[145,146] with α-halogenocarbonyl compounds, Safonova and coworkers obtained in most cases only the most stable isomer [either (XLIVA) or (XLIVB)] and their dehydration products.



Electron-accepting substituents R^4 and electron-donating substituents in the heterocycle (R and R^1) stabilise the cyclic form[137,142,144-146]. Phenylacyl derivatives show a smaller tendency towards the formation of the cyclic form (XLIVB) than the products of the condensation with aliphatic halogenoketones. Both isomers were isolated in reactions of 5-amino-4-chloro-6-mercaptopyrimidine (XLIIIb, R = R^1 = H, R^1 = Cl) with phenylacyl bromides ($R^4 = C_6H_4X$, X = H, 4-Br, 3-NO_2, or 4-NO_2)[88,141] and of 3-amino-6-chloro-2-mercaptopyridine (XLIIIa, $R^1 = R'$ = H, R = Cl) with *o*-substituted (F, Br, Me) phenylacyl halides[140]. In a medium close to neutrality 5-amino-4-chloro-6-phenylacylmercaptopyrimidines (XLIVb – A) are formed. The isomerisation (XLIVb – A) → (XLIVb – B) is base-catalysed. However, after the introduction of a methyl group into the amino group (R^1 = Me), such isomerisation could not be achieved[88].

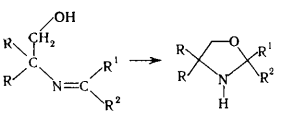
Tautomeric equilibria in solutions of 6-alkyl-4-chloro-6-hydroxy-5,6-dihydropyrimido[4,5-*b*][1,4]thiazines (XLIVb – B, R = R^1 = R^2 = R^3 = H, R′ = Cl, R^4 = Me, CH_2Cl, or CH_2COOEt) were not observed by infrared and ^1H NMR spectroscopic methods[144]. The derivatives of these compounds having a methyl group at the nitrogen atom (R^1 = Me) form equilibrium mixtures in solution. In deuteriochloroform solution of the 6-methyl derivatives (XLIVb, R^1 = R^4 = Me, R′ = Cl) the equilibrium is displaced towards the open-chain form and in solutions of the compounds (XLIVb, R^1 = Me, R′ = Cl, R^4 = CH_2Cl or CH_2COOEt) it is displaced towards the cyclic form. The addition of a proton-accepting agent (C_5H_5N-d_5) to the solutions displaces the equilibrium towards the cyclic form. The destabilising effect of the methyl group (R^1 = Me) at the nitrogen atom on the cyclic form cannot be accounted for in terms of electronic hypotheses, because the methyl group enhances the nucleophilic properties of the nitrogen atom and consequently should have the opposite effect. The experimentally observed influence of the methyl group can be explained[144] by the steric interaction of *peri*-substituents in the cyclic form (XLIVb – B, R′ = Cl, R^1 = Me), which destabilises the 1,4-thiazine ring.

Apart from the examples discussed above, there is evidence for ring–chain tautomerism (IA ⇌ IB, X = NR) in the series of monohydrazones of 1,3-dicarbonyl compounds[147,148], *N*-(2-oxoalkyl)triazenes[149,150], *N*-acylmalonodianilides[151], *O*-(3-oxoalkyl)hydroxylamines[152], urethanes derived from benzoin[153], 2-benzoylbenzenesulphonamide and 2-phenylacylbenzenesulphonamides[154], *NN*′-dimethylhydrazides of 2-acylbenzoic acids[155], and 6-hydroxycrinamines[156].

III. IMINES AND HYDRAZONES

Hydroxy-derivatives (IIA ⇌ IIB, IIIA ⇌ IIIB, X = O)

The tautomeric equilibrium (XLVA) ⇌ (XLVB) is observed in solutions of oxazolidines[1,157-161]. An increase in the steric bulk of the substituents R^1 and R^2 stabilises the open-chain form. It has been established that an enhancement of the electron-accepting properties of the substituents X in the aromatic ring in the series of 2-(3′- or 4′-X-phenyl)-4,4-dimethyloxazolidines (XLV, R = Me, R^1 = H, R^2 = 3′ or 4′-XC_6H_4) displaces the equilibrium towards the cyclic form[160]:

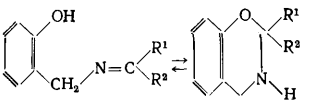


(XLVA) (XLVB).

A linear correlation has been observed between the tautomeric equilibrium constants K_T = [B]/[A] and the σ or better σ* constants of the substituents X in the aromatic ring [$\lg(K_T/K_0) = 0.86\sigma$, $r = 0.973$; $\lg(K_T/K_0) = 0.54\sigma^*$, $r = 0.999$]. The equilibrium constants were determined from the intensities of the signals of the geminal proton relative to the aryl group (R^1 = H) in both tautomeric forms[159,160].

The products of the condensation of 3-aminopropanol with carbonyl compounds were obtained either in an open-chain form or as tetrahydro-1,3-oxazines[162,163]. They show a greater tendency towards cyclisation than *N*-(2-hydroxyethyl)imines. 4-Aminobutanol gives rise to hexahydro-1,3-oxazepine in the reaction with formaldehyde and the products of its condensation with benzaldehyde and acetophenone have an open-chain structure[164].

In the crystalline state *N*-(2-hydroxybenzyl)imines of aromatic aldehydes (XLVI, R^1 = H, R^2 = 4′-XC_6H_4) have the open-chain structure (XLVIA), while in solutions the equilibrium (XLVIA) ⇌ (XLVIB) is established rapidly[165,166]:



(XLVIA) (XLVIB).

The tautomeric equilibrium constants are satisfactorily correlated with the σ or σ* constants of the substituents X [$\lg(K_T/K_0) = 0.74\sigma$, $r = 0.993$; $\lg(K_T/K_0) = 0.68\sigma^*$, $r = 0.999$].[160,166]. The *N*-(2-hydroxybenzyl)imines derived from aliphatic aldehydes and ketones have the cyclic structure (XLVIB) and in solutions the equilibrium is almost entirely displaced towards the cyclic form. It has been established by ^1H NMR [167] that protonation of the compounds (XLVI, R^1 = H, R^2 = alkyl or aryl; R^1 = R^2 = alkyl) in solution in trifluoroacetic acid results in the formation of open-chain immonium ions. Protonated cyclic forms were obtained only for the imines derived from formaldehyde and trichloroacetaldehyde.

The 1,3-oxazine–Schiff base tautomerism was observed also in solutions of the products of the condensation of 2-hydroxybenzylamine with α-dicarbonyl compounds[168]. 2,4-Diaryl-2,3-dihydro-1*H*-nathpho[1,2-*e*]-1,3-oxazines obtained[169] by the condensation of 1-(α-aminobenzyl)-2-naphthol with aromatic aldehydes have a cyclic structure in the crystalline state and in solution give rise to equilibrium mixtures; an equilibrium has also been observed between the cyclic and open-chain protonated forms in solution in trifluoroacetic acid.

Table 2. Effect of the proton-accepting properties of solvents on the constants of the tautomeric equilibrium (XLVA) ⇌ (XLVB) (R = Me, R^1 = H, R^2 = Ph).[159]

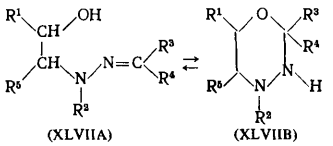
Solvent	$\Delta\nu^*_{OH}$, cm^{-1}	K = [B]/[A]**	Solvent	$\Delta\nu^*_{OH}$, cm^{-1}	K = [B]/[A]**
Carbon tetrachloride	0	1.89	Acetone	110	0.42
Chloroform	8	1.72	Tetrahydrofuran	156	0.51
Dimethyl carbonate	69	0.80	Dimethylacetamide	193	0.12
Acetonitrile	87	0.62	Dimethyl sulphoxide	224	0.10

* The shift of the hydroxyl band frequency in the infrared spectra of solutions of di-t-butylmethanol as a measure of the proton-accepting properties of the solvent.
** Determined by ^1H NMR at 38°C.

Under the influence of solvents, the constants of the tautomeric equilibria (XLVA) ⇌ (XLVB) and (XLVIA) ⇌ (XLVIB) vary over a wide range, but they are not correlated either with the dipole moments, or with the dielectric constants, or with Kosower's *Z* constants of the solvents[166]. A satisfactory correlation has been found[159], between the frequency shifts of the hydroxyl band $\Delta\nu$(OH) in the infrared spectra of solutions of di-t-butylmethanol on formation of intermolecular hydrogen bonds with the

solvent and the activation enthalpies ΔH° for the tautomeric transformations (XLVA) ⇌ (XLVB) (R = Me, R^1 = H, R^2 = Ph) in the same solvents. Consequently the ability of the solvents to form intermolecular hydrogen bonds with the hydroxy-group of the Schiff base plays the main role in determining the state of equilibrium. The enhancement of the proton-accepting properties of the solvent displaces the equilibrium towards the open-chain form (Table 2).[159]

Potekhin and coworkers[170-175] made a systematic study of the tautomerism (XLVIIA) ⇌ (XLVIIB) of *N*-(2-hydroxyalkyl)hydrazones. The tautomeric composition was determined by measuring the molecular refraction and by ^{1}H NMR. Freshly prepared products of the condensation of *N*-alkyl-*N*-(2-hydroxyalkyl)hydrazines with aldehydes and ketones in most cases have the cyclic structure of alkyl-substituted perhydro-1,3,4-oxadiazines (XLVIIB). On storage and in solution, they form the equilibrium mixtures (XLVIIA) ⇌ (XLVIIB). The equilibrium concentration of the open-chain form (XLVIIA) increases with increase of the number and steric bulk of the alkyl substituents at the carbon atom of the C=N bond (R^3, R^4).



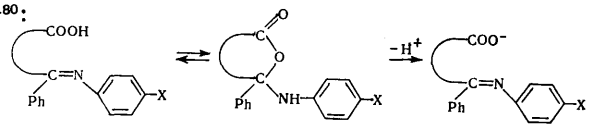
(XLVIIA) (XLVIIB)

The introduction of the methyl group in the hydroxyethyl group (R^1 = Me), the introduction of an alkyl substituent at the nitrogen atom (R^2 = alkyl), and an increase of the steric bulk of the latter substituent shift the equilibrium towards the cyclic form (XLVIIB). *N*-Unsubstituted 2-hydroxyethyl- and 2-hydroxypropyl-hydrazones (XLVIIA, R^1 = H or Me, R^2 = H) [172,173] and also products of the condensation of lactic acid hydrazide with carbonyl compounds[176] do not give rise to the cyclic form. In the series of *N*-aryl-*N*-hydroxyethylhydrazones (XLVII, R^1 = H, R^2 = *p*-XC_6H_4) a shift of the equilibrium towards the cyclic form was observed[175] with enhancement of the electron-accepting properties of the substituent X in the aromatic ring.

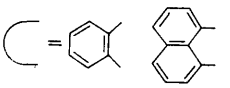
The greater tendency of aldehyde hydrazones to form the cyclic form (XLVIIB) compared with ketone hydrazones can be explained[172] by the fact that perhydro-1,3,4-oxadiazines with two alkyl substituents at $C_{(2)}$ have an increased conformational energy. An important factor facilitating intramolecular cyclisation is also the higher electrophilicity of the carbon atom in the C=N bond in aldehyde derivatives compared with ketone derivatives[38,177].

The tautomeric equilibrium constants of the products of the condensation of *N*-amino-(-)-ephedrine with aliphatic aldehydes (XLVII, R^1 = Ph, R^2 = R^5 = Me, R^3 = H, R^4 = alkyl) at different temperatures in solution in tetrachloroethylene were measured by ^{1}H NMR [178] in the presence of an acid catalyst (0.1% CF_3COOH), which increases the rate of tautomerisation. An increase of the polarity of the solvent, an increase of solution temperature (cf. Potekhin and Zaitsev[173]), and also an increase of the steric bulk of the alkyl substituent R^4 displace the equilibrium towards the open-chain form.

In the crystalline state the anils of 2-benzoylbenzoic acid[179,180] have the cyclic structure of 3-arylamino-3-phenylphthalides (XLVIIIa – B), while in solution the equilibrium (XLVIIIa – A) ⇌ (XLVIIIa – B) is appreciably displaced to the right. Electron-accepting substituents in the aromatic ring stabilise the cyclic form. The enhancement of the polarity and proton accepting properties of the solvents shift the equilibrium to the open-chain form[180]:



(XLVIIIA) (XLVIIIB) (XLIX)

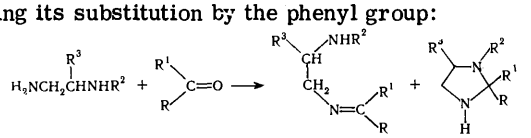


(a) (b)

Compared with the molecule of the anil of 2-benzoylbenzoic acid (XLVIIIa – A), in the (XLVIIIb – A) molecule the interacting COOH and C=N groups are sterically in greater proximity and therefore the equilibrium in solutions of 2-benzoylnaphthoic acid anils is fully displaced towards the cyclic form (XLVIIIb – B).[181] When (XLVIIIa) and (XLVIIIb) are treated with bases, the open-chain anions (XLIX) are formed.

Amino-derivatives (IIA ⇌ IIB, IIIA ⇌ IIIB, X = NR)

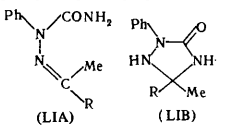
Mixtures of open-chain and cyclic isomers, (LA) and (LB), are formed in reactions of ethylenediamines with aldehydes and cyclic ketones. However, Chapuis et al.[182] were unable to confirm the existence of the tautomeric equilibrium (LA) ⇌ (LB) in solution. It has been shown by ^{1}H NMR that the fraction of the cyclic isomer in the mixture of reaction products decreases with increase of the steric bulk of the alkyl substituent R^1 (for R = H) or following its substitution by the phenyl group:



(LA) (LB)

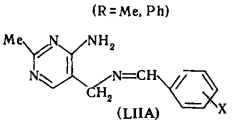
Acetone and acetophenone 2-phenylsemicarbazones have been obtained[183] in both the open-chain (LIA) and cyclic (LIB) forms. The isomerisation (LIA) → (LIB) takes place in the presence of acid.

The reactions of 4-amino-5-aminomethyl-2-methyl-(or phenyl)pyrimidine with aromatic aldehydes give rise to open-chain (LIIA) or cyclic (LIIB) condensation products or their mixtures[184]. However, it is impossible to find a relation between the electronic properties of the substituent in the aromatic ring of the aldehyde and the structure of the isomer formed.



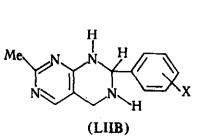
(LIA) (LIB)

(R = Me, Ph)



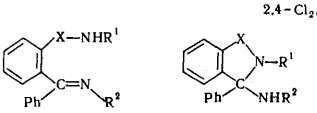
(LIIA)

(X = 4-Cl, 4-Br, 4-F)



(LIIB)

(X = 4-F, 4-MeO, 4-NO_2, 2,4-Cl_2, 3,4-Cl_2)



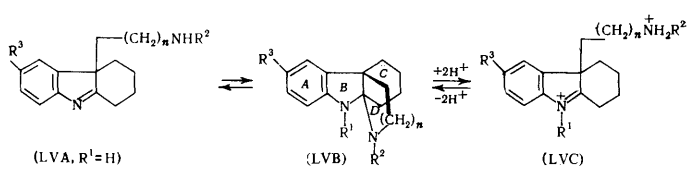
(LIIIA, LIVA) (LIIIB, LIVB)

(LIII, X = CO; LIV, X = SO_2)

Both isomers have been obtained in the series of imines[154] and anils[185] derived from 2-benzoylbenzamides—(LIIIA) and (LIIIB). The imine derived from 2-benzoyl-*N*-methylbenzamide has been obtained only in the cyclic form (LIIIB, R^1 = Me, R^2 = H). The anilide has been isolated in the open-chain form (LIIIA, R^1 = Ph, R^2 = H). When its solution in deuteriochloroform is stored at room temperature or its solution in ethanol is heated, the isomerisation (LIIIA) → (LIIIB) takes place readily. A similar isomerisation occurs in a series of anils of *N*-alkyl-2-benzoylbenzamides (LIII, R^1 = n-Pr, $PhCh_2$, i-Pr, or t-Bu, R^2 = Ph[5]), obtained by treating 3-chloro-2,3-diphenylisoindolinone with alkylamines[185]. An increase of the steric bulk of the substituent R^1 hinders the isomerisation (LIIIA) → (LIIIB): the *N*-benzylamide isomerises more slowly at room temperature in ethanol solution than the *N*-propylamide, while the *N*-isopropyl- and *N*-t-butyl-amides are stable under these conditions. They isomerise on refluxing the ethanol solutions with added triethylamine. In solutions in dioxane at room temperature both isomers (LIIA and LIIIB, R^1 = alkyl, R^2 = Ph) are stable and equilibrium mixtures are not formed when the solutions are stored for 24 h.

The imine derived from *N*-methyl-2-benzoylbenzenesulphonamide has been obtained[154] in the cyclic form (LIVB, R^1 = Me, R^2 = H) and the *N*-phenyl derivative has been obtained as a mixture of both isomers with the open-chain form predominating.

Ring—chain tautomerism has been observed[186] for echiboline (LVB, $R^1 = R^2 = R^3$ = H, n = 1) and its derivatives. In all cases protonation results in the open-chain dication (LVC) and deprotonation is accompanied by cyclisation:

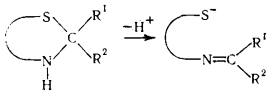


(R^1=H, Me; R^2= H, Me; R^3=H, OMe; n=1,2,3)

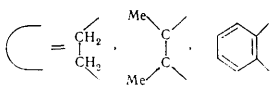
Certain echiboline derivatives (LV, R^1 = H, R^2 = H or Me, R^3 = MeO) exist in the cyclic form in solvents of low polarity, while in methanol solutions they form equilibrium mixtures with the open-chain form. Ring opening is facilitated by the presence of unsubstituted nitrogen atoms ($R^1 = R^2$ = H), by the introduction of the methoxy-group into the aromatic ring (R^3 = MeO) which decreases the electrophilicity of the carbon atom of the C=N bond in the molecule of (LVA), and by increase of ring size. Echiboline itself (LVB, $R^1 = R^2 = R^3$ = H, n = 1) exists in the cyclic form in solution, an equilibrium is observed with n = 2, and on further increase of ring size (n = 3) the cyclic form is not formed at all.

Mercapto-derivatives (IIA ⇌ IIB, X = S)

The products of the condensation of 2-mercaptoethylamine[187-189], 2-mercapto-3-butylamine[187], and 2-mercaptoaniline[190-192] with carbonyl compounds have exclusively the cyclic structure (LVIB). The formation of open-chain derivatives when the alkylation reactions are carried out in highly alkaline media is indirect evidence for the open-chain structure of the anionic form (LVIC):



(LVIB) (LVIC)

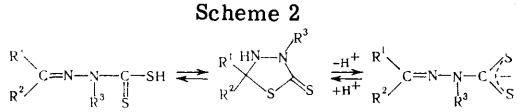


In reactions with formaldehyde and cyclohexanone, 3-mercaptopropylamine forms the corresponding tetrahydro-1,3-thiazines and the reaction with benzaldehyde gives a mixture of both isomers with the Schiff base predominating[193]. The reaction of 4-mercaptobutylamine with cyclohexanone gives rise to hexahydro-1,3-thiazepine[164].

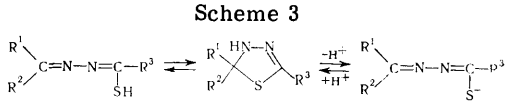
The concept of the ring—chain equilibrium of mercaptoalkylimines has been used[194] to explain the mechanism of ring contraction in the 5,6-dihydro-1,4-thiazines under the influence of hydrogen sulphide as well as the reverse reaction—the expansion of the rings of thiazolidines under the influence of elemental sulphur.

Mayer and Lauerer[195] quote interesting examples of the ring—chain tautomerism in the series of 1,3,4-thiadiazolidine and 1,3,4-thiadiazoline derivatives (Schemes 2—4). The state of equilibrium depends on the pH of the medium. The anionic forms (Schemes 2 and 3) have the open-chain structure.

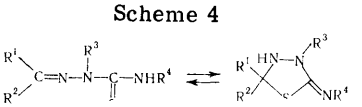
Scheme 2



Scheme 3



Scheme 4



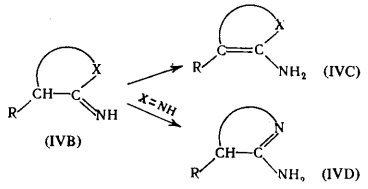
IV. NITRILES

(IVA → IVB, X = O, NR, or S)

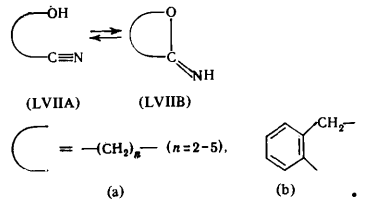
Numerous ways of synthesising heterocyclic imines or amines whose final stage is intramolecular nucleophilic addition of OH, NH, and SH groups to the C≡N bond have been developed[196,197]. The intermediates formed in these syntheses, namely hydroxy-, amino-, or mercapto-nitriles (IVA, X = O, NR, or S), were frequently not isolated.

Examination of studies where the compounds (IVA) were isolated in a pure form shows that the isomerisation (IVA) → (IVB) takes place readily and irreversibly on heating in polar solvents[198-200], in the presence of acids[201-206] and bases[197,207-218], or simply on heat treatment[198,200,203,218-220]. Double melting points, i.e. the crystallisation of the substance after fusion and its second fusion ar the melting point of the cyclic isomer, are important phenomena in the thermal isomerisation of

2-cyanobenzamide[219] and 2-thioureidobenzonitrile[198]. The heterocyclic imines (IVB) formed frequently isomerise to heterocyclic amines (IVC or IVD) as a result of the migration of the double bond to the ring:

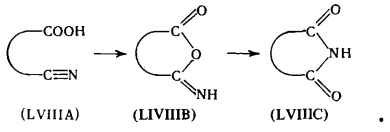


Matsui and also Renson observed $\nu(C\equiv N)$ and $\nu(C=N)$ bands in the infrared spectra of the ω-cyanoalcohols (LVIIa)[221] and 2-hydroxymethylbenzonitrile (LVIIb) [222] and concluded that the ring–chain tautomeric equilibrium (LVIIA) $\rightleftharpoons$ (LVIIB) occurs:



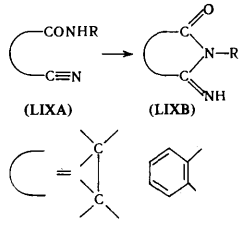
This conclusion requires additional confirmation, which can be secured by spectroscopic study of solutions of (LVIIa) and (LVIIb) in various solvents. Numerous data on the cyclisation reactions of hydroxynitriles[196,197,201] suggest that the isomerisation (IVA) → (IVB) (X = O) is irreversible. One cannot rule out the possibility that some investigators[221,222] did not work with the equilibrium system (LVIIA) $\rightleftharpoons$ (LVIIB) but with a mixture of isomers (LVIIA) and (LVIIB) (cf. des Abbayes[214]).

The mononitriles of phthalic[219], homophthalic[223], and other γ- and δ-dicarboxylic acids[197] readily isomerise to the imides (LVIIIC). This isomerisation can proceed through the stage involving the formation of the relatively unstable iminolactone (LVIIIB).[216,223] A study[218] of the infrared spectra of 2-cyanobenzoic acid in various solvents showed that the acid is stable in solution at room temperature and the equilibrium (LVIIIA) $\rightleftharpoons$ (LVIIIB) is not observed.

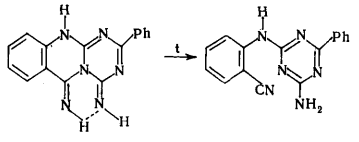


Both γ-and δ-aminonitriles[202,203,209,217,224-226], β-hydrazinonitriles[213,217,227], the hydrazones of cyanoketones[200], and β-cyanoacid hydrazides[190] isomerise to the corresponding heterocyclic imines or amines. The amides of β-cyanopropionic[208,210,215] and 2-cyanobenzoic acids (LIXA) [218-220] isomerise in the presence of bases (sodium alkoxides or triethylamine) or by a thermal process to the iminolactams (LIXB).

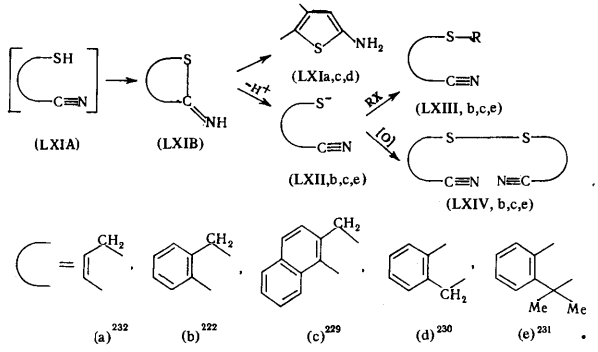
It has been shown that an increase in the bulk of the substituent R at the nitrogen atom in the series of 2-cyanobenzamides hinders the isomerisation (LIXA) → (LIXB) and for this reason *N*-(t-butyl)- and *N*-(1-adamantyl)-2-cyanobenzamides do not cyclise. In solutions in dioxane 2-cyanobenzamides and their cyclic isomers (LIXB) are stable and the equilibrium (LIXA) $\rightleftharpoons$ (LIXB) has not been observed by infrared spectroscopy[218]. 2-Ureido and 2-thioureido-benzonitriles[198,212,228] as well as urethanes derived from α-cyanohydrins[211] isomerise similarly.



Among amino-derivatives of nitriles, there is one unusual example[226] where the cyclic form undergoes thermal isomerisation to the open-chain form [(LXB) → (LXA)]. Evidently the gain of the aromatisation energy on formation of the *s*-triazine ring in the open-chain isomer (LXA) is of decisive importance here:



At the instant of their formation γ-mercaptonitriles (LXIA) cyclise[196,222,229-232] to iminothiophen derivatives (LXIB). If there is a hydrogen atom attached to the carbon atom which is α to the C=N bond, the latter undergo spontaneous further isomerisation to the aminothiophens (LXIa – c) and (LXId – C).[230,232] Stacy[229,231] and Renson[222] speak of the ring–chain tautomerism (LXIA) $\rightleftharpoons$ (LXIB), since the compounds (LXIb – B), (LXIc – B), and (LXIe – B) form both cyclic and open-chain derivatives. For example, alkylation in an alkaline medium gave the open-chain *S*-alkyl derivatives (LXIII, b, c and e) and on oxidation the products were the open-chain disulphides (LXIV, b, c, and e). Evidently the open-chain anion (LXII) is formed in an alkaline medium. However, the presence of the open-chain form either in the crystalline state or in solution could not be demonstrated by spectroscopic methods (Raman spectroscopy and ^{1}H NMR), i.e. the tautomeric equilibrium (LXIA) $\rightleftharpoons$ (LXIB) does not occur within the limits of the sensitivity of these methods.



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Thus the application of infrared, ^{1}H NMR, and ultraviolet spectroscopic methods permits a quantitative characterisation of the phenomenon of ring–chain tautomerism. However, few such studies have been made in this field. A quantitative assessment of these processes,

based on at least two spectroscopic methods, is of greatest interest and evidently such investigations will be the first to develop.

A common defect of the majority of the experimental studies carried out to date in this field is the narrow range of test systems. Whereas the influence of the substituents on ring–chain equilibrium has been very thoroughly characterised[160,166,233-237] by correlation constants, attempts to assess quantitatively the influence of the structure of the link joining the two interacting groups are not described in the literature. Nevertheless, the study of the relation between the quantitative characteristics of intramolecular reversible addition reactions and the steric disposition of the reacting functional groups in the presence of a fairly rigid connecting link is of great theoretical interest.

ADDED IN PROOF

During the preparation of the review for the press, a number of studies on the ring–chain tautomerism of hydroxyketones[238-241], hydroxyiminoketones[242,243], 2-oxoalkyltriazenes[244,245], and *N*-(β-hydroxyalkyl)hydrazones[246] were published.

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The Ullmann Ether Condensation

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The review deals with the Ullmann condensation as the most important method for the synthesis of aromatic ethers. The available information about the dependence of the reactivity of the reactants on structure and the reaction mechanism is examined and the experimental condensation conditions are discussed.
The bibliography includes 241 references.

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1. INTRODUCTION

In 1904 Ullmann[1] observed that the presence of metallic copper greatly facilitates the substituion of a halogen atom in an aromatic ring by a phenolic residue:

$$ArX + KOAr' \xrightarrow[Cu]{t^\circ} ArOAr' + KX \ .$$

This catalytic method for the synthesis of aromatic ethers, usually referred to as the Ullmann condensation[2], has become widely used in catalysis and industrial chemistry.

The Ullmann condensation is a method for the synthesis of phenyl ether (used to prepare heat exchangers and in the perfume industry[3-8]), substituted phenyl ethers (monomers for thermostable polymers[9-11]), and polyphenyl ethers, which have found important applications in various branches of modern engineering, for example, as oils for the creation of an ultrahigh vacuum, as high-temperature greases, hydraulic liquids, etc.[12-20]

A wide variety of aryl ethers, including intermediates in the synthesis of complex natural products such as alkaloids[21-36] and also diphenylene dioxides, have been synthesised on a preparative scale by the Ullmann condensation[37-41].

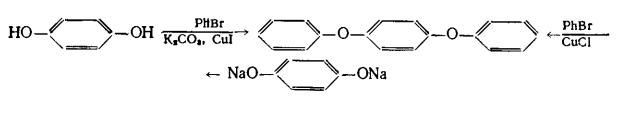
During the last ten years, a number of studies undertaken to determine the principal characteristics of this reaction and to elucidate its mechanism, have been published. Despite the extensive applications of the Ullmann condensation, there is no special review in the literature dealing with the synthetic aspects of this reaction.
The Ullmann ether condensation has been only briefly examined among other reactions in reviews on the synthesis and properties of phenyl[6] and polyphenyl[13,14] ethers, nucleophilic substitution[42], and copper-catalysed processes[43].

2. EXPERIMENTAL CONDENSATION CONDITIONS

The condensation is carried out by heating the initial reactants at 100-300°C in the presence of a copper catalyst in a solvent or without one (in the absence of a solvent, the optimal temperature is usually 180-220°C). To avoid the oxidation of the phenol, the reaction is sometimes performed in an inert atmosphere[44-51].

The phenolic components are frequently introduced in the form of salts, which are obtained by treating phenols with alkalis, alkali metals, and their alkoxides as well as sodamide[52] and sodium hydride[53]. Potassium salts are apparently more reactive. They are employed more frequently than sodium phenoxides[44,45,50,54]. However, a rigorous quantitative estimate of the comparative reactivities of different salts has not been made.

Free phenols can also be introduced into the reaction with aromatic halogeno-derivatives. Potassium carbonate is then added to the mixture and the method of synthesis is greatly simplified without reducing the yield of ethers[50,55]. This version of the condensation has undoubted advantages in the synthesis of aromatic polyethers. The difficulties in the preparation of such ethers are associated with the instability of the alkali metal salts of dihydric phenols which char to a considerable degree[56]. This can be partly avoided by preparing dry phenoxides beforehand under special conditions[53], which, however, complicates the synthesis. The use of K_2CO_3 and of free phenols eliminates altogether the stage involving the preparation of phenoxides and as a rule leads to higher yields of polyethers[57,58]. Thus bromobenzene condenses with hydroquinone in the presence of K_2CO_3, forming *p*-diphenoxybenzene in 63% yield[57], while the disodium salts of hydroquinone gives rise to the same product in a yield of only 0.3%:[53]



It is interesting that other salts, for example $Na_2B_4O_7$, MeCOOLi, MeCOONa, MeCOOK, $(NH_4)_2CO_3$, Na_2CO_3, and $CaCO_3$, are ineffective[57].

The oxides Cu_2O and CuO, which evidently combine the functions of a catalyst and a base, have an unusual effect[45,55,59,60]:

$$2ArX + 2Ar'OH + Cu_2O \rightarrow 2ArOAr' + 2CuX + H_2O \ .$$

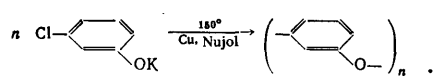
The rate of condensation is in this case lower than in the presence of K_2CO_3 and copper salts [57].

3. THE CATALYST

Metallic copper [1,10,11,15-17,20,21,23-29,35,36,41,47-52,55,56,61-166], the copper salts $CuCl_2$, [15,16,166-170] $Cu(OCOMe)_2$, [46,57,58,61,171-174] $CuSO_4$, [175-179] CuCl, [53,57,180,181] CuBr, [57,182,183] CuI, [57] $CuCO_3$, [7,184,185] and the copper oxides CuO [34,55,186,187] and Cu_2O [45,55,56,62,63,188-190] have been used as catalysts. In addition the copper salts of alkylnaphthalenesulphonic acids [191], alkylbiphenyldisulphonic acids [191], and phenols [192-194] as well as the copper(II) complexes $(C_5H_5N)_2 \cdot CuCl_2$ and $Cu(OCH_3)_2$ [51] have been proposed as catalysts of the Ullmann condensation. Powdered copper is obtained by reducing $CuSO_4$ with zinc [64] or by electrolytic deposition [65,195]. Copper comminuted mechanically, the so called copper bronze [22,66,67,196-211], is also used. Sometimes copper is employed in combination with its salts, for example with $Cu(OCOMe)_2$, [22,39,40,68-70,212-251] CuCl, [222] CuI, [197] and $CuNO_3$. [37,38]

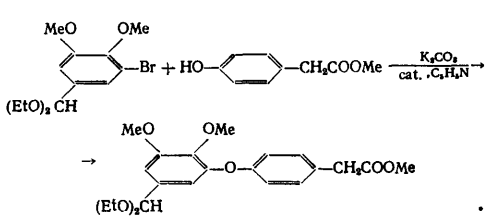
Attempts have been made to replace copper catalysts by other metals, salts, and oxides: titanium [223], iron [224], $Co(OCOMe)_2$, [225] $Ni(NO_3)_2$, [225] and Al_2O_3, [224] but these catalysts have not been widely used, probably owing to their low activity.

Despite the initial view [166], the relative catalytic activities of various forms of copper depend significantly on the method of preparation of the catalyst, the reaction conditions, and many other factors [44,53,55,71,195]. Thus, in a study of the polycondensation of potassium *m*-chlorophenoxide in Nujol in the presence of metallic copper, Brown and Goldman [195] observed that the method of preparation of the catalyst ("chemically" reduced or electrolytically precipitated copper with an admixture of 1% of zinc) and its preliminary treatment have a significant influence on the course of the reaction and the properties of the resulting polymer:



Under these conditions, copper oxides have an insignificant catalytic activity.

On the other hand, in the condensation of phenols and methyl *p*-hydroxyphenylacetate with certain aryl bromides, copper oxides proved to be more active [55]. An appreciable difference between CuO and Cu_2O was not observed and the relative efficiency of the catalyst depended on the nature of the initial compounds and the solvent. For example, in the condensation of the diethyl acetal of 5-bromoveratraldehyde with methyl *p*-hydroxyphenylacetate in boiling pyridine in the presence of copper, Cu_2O, and CuO the yields were 10, 30, and 35% for reaction times of 15, 10, and 9 h respectively:



In a study of the condensation of α-bromonaphthalene with phenols in collidine, Bacon and Stewart [45] also concluded that copper oxides are more active than copper and its salts (Table 1):

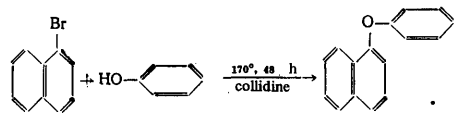


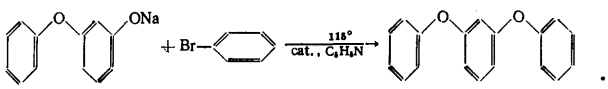
Table 1.

Catalyst	Cu_2O	CuO	Cu	CuCl	CuBr	$CuCl_2$
Yield of α-phenoxynaphthalene, %	50	31	23	traces	traces	0

However, in this case the condensation was carried out in the absence of potassium carbonate and the enhanced activity of copper oxides may have been due to the fact that they are capable of behaving as both catalysts and bases. The presence of oxidised species in finely divided metallic copper also cannot be ruled out.

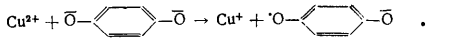
According to Weingarten [44], $CuBr_2$, $CuCl_2$, $Cu(OCOMe)_2 \cdot H_2O$, CuI, CuBr, and CuCl are equally effective as catalysts of the condensation of bromobenzene with potassium phenoxide in diglyme. Metallic copper, Cu_2O, CuO, and $CuSO_4$ are inactive in this reaction.

Copper(I) and copper(II) salts exhibit approximately equal catalytic activities also in the condensation of sodium *m*-phenoxyphenoxide with bromobenzene in pyridine, while copper is ineffective [53]:



The first attempt to discover the catalytically active form of copper [226] did not elucidate the problem appreciably. More convincing results were obtained later [44] in a study of the condensation of bromobenzene with potassium phenoxide in diglyme in the presence of CuBr and $CuBr_2$. These salts showed equal catalytic activities and the ESR spectra and antimagnetic susceptibilities of the catalytic solutions were similar in the two cases. However, a CuBr solution prepared in an atmosphere of nitrogen gave a weaker ESR signal than a $CuBr_2$ solution and its magnetic susceptibility was negligible. On the other hand, when the condensation was carried out in an inert atmosphere, the reaction rate increased. Hence it followed that the active form of the copper catalyst is univalent copper. The catalytic activity of bivalent copper may have been due to its reduction by the phenoxide anion, which was then oxidised to a relatively stable free radical. The latter in fact made the reaction mixture paramagnetic. Indeed, the white precipitate deposited when the solution of $CuBr_2$ and potassium phenoxide in diglyme was poured into water proved to be a copper(I) salt and the addition to the catalytic solution of 2,6-di-t-butyl-4-methylphenol, 2,5-di-t-butylhydroquinone, or phenothiazine—compounds which trap free radicals—resulted in appreciable changes in the ESR spectrum but did not affect the rate of the Ullmann ether condensation.

It has been found[53] that metallic copper does not catalyse the condensation of bromobenzene with sodium *m*-phenoxyphenoxide in boiling pyridine and that, when CuBr is used as a catalyst, the introduction of copper powder into the reaction mixture does not affect the rate of this reaction. Since powdered copper completely reduced bivalent copper to the univalent state under these conditions, the authors[53] concluded that the only possible active form of the catalyst is univalent copper. These workers also believe that bivalent copper may be reduced by phenoxide anions. The low yields of products and the formation of large amounts of resins in the condensation of readily oxidised polyhydric phenols (catechol, hydroquinone, 2,6- and 1,5-dihydroxynaphthalenes and phloroglucinol) were explained by polymerisation processes involving radical-ions of the semiquinone type:



Thus the available literature data show that the active principle of the catalyst is probably univalent copper. On the other hand, bivalent copper compounds and metallic copper are active by virtue of the oxidation-reduction processes occurring in the reaction medium.

However, in the practical selection of the catalyst, one probably should not ignore also the role of factors such as the solubility of copper compounds, the effects of the chemical nature of the solvent and the reactants, etc.

4. THE SOLVENT

An excess of the phenol[7,49,67,72-79,184,185,198,200,220], heavy unsaturated and aromatic hydrocarbons[48,80,172,177-179], alcohols and glycols[22,63,81,82,197,224], diglyme[15,42,44,222], dioxan[22,171,173,174,176], ketones[65,83,169,180], dimethylformamide[11,55,187,189], dimethyl sulphoxide[11,227], nitrobenzene[84,197,204], pyridine and its derivatives[23,26,28,29,34,46,55,57,58,85,86,172,188], quinoline[63], and certain other organic compounds[11,55,63,169] have been used as solvents.

One of the best solvents is pyridine[53,55,57,58]. Thus, in the condensation of bromobenzene with the sodium salt of *m*-resorcinol in pyridine, the yield of *m*-diphenoxybenzene was 74% and the overall yield of this ether and *m*-phenoxyphenol reached 89%. In other solvents the yields were significantly lower[53] (Table 2):

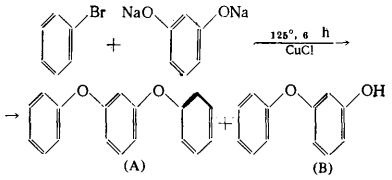


Table 2.

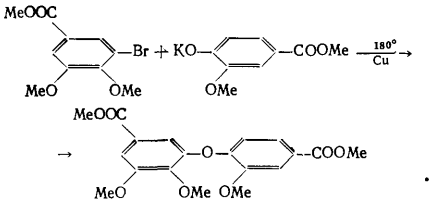
Solvent	Yield, %		Solvent	Yield, %	
	ether (A)	ether (B)		ether (A)	ether (B)
Pyridine (117°C)	74	15	Dimethylformamide	4	34
Pyridine + 2% of water (112°C)	4	22	Hexamethylphosphoramide	5	47
2,4,6-Collidine	17	25	Methyl sulphoxide	14	42
Pyridine *N*-oxide	18	40	n-Propyl sulphone	42	33
Di-n-butylamine	32	19	2-Methoxyethyl ether	21	25
1-Methyl-2-pyrrolidinone	11	46			

Attempts to find rigorous correlations between the effectiveness of the solvent and its characteristics, for example its basicity, have been unsuccessful[45].

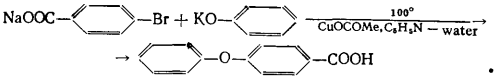
On the other hand, it is significant that the majority of the solvents employed contain in their molecules a heteroatom having a lone electron pair. The dissolution of the copper catalyst is apparently accompanied by complex formation in which the solvent participates via its heteroatom[53]. If it is presumed that the action of the catalyst is also in some way related to the formation of complexes with the reactants, then it is necessary that the copper–solvent complex should be dissociated to a fairly high extent. Indeed, in the above example of the condensation of bromobenzene with the sodium salt of *m*-resorcinol the replacement of 9% pyridine by $\alpha\alpha'$-bipyridyl, which is a more powerful ligand, reduces the yield of *m*-diphenoxybenzene from 74 to 31%. Thus the solvent plays to some extent the role of a cocatalyst[53].

In the light of these findings the promoting effect of the addition of compounds with a tertiary nitrogen atom[87,169,180,211] and the enhanced activity of the complex catalyst $(C_5H_5N)_2CuCl_2Cu(OMe)_2$ [51] become understandable. Admixtures which may be present in the solvent probably also have the same type of effect on the rate of reaction. Thus it has been shown that the reaction of bromobenzene with potassium phenoxide is faster in unpurified diglyme. After the solvent has been purified by distillation from $LiAlH_4$, the rate of reaction falls[44]. The active ingredient was isolated chromatographically; it is suggested[44] that it has the structure of the diester $CH_3OCH_2COOCH_2CH_2.OCHO$. It was observed that the addition of certain other esters, namely ethylene carbonate, the diacetate of propylene glycol, 1,2-diacetoxycyclohexane, etc. to the solvent has a similar activating effect.

The possibility of carrying out the reaction in aqueous media is not altogether clear. An example was quoted above (Table 2) where the addition of 2% of water to pyridine reduced the yield of condensation products almost threefold. Small amounts of water also inhibit the reaction between methyl 5-bromoveratrate and 4-hydroxy-3-methoxybenzoate; however, the process does not require the complete absence of water[71]:



On the other hand, a favourable effect of water on the reaction has also been noted[88,228]. For example, according to Vainshtein et al.[228], sodium *p*-bromobenzoate condensed in aqueous pyridine with potassium phenoxide to give a 90% yield of 4-carboxyphenyl phenyl ether, while in anhydrous pyridine the reaction did not occur at all:



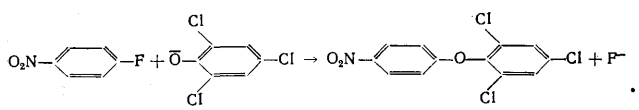
There are data concerning both unsuccessful[173,175] and successful[177] attempts at condensation in aqueous solutions. Instances are also known of its successful achievement in mixtures of organic solvents with water[172,179].

5. THE REACTIVITY OF ARYL HALIDES

As in the majority of copper-catalysed reactions of aryl halides[43,229,230], the case of substitution of halogen atoms in the Ullmann condensation decreases in the sequence I > Br > Cl ≫ F.[45,50,60,65,167,227] Thus, under standard conditions (170°C, 72 h, Cu_2O, collidine), the yields of phenyl ether in the condensation of iodo-, bromo-, and chloro-benzene with phenol were 70, 42, and 10% respectively[60].

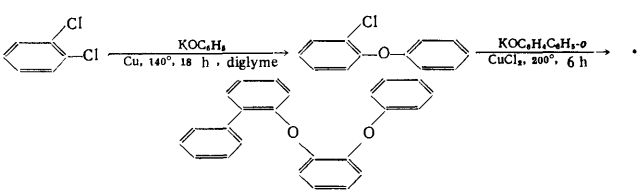
The relative rates of condensation of halogenobenzenes with potassium phenoxide in diglyme at 160°C in the presence of $CuCl_2$ have been determined[167]. For iodo-, bromo-, chloro-, and fluoro-benzenes, they are respectively 40, 40, 1, and 0.001% and more refined kinetic measurements showed that the rate for iodobenzene is approximately threefold higher than for bromobenzene.

On the other hand, there are literature data demonstrating a high reactivity of certain aryl fluorides[89,231]. For example, according to Dahlgard and Brewster[231], *p*-chloronitrobenzene and 2,4,6-trichlorophenol do not condense in an alkaline medium in the presence of a copper catalyst, but the condensation does proceed when *p*-fluoronitrobenzene is used as the halogen-containing component:

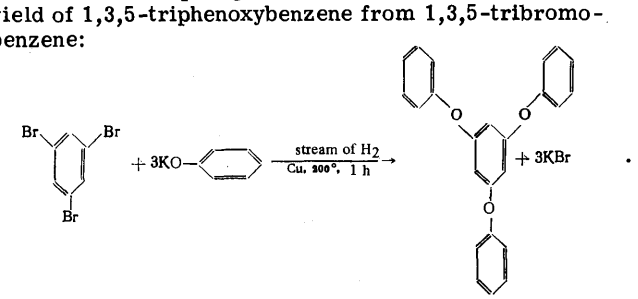


However, one cannot rule out the possibility that in this case the main role is assumed by the non-catalytic halogen-substitution reaction, which fluoro-derivatives in fact tend to undergo to the greatest extent[42,232].

The Ullmann ether condensation usually permits the introduction of several aryloxy-groups into the benzene ring[16,37,50,61,90-92,171]. In this case a stepwise substitution of halogens is possible. Thus 1,2-dichlorobenzene was condensed in succession with phenol and *o*-hydroxybiphenyl; the yield of the intermediate 2-chlorophenyl phenyl ether reached 70% and the yield of the final ether with four benzene rings, formed from the latter, was 62%:[15]

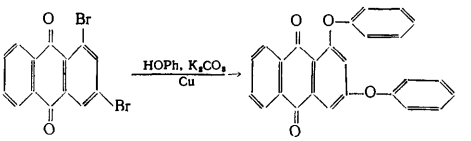


Ullmann and Sponagell[50] succeeded in obtaining a 90% yield of 1,3,5-triphenoxybenzene from 1,3,5-tribromobenzene:



However, the attempt to substitute the four bromine atoms in 1,2,3,5-tetrabromobenzene was unsuccessful. Owing to a dehalogenation side reaction, the initial tetrabromo-compound was reduced to 1,3,5-tribromobenzene and the only condensation product was 1,3,5-triphenoxybenzene (50% yield).

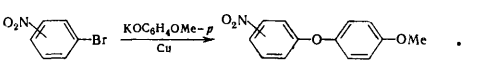
The condensations of various dihalogenoanthraquinones have been described: the yields of the diethers were 64 to 97%.[61,84] For example, 1,3-diphenoxyanthraquinone was synthesised from the corresponding dibromo-derivative by refluxing for 2 h with an excess of phenol in the presence of copper and potassium carbonate, the yield being 97%:[61]



Aryl halides containing a wide variety of substituents in the aromatic ring have been successfully employed in the Ullmann condensation. Even chemically reactive groups such as CHO,[36,85,93-95,211] OH,[15,24,37,49,67,68,78,90] and NH_2[61] do not then require special protection.

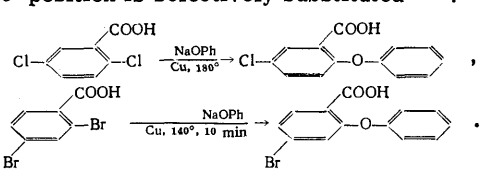
The nature and positions of the substituents have a significant influence on the reactivity of aryl halides. Highly electronegative groups in the *ortho*-position relative to the halogen have a marked activating effect on the latter. Unfortunately, the available literature data are insufficient for a comparison of the activating effects of these groups.

The nitro-group apparently has one of the most powerful activating effects. Its influence is clearly shown when it is present not only in the *ortho*- but also the *para*-position. The *meta*-nitro-group is in this respect less effective. Whereas *p*-bromonitrobenzene condensed with the potassium salt of the monomethyl ether of hydroquinone to give 4-methoxyphenyl 4-nitrophenyl ether in 80% yield, the yield of the corresponding phenyl ether from *m*-bromonitrobenzene under comparable conditions was only 31%:[96]

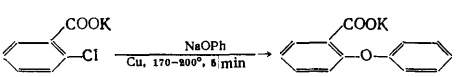


Owing to the enhanced reactivity of *o*- and *p*-halogenonitrobenzenes, the yields of their condensation products as a rule reach 80–90%.[45,64,89,93,96,197]

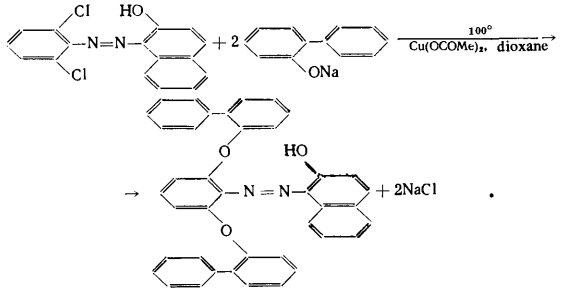
The activating effect of the carboxy-group is shown mainly when it is in the *ortho*-position with respect to the halogen. In dihalogenobenzoic acids the halogen atom in the *ortho*-position is selectively substituted[97,98]:



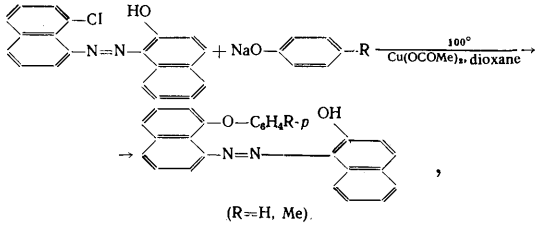
It is also instructive that in preparative syntheses the yields of *o*-aryloxybenzoic acids frequently exceed 80 to 90%.[99,100,166,197] For example, *o*-chlorobenzoic acid (in the form of a salt) condenses with sodium phenoxide on brief heating to 170–200°C in the presence of copper powder to give 90% of *o*-phenoxybenzoic acid[166]:



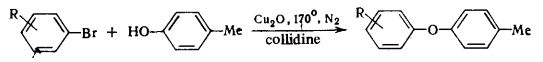
The *ortho*-halogen in azo-compounds exhibits a high reactivity [171-174,176-179]. The condensation of such compounds proceeds at comparatively low temperatures (93° to 110°C) and reaches completion in 4–16 h; the yields of the ethers are invariably high (70–100%). For example the reaction of 2,6-dichlorobenzene(1-azo-1′)-2′-naphthol with the sodium salt of 2-hydroxybiphenyl in boiling dioxan resulted in the quantitative substitution of both chlorine atoms in 4 h: [171]



The azo-group in the *peri*-position of α-chloronaphthalene has a similar effect [173]:



(R=H, Me).



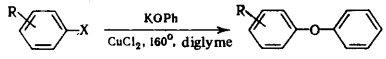
(R=o-Me, p-Me, H, p-OMe)

The presence of electron-donating substituents in the aryl halide molecule does not affect significantly the mobility of the halogen [45,53,101,167,233]. Thus the reaction of *p*-cresol with bromobenzene, *o*- and *p*-bromotoluenes, and *p*-bromoanisole in the presence of Cu_2O in collidine at 170°C in the course of 16 h gave similar yields of ethers: 43, 42, 41, and 54% respectively [45].

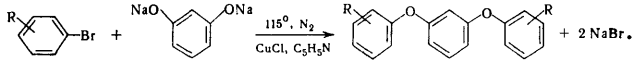
Table 3.

R(X=Cl)	H	*o*-Cl	*m*-Cl	*p*-Cl	*p*-Me	*p*-OMe
Relative rate	1.0	1.4	2.5	1.9	0.78	1.2
R(X=Br)	H	*o*-Me	*m*-Me	*p*-Me		*m*-Br
Relative rate	40	15	31	31		130

Nevertheless in the measurements of the relative rates of condensation of potassium phenoxide in diglyme at 160°C (Table 3) it was possible to observe a weak deactivating effect of the methyl group in various positions of the substituted halogenobenzene, which is typical for nucleophilic aromatic substitution. A slight activating effect of the second halogen atom, which increases in the series of isomers $o < p < m$, was also noted [167]:



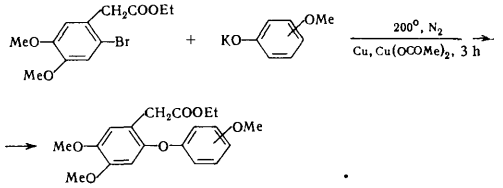
In agreement with this, Williams et al. [53] found that in the condensation of substituted bromobenzenes with the sodium salt of resorcinol the effect of substituents is in general typical for nucleophilic substitution and is described satisfactorily by the Hammett equation with the reaction constant $\rho = +1.4$:



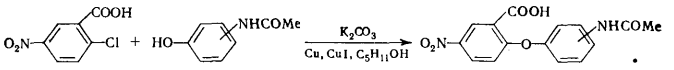
In this reaction the *p*-methoxy-group has a deactivating effect on the halogen and therefore, contrary to other data [45,167], also does not deviate from the general rule. However, one must emphasise that all these quantitative or semiquantitative determinations were made for extremely limited series of substituents.

6. THE PHENOLIC COMPONENT

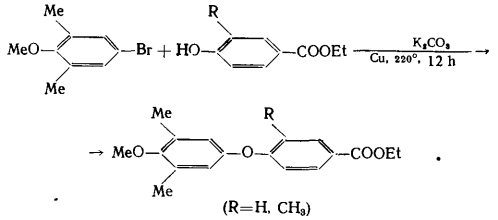
There are almost no literature data on the effect of the structure of the phenolic component on the rate of condensation. Electron-donating groups in the *ortho*-position probably reduce its reactivity. Thus potassium *o*-, *m*-, and *p*-methoxyphenoxides react under identical conditions with ethyl 2-bromo-4,5-dimethoxyphenylacetate, forming the corresponding phenyl ethers in yields of 6, 42, and 46% respectively [212]:



The reaction of *p*-*N*-acetamidophenol with 2-chloro-5-nitrobenzoic acid (boiling pentyl alcohol, potassium carbonate, copper powder, and CuI) resulted in the formation of 2-(*p*-*N*-acetamidophenoxy)-5-nitrobenzoic acid in 79% yield, while only 19% of the ether was obtained from *o*-*N*-acetamidophenol [197]:

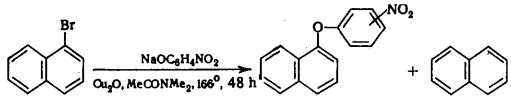


Whereas the introduction of one methyl group in the position adjoining the hydroxyl in ethyl *p*-hydroxybenzoate had only a slight effect on the yield of the product of its condensation with 4-bromo-2,6-dimethylanisole, two *ortho*-methyl-groups completely inhibited this reaction [102]:

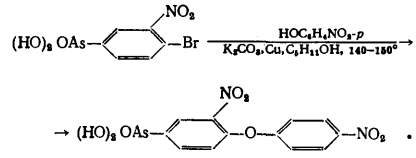


(R=H, CH_3)

Nitrophenols as a rule enter with difficulty into the Ullmann condensation. Thus potassium *p*- and *m*-nitrophenoxides condensed with α-bromonaphthalene in boiling dimethylacetamide in the presence of Cu_2O to give 9 and 38% yields of α-nitrophenoxynaphthalenes after 48 h. The *o*-nitrophenoxide did not condense but the initial bromo-derivative was reduced to naphthalene in all three cases to the extent of 9, 20, and 50% respectively[45]:



A relatively low yield of the ether was obtained also in the condensation of *p*-nitrophenol with 4-arsono-1-bromo-2-nitrobenzene: 10% against 54% for the unsubstituted phenol under the same conditions[82]:



The deactivating effect of the *p*-nitro-group was also noted by McRue et al.[22]

It is very difficult to obtain information concerning the influence of other substituents in phenol on its reactivity by comparing the available data. The differences between the reactivities of phenols based on the results of condensations with α-bromonaphthalene and 4-arsono-1-bromo-2-nitrobenzene under the conditions indicated above for the reactions with nitrophenoxides (in the condensation with α-bromonaphthalene, collidine was employed as the solvent instead of dimethylacetamide) are instructive in this respect, the yields (expressed as percentages) are indicated in brackets:

$$p\text{-MeO}(72) > p\text{-Me}(62) > p\text{-Cl}(49) > o\text{-COOH}(32) > p\text{-COOH}(11) \simeq$$
$$\simeq m\text{-NO}_2(12) \simeq p\text{-NO}_2(12)^{45};$$
$$o\text{-COOH}(82) > p\text{-Cl}(78) > p\text{-COOH}(60) > \text{H}(54) > p\text{-Me}(46) >$$
$$> o\text{-Me}(25) > p\text{-NO}_2(10)^{82}.$$

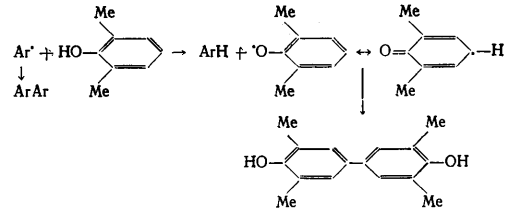
7. SIDE REACTIONS

Typical side reactions accompanying the Ullmann ether condensation are reductive dehalogenation[45,57,65,66,79,103,104,196,234,235], the Ullmann coupling process[45,86,235], and the exchange of halogens between the aryl halide and the copper salt[45].

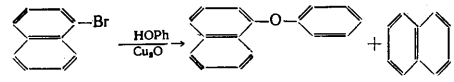
In the reduction process the phenolic component can behave as a hydrogen donor[45,235]. The importance of the side reaction probably increases when the reactivity of the phenol in the condensation is low. For example, the reaction of equimolar amounts of *o*-bromonitrobenzene with *p*-cresol in boiling collidine in the presence of Cu_2O gives a 48% yield of the ether together with 22% of nitrobenzene and 3% of *oo'*-dinitrobiphenyl as by-products. In the reaction with 2,4- and 2,6-dimethylphenols the yield of the ether falls to 0–2%, while that of nitrobenzene increases to 70–80%. At the same time bisphenols were identified in the reaction products, the yield of 4,4'-dihydroxy-3,5,3',5'-tetramethylbiphenyl reaching 20% in the latter case.

Bacon and Stewart[235] proposed the following mechanism for the formation of by-products:

$ArBr + Cu^+ \rightleftharpoons$ complex on the surface of $Cu_2O \rightleftharpoons Ar^\cdot + Cy^{2+} + Br^-$,



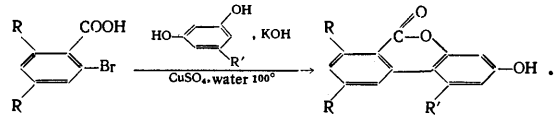
The solvent has an appreciable influence on the relative contributions of the main and side reactions. Thus, the reaction of α-bromonaphthalene with phenol in the presence of Cu_2O gives 61% of α-phenoxynaphthalene in 2,4,6-collidine, 46% in quinoline with 12% of naphthalene as a second product, while in pyridine *N*-oxide the yields are 38% of the ether and 36% of naphthalene[45]:



It is important to note that the characteristics of the structure of the aryl halide, which are responsible for its high reactivity in the Ullmann ether condensation, are probably favourable also for the side reactions.

The reactions enumerated above, occurring under the conditions of the Ullmann ether condensation as side processes, acquire independent synthetic value under special conditions[45,229,230,235,236].

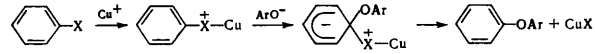
Among other side reactions, mention should be made of condensations involving the mobile hydrogen atoms in the aromatic ring of one of the reactants. An interesting illustration of the possibility of reactions of this kind is provided by the formation of the lactones of substituted 2',4'-dihydroxybiphenyl-2-carboxylic acids in an aqueous alkaline medium in the presence of $CuSO_4$:[175,237,238]



(R=OMe, R'=Me, R=R'=H)

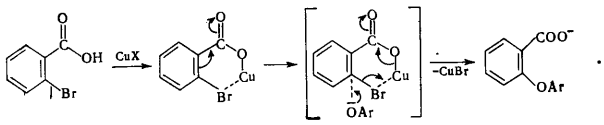
8. THE REACTION MECHANISM

In 1941 Bunnet and Zahler[42] put forward a hypothesis concerning the mechanism of the Ullmann ether condensation according to which the action of the copper catalyst reduces to the formation of a halogenonium compound and a consequent increase in the mobility of the halogen under nucleophilic attack:

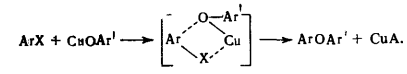


Bunnet and Zahler's mechanism had the importance of a general principle only and, owing to the lack of experimental data, could not specify the valence state of the catalytically active form of copper.

Later this hypothesis was used to account for the high activating effect of the *ortho*-carboxy-group and its almost total absence for the *para*- and *meta*-carboxy-groups [73]:

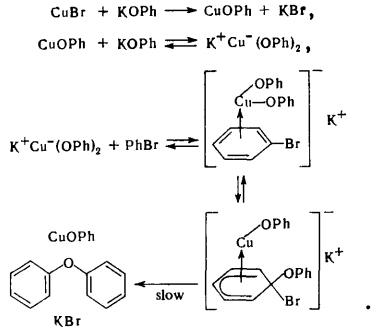


An essentially similar idea constituted the basis of the hypothesis [192] that the condensation proceeds via the usual four-centre mechanism, proposed for the exchange reactions of aryl halides with copper salts [43]:



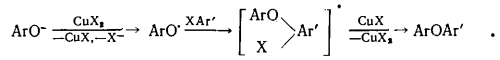
According to this hypothesis, copper(I) phenoxide is formed in the reaction. The possibility of the direct formation of ethers from aryl halides and copper phenoxides has been demonstrated experimentally [192,194].

The condensation mechanism proposed by Weingarten [44] is based on a somewhat different principle. The author begins with the following experimental findings: (1) the catalytically active form of the copper catalyst is univalent copper; (2) the effect of the nature and positions of the substituents in the aryl halide on the mobility of the halogen atom is typical for nucleophilic substitution; (3) the mobility of the halogen decreases in the series I > Br > Cl > F, which is correlated with the ease of dissociation of the carbon–halogen bond. According to Weingarten, the catalytic effect of copper is determined by its interaction (as the phenoxide) with the π electrons of the aromatic system of the aryl halide and not with the halogen atom undergoing substitution. Copper thus plays the role of, as it were, an additional electron-accepting (i.e. activating) substituent:



The main idea of this mechanism is seen to be confirmed by data demonstrating the existence of a copper(I)–benzene complex [239] and the greater ease of substitution of the halogen by the nucleophilic agent in the π-complexes of aryl halides with transition metals, such as the complex of chlorobenzene with chromium tricarbonyl [240]. The proposed mechanism is consistent with kinetic data obtained in a study of the condensation of bromobenzene with potassium phenoxide in diglyme in the presence of CuBr: the reaction is of first order with respect to the aryl halide and the copper salt and of a fractional order with respect to the phenoxide, which increases from a value close to zero at high concentrations to approximately unity at low concentrations. The reaction equation, describing satisfactorily the experimental findings and reflecting the variable order with respect to the phenoxide, may be based either on the hypothesis that at high concentrations the phenoxide is associated but only the monomeric species are reactive or on the hypothesis of a salt effect due to the phenoxide itself. The author was unable to make a choice between these two alternatives.

Kopylov [241] suggested a free-radical mechanism of the Ullmann ether condensation:



This mechanism essentially reflects the tendency to combine within the framework of a fundamentally the same mechanism oxidative polycondensation of phenols [13], oxidative substitution at the halogen in halogenophenols [13], and the Ullmann ether condensation. The validity of this attempt is doubtful and conflicts with experimental data showing that free radicals are not involved in the Ullmann reaction and that the true catalyst of this reaction is univalent and not bivalent copper. Moreover, the first two reactions can occur also under the influence of non-copper oxidants, whereas copper is a specific condensation catalyst. It is more likely that the free radicals, whose formation is indeed possible under the conditions of the Ullmann reaction, are not responsible for the main process but only for the accompanying side reactions.

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Immobilised Enzymes

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Adsorption, covalent bonding, and occlusion into the structure of a gel can be used to attach enzymes to insoluble carriers in order to obtain heterogeneous enzymic catalysts. The kinetic characteristics of the enzymes are affected by immobilisation, but these changes—quite often more apparent than real—are due to changes not in the properties of the enzyme molecules themselves but in their microenvironment. Immobilised enzymes possess enhanced stability, and can be employed in technical processes, biochemical analyses, and medicine. A list of 506 references is included.

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I. INTRODUCTION

Artificial insoluble derivatives of enzymes are attracting increasing interest from chemists, biochemists, technologists, and medical men. These products—which, according to the recommendations of an international symposium[1], should be termed *immobilised enzymes*—have been recommended for use in technical processes, analytical chemistry, and medicine. Immobilised enzymes, especially in the form of membranes, may serve as models for subcellular structures. The prospects for the application of immobilised enzymes and certain convenient aspects for theoretical investigations have already been reflected in hundreds of papers and patents, which have been covered in dozens of reviews. Disregarding popular reviews and publicity, as well as relatively inaccessible publications, we can refer to several extremely serious and thorough surveys[2-20].

The immobilisation of enzymes forms part of the broader problem of the purposeful modification of biologically active substances. The present Review deals mainly with immobilised enzymes and insoluble complexes of enzymes with polymers. However, the immobilisation of enzyme inhibitors, antibodies, antigens, nucleic acids, hormones, and other biologically active substances is omitted, as well as the chemical modification of enzymes with simple substances. It must be emphasised here that the immobilisation of various biologically active substances capable of specific complex formation with biopolymers has become the foundation of an extremely effective technique for separating and purifying proteins and other biologically important substances by affinity chromatography (chromatography based on specific sorption). This method has developed especially rapidly during recent years, and has formed the subject of several detailed reviews[21-28].

The ability of enzymes to function when present in cell membranes has been known since the establishment of enzymology as a science. It may be supposed that most enzymes act in an insoluble form in cells, and that their total quantity contained in membrane structures exceeds the quantity present in dissolved form in the protoplasm. McLaren illustrates[11] the antiquity of heterogeneous enzymic catalysis by the use even in the nineteenth century of columns filled with earths to investigate nitrification. On the other hand, good yields of enzymic activity in adsorption chromatography have proved that the binding of enzymes with insoluble materials may not involve irreversible inactivation.

However, we can speak of the immobilisation of enzymes only after the specific catalytic action of intentionally prepared insolubilised enzymes with a substrate had been proved. The first results of this kind were published during the first half of the present century by Nelson[29,30] and by Langmuir[31,32]. The instability of enzymic adsorption complexes limited their application, and a broad investigation of immobilised enzymes began only in the 1950s, when the covalent bonding of enzymes and the occlusion of biological macromolecules in the three-dimensional structure of various gels came to be employed as well as adsorption. Methods for the retention of dissolved enzymes in microcapsules made of semipermeable membranes, in hollow fibres, and also in large-scale reaction vessels fitted with ultrafiltration membranes have now been developed together with molecular immobilisation (the immobilisation of each molecule).

Many immobilisation procedures are now known, hundreds of insoluble derivatives of enzymes have been obtained, and the possibility of their repeated and prolonged use has been shown. Technical processes, analytical techniques, and several therapeutic procedures have been based on the use of immobilised enzymes. The value of these products in industrial biochemistry is stressed in a special resolution of the Presidium of the USSR Academy of Sciences[33].

At the present time there are more than a thousand publications and two hundred patents on immobilised enzymes. It is clearly impossible to mention all these references in this Review, and the literature is therefore cited selectively. Since complete patent specifications are comparatively inaccessible and patented results are quite often published subsequently in the open press, a restriction was first imposed on the number of references to the patent literature. Nevertheless, the absence of an exhaustive bibliography does not prevent the reader from obtained a sufficiently general idea of the present position of the problem.

II. METHODS FOR THE IMMOBILISATION OF ENZYMES

1. Principles of Immobilisation

Methods of immobilising biologically active substances can be divided into two main groups: in molecular immobilisation each molecule is attached to the carrier individually; immobilisation occurs in solution when larger or smaller volumes of the enzyme solution are separated from the external medium by a semipermeable membrane. Molecular immobilisation can in turn be effected in three ways, according as the molecules are retained on the carrier by adsorption or covalent bonds or are held mechanically in the three-dimensional network of chains in the macromolecules of a polymeric carrier. Methods are also possible in which several of the above principles are combined.

2. Immobilisation of Enzymes by Adsorption

Ion exchangers and "neutral" adsorbents, which are not well defined exchangers, are used for the immobilisation of enzymes by adsorption.

Silicon dioxide as silica gel or glass is most often used as neutral carrier. Such materials have been applied to the immobilisation of glucose oxidase[34,35], cytochrome-c[36-38], malic dehydrogenase[39], succinic dehydrogenase[40-42], glucose 6-phosphate dehydrogenase[43], catalase[40-42], hexokinase[40-42,44,45], amyloglucosidase[34], trypsin[46,47], chymotrypsin[46], papain[35,48], alkaline protease[49], acid phosphatase[40-42,50], ribonuclease[46,51,52], aminoacylase[53], and phosphoglucomutase[40-42]. Interesting work has been done by Poltorak and his coworkers[54,55], who adsorbed enzymes on silica gel by means of an intermediate lipid layer. They thus achieved tenfold increases in activity of several enzymes, which is a very rare concomitant of immobilisation[40-42]. These results have been summarised and discussed in reviews by the same workers.

Various clays are suitable for obtaining active adsorbents. They have yielded immobilised glucose oxidase[56,57], catalase[56], glucoamylase[58,59], lysozyme[60], invertase[56], neuraminidase[56], trypsin[61], chymotrypsin[61-63], alkaline protease[49], bacterial protease[64], phosphatase[65,66], urease[67-69], and penicillinamidase[70]. Enzymes which have been immobilised on the mineral supports are nicotinamide—adenine dinucleotide pyrophosphorylase[71], invertase[30], proline iminopeptidase[72], alkaline protease[49], leucine aminopeptidase[73], aminoacylase[53,74], and penicillinamidase[75].

Activated carbon has been used as carrier for glucose oxidase[34], succinic dehydrogenase[40], invertase[29,30], glucoamylase[34,58,59,76], catalase[41 42 77], alkaline phosphatase[78], acid phosphatase[42,77], hexokinase[42,77], and phosphoglucomutase[42,77]. Peroxidase[79], cellulase[80], and deoxyribonuclease[81] have been adsorbed on cellulose; and glucose 6-phosphate dehydrogenase[82] and adenosine triphosphatase[83] have been immobilised on cellulose nitrate. Liver cells adsorbed on cellulose nitrate have been used to obtain material having ribonucleic-acid synthetase activity[84]. The efficiency of adsorption of amylase on Millipore filters can be enhanced by preliminary acylation of the enzyme with aliphatic acids[85,86]. Glycerol dehydrogenase has been adsorbed on a dextran gel—Sephadex[87].

Ion-exchange resins are used far more often than neutral carriers for immobilising enzymes. Insoluble derivatives of catalase[88], invertase[89], glucoamylase[90,91], aminoacylase[53,74,92-95], β-galactosidase[96], pepsin[96], kidney proteinase[96], asparaginase[97], adenosine triphosphate deaminase[98], glucose isomerase[99], and D-oxynitrilase[100] have been obtained on di- and tri-ethylaminoethylated celluloses. The enzyme column for the first industrial installation having an insoluble enzyme was obtained by adsorbing aminoacylase on diethylaminoethylated Sephadex[53,74,101,102]. Dextransucrase has been immobilised by the same method[103]. Catalase[104], glucose oxidase[34], glucoamylase[34,105], ribonuclease[51,52], aminoacylase[53], and penicillinamidase[106] have been attached to synthetic polymeric anion-exchange resins.

Among cation exchangers, carboxylated carriers are most often employed for immobilising enzymes. Carboxymethylcellulose has served for the immobilisation of catalase[88], peroxidase[107], asparaginase[108], and phosphomonoesterase[109]; and carboxymethylated Sephadex for glucose oxidase and glucoamylase[34], as well as aminoacylase[74]. Glucose oxidase[34], glucoamylase[34], ribonuclease[51,52,110], and trypsin[111] have been immobilised on carboxylated polymeric cation-exchange resins. Among special carboxylated carriers mention may be made of a copolymer of alanine and glutamic acid, as well as polygalacturonic acid for the immobilisation of acetylcholine esterase[112] and succinylated glass for binding lactate dehydrogenase[113]. Aminoacylase[74] and ribonuclease[114] have been immobilised on sulphonated cation-exchange resins.

Soluble polyelectrolytes are used, as well as insoluble exchangers, for the modification of enzymes. The resulting soluble polymer—enzyme complexes also possess enhanced stability[115-118].

3. Occlusion of Enzymes into Gel Structures

When enzyme and substrate differ considerably in size, a gel can be chosen whose pores are sufficiently large for diffusion of the substrate but completely exclude that of the large enzyme molecules. Such a situation ensures irreversible bonding of the enzyme with retention of its activity. A limited number of gel-forming substances have hitherto been used in this method of immobilisation. Trypsin[119] and acetylcholine esterase[120] have been occluded into gelatinous silicic acid. A process for obtaining choline esterase, alkaline phosphatase, trypsin, lipoxidase, urease, catalase, and prostaglandin synthetase occluded in silica gel has also been patented[121,122]. Aminoacylase has been trapped in hydroxymethylcellulose[53], acylase[123] and choline esterase[124] in agar-agar, choline esterase[124-126] and urease[127] in starch, trypsin[128], chymotrypsin[128], acetylcholine esterase[129], and a complex of glucose oxidase with peroxidase[129] in silastic silicone, and penicillinamidase[53] in polyurethane. An unusual method for obtaining complexes of this type is the electrodeposition of collagen fibres in a solution of the enzyme, which has been used to immobilise urease[127,130], α-amylase[131], amyloglucosidase[132], and invertase[132].

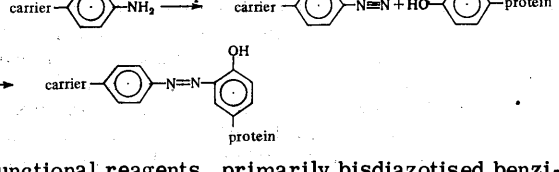
The most widely used carrier for obtaining enzymes enclosed in a gel is cross-linked polyacrylamide. Acrylamide and methylene-*NN*-bisacrylamide in various proportions are readily polymerised by a free-radical mechanism. The free radicals required are most often provided by a photochemical or a redox reaction, but ionising radiation is sometimes used[133,134]. Capture in a polyacrylamide gel has served for the immobilisation of glucose oxidase[135-139], L-amino-acid oxidase[140-142], D-amino-acid oxidase[143-147], xanthin oxidase[143], alcohol

dehydrogenase[143,144], lactic dehydrogenase[137,143,144], catalase[137,144], glucose 6-phosphate dehydrogenase[145,146], glyceraldehyde 3-phosphate dehydrogenase[143], peroxidase[148], hexokinase[146,149], phosphofructokinase[149], α-amylase[150], β-amylase[150], glucoamylase[151,152], invertase[153-155], β-glucosidase[156,157], β-galactosidase[158], trypsin[133,134,150,158,159], chymotrypsin[150], papain[150], urease[126,142,160,161], asparaginase[147], choline esterase[126,162], aminoacylase[53,163], phosphatases[164,165], adenosine trisphosphate diphosphohydrolase[166], ribonuclease[150], aldolase[149,150,167,168], enolase[167-169], decarboxylase[143,159], aspartase[170], phosphoglycerate mutase[167,168,171], glucoisomerase[172], phospho-gluco-isomerase[149], citrate synthetase[173], thiocyanase[174], and injectase[174]. Other polyacrylic gels have been used, e.g. hydroxyethyl methacrylate for the fixation of glucose oxidase[175], but considerably more rarely than polyacrylamide. The extremely long list of products obtained indicates the universality of this method. Polyacrylamide gel has been used to immobilise not only individual enzymes but also enzymic complexes[145,146,149,176-178] and entire cells of micro-organisms[159,179,180].

4. Covalent Bonding of Enzymes

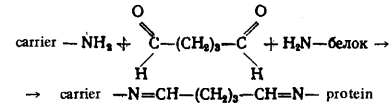
Covalent immobilisation is often considered separately for cases in which the new covalent bonds are formed between activated groups of the carrier and reactive groups in side-chains of the protein and for those in which the protein is cross-linked by a bifunctional reagent into an insoluble "superpolymer" in the pores or on the surface of an unreactive carrier or else in the complete absence of such a carrier. The distinction between these processes disappears when the carrier contains the same reactive groups as the protein, while immobilisation is effected by means of a bifunctional reagent. In such cases covalent bonding of the protein molecule with the carrier and immobilisation by formation of a superpolymer may take place simultaneously. In the present Review all these cases are regarded as the single method of covalent immobilisation. "Superpolymerisation" of an enzyme involves immobilisation in the absence of a carrier, although the resulting insoluble, intermolecularly cross-linked enzyme can then be regarded as a carrier.

One of the first processes suggested was the covalent bonding of proteins by azo-coupling, primarily with tyrosine residues of the protein molecule:



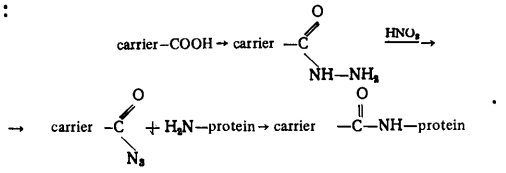
Bifunctional reagents, primarily bisdiazotised benzidine-2,2′-disulphonic acid, have also been used in this process. Immobilisation has thus been applied to papain in the absence of a carrier[181], glucose oxidase[182,183], trypsin[182], chymotrypsin[182], papain[184,185], apyrase[83], adenosine triphosphatase[83], and carbonic anhydrase[182,183] on cellulosic carriers, and papain on collagen[181]. Enzymes are more often bonded to an already diazotised carrier. Thus glass treated with 3-triethoxysilylpropylamine and *p*-nitrobenzoyl chloride, and then subjected to reduction and diazotisation, has been used for the fixation of glucose oxidase[186], peroxidase[186], L-amino-acid oxidase[187], invertase[188], trypsin[186,189], papain[189], ficin[186], pronase[190], alkaline phosphatase[186,191,192], urease[186,193], acetylcholine esterase[194], aminoacylase[52], aryl sulphatase[195], steroid esterase[196], and glucoisomerase[197]. Immobilisation of the coenzyme, nicotinamide–adenine dinucleotide, has been accomplished in the same way[198,199]. Carriers which already contain benzene rings are merely nitrated and reduced. Polystyrene has been used in this way for the immobilisation of glucose oxidase[200], catalase[201,202], lipase[201], α-amylase[203,204], pepsin[204], ribonuclease[204], carboxypeptidase[204], and aminoacylase[205]; and copolymers of *p*-amino-DL-phenylalanine with aliphatic amino-acids for that of trypsin[206,207], chymotrypsin[207], papain[181,207], thrombin[208], prothrombin[206,208], pronase[107,209], urease[207,210], and plasminogen[211]. Polytyrosyl derivatives of the enzymes—trypsin[212-214] and papain[215]—have been fixed by the same procedure. Polytyrosyl derivatives containing a larger number of phenolic groups attackable by diazo-compounds are obtained by treating the enzyme with *N*-carboxy-L-tyrosine anhydride. Diazotised *p*-aminobenzylcellulose has been attached to invertase[188], various amylases[216,217], pullulanase[218], dextranase[218], β-glucosidase[216], chymotrypsin[219], trypsin[216], thrombin[220], ficin[219], papain[218], carboxypeptidase[218], aminoacylase[53,205], and ribonuclease[219]. Aromatic amino-groups are present in the polyacrylic resin Enzacryl AA, which is marketed especially for the immobilisation of enzymes[221]. The diazotised resin has been used to bind amylase[222,223], cathepsin[224], aminoacylase[53], and adenosine deaminase[225,226]. Mention must be made also of the immobilisation of enzymes on diazotised polysaccharide anthranilates[227,228].

Most procedures for the covalent immobilisation of enzymes are based on the reactions of nucleophilic groups in the proteins—in particular their primary amino-groups—with electrophilic groups of an activated carrier on a bifunctional reagent. We shall firstly consider the reaction of amino-groups with aldehydes



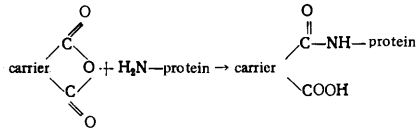
Dialdehydes, mainly glutaraldehyde, are mostly used in this reaction. This bifunctional reagent has been employed to immobilise, in the absence of a carrier, catalase[229-232], glucose oxidase[232], peroxidase[232], trypsin[232-234], chymotrypsin[233,235,236], papain[237-241], carboxypeptidase[242-244], lysozyme[127,232,236], subtilysine[245], urease[230], asparaginase[230], ribonuclease[232], aminoacylase[53], and certain zymogens[128,234,236]. The use of glutaraldehyde to cross-link a protein adsorbed on a neutral carrier has served to immobilise glucose oxidase, urate oxidase, trypsin, chymotrypsin, urease, carboanhydrase[246], and adenylate cyclase[247] on cellulose, as well as trypsin on silica gel[248]. Enzymes are more often cross-linked by glutaraldehyde with a carrier containing amino-groups: trypsin[234,249,250], pepsin[251], rennin[252], and aldolase[253] have been attached to aminoethylcellulose; alcohol dehydrogenase[217], lactate dehydrogenase[217], glucose oxidase[254], uric oxidase[255], urease[254,255], and L-asparaginase[256,257] to a partly hydrolysed polyamide; peroxidase[258], glucose oxidase[259], cytochrome[258,259], trypsin[258,259], chymotrypsin[259], acid phosphatase[259], and ribonuclease[260] to polyacylamide; and adenylate cyclase to aminopolystyrene[247]. Aldehyde-containing carriers are used considerably more rarely: e.g. poly(acrylamidoacetaldehyde dimethylacetal) has been employed for binding trypsin[260], papain[260], α-amylase[260,261], and dextranase[260,261], and an acrylaldehyde–styrene copolymer to bind invertase[262].

The reaction of acid azides with the amino-groups of a protein finds widespread use for the immobilisation of enzymes:



Diazides are seldom employed as bifunctional reagents because of their sparing solubility in water. It is preferred to convert carboxy-groups of a hydrophilic carrier, generally carboxymethylcellulose, into azides. Insoluble derivatives have been obtained by this method from catalase[263], chymotrypsin[219,264-269], trypsin[269], ficin[219,270], bromelain[56], pronase[271], ribonuclease[219,272], adenosine triphosphatase[83], alkaline phosphatase[273], apyrase[83,274], aminoacylase[53], penicillinamidase[275], asparaginase[276], streptokinase[277], adenylate cyclase[247], and various amylases[203,278,279]. Another widely used carrier of this type is polyacrylohydrazide, known also under the proprietary name Enzacryl AH,[221] on which have been fixed glucose oxidase[280], luciferase[281], α- and β-amylases[272,282], trypsin[283-286], chymotrypsin[286], aminoacylase[285,286], and ribonuclease[287]. Other carriers are comparatively rarely used in the azide method of immobilisation: carboxymethyldextran has given insoluble acetylcholine esterase[112], asparaginase[288], and streptokinase[277]; pectin has been used for trypsin and chymotrypsin[289]; and nylon for trypsin[290].

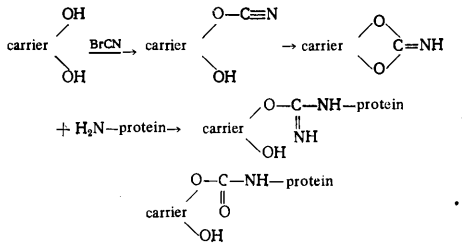
Reaction with anhydrides of dibasic acids is also extremely popular:



Since this involves the formation not only of a covalent bond but also of an ionisable carboxy-group, electrostatic interaction may be observed between protein and carrier molecules. Carriers of this type are usually obtained by the copolymerisation of maleic anhydride and ethylene, and are simply termed EMA polymers. This method of immobilisation has been applied predominantly to proteolytic enzymes, mainly trypsin[2,144,181,212,213,292-298], and a special review has been devoted to derivatives of this type[291]. Other proteinases are represented by chymotrypsin[2,144,297,298], pepsin[299], plasmin[2], kallikrein[144], papain[297,299,300], bromelain[300], ficin[300], pronase and neutral proteinase[299], and Novo and Carlsberg subtilisines[297].

Proteinases inhibited by mercury compounds have in certain cases been immobilised in order to protect the active centres of the enzymes from acylation: attachment of the enzymes to the carrier was followed by reactivation[300]. Immobilisation has been applied not only to proteolytic enzymes but also to catalase[298], D-amino-acid oxidase[298], xanthine oxidase[298], amylase[299,301], dextranase[301], cellulase[298,301], β-glucosidase[298], naringinase[302], ribonuclease[303], acetylcholinesterase[304], lipase[299,301], penicillinamidase[106,302], asparaginase[298,301], urease[301], alkaline phosphatase[273], pyrophosphatase[298], hexokinase[298], adenylate cyclase[247], and oxynitrilase[301]. Soluble EMA polymers have served for the preparation of soluble polymer—enzyme complexes[301]. Among other polymeric anhydrides only that of polymethacrylic acid has been used, to immobilise trypsin, chymotrypsin, and papain[362,386].

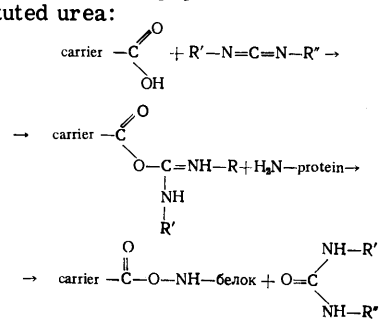
The activation of hydroxylated carriers with cyanogen bromide, proposed by Porath et al.[305], has gained very great popularity during recent years. This reagent acts on the carrier surface to form iminocarbonate groups capable of bonding with the amino-groups of proteins:



This method is mostly used to activate agarose (Sepharose), which, because of its ability to swell strongly in water (dry content 2%, 4%, or 6%), has an extremely large-pored structure. This ensures that large enzyme molecules are trapped in the pores of the carrier, and that diffusion coefficients shall be high even for substrates of high molecular weight. Enzymes which have been immobilised in this way are glucose oxidase[306], lactoperoxidase[307], lipoxygenase[308], isocitrate dehydrogenase[309,310], pyridine nucleotide transhydrogenase[311], protocatechuate 3,4-dioxygenase[312], glucose 6-phosphate dehydrogenase[146], glucoamylase[306], trypsin[313-317], chymotrypsin[252,305,316,318,319], pepsin[320,321], rennin[252,322], cathepsin[224], elastase[323], leucine aminopeptidase[324,325], amino- and carboxy-peptidases[326], papain[316], bacterial proteinase[327], various nucleases[328-334], choline esterases[335], aminoacylase[53], penicillinamidase[336], aldolase[337], glucogen phosphorylase[338], and transfer ribonucleic acid histidine[339] and isoleucine[340] synthetases.

Although Sepharose activated with cyanogen bromide enables extremely high activities to be attained with many immobilised enzymes, the poor mechanical and thermal stability of this material must not be overlooked. In order to obtain insoluble enzymes more suitable for technical application, other polysaccharide materials have been activated with cyanogen bromide. Thus cellulose has served for the attachment of glucoamylase[341], pronase[271], acetylcholinesterase[112], penicillinamidase[336], asparaginase[276], polynucleotide phosphorylase[342], and streptokinase[277]. The dextran gel Sephadex has been used to immobilise glucose oxidase[343], catalase[343], lipoxygenase[344], glucose 6-phosphate dehydrogenase[345], isocitrate dehydrogenase[309], glucoamylase[343], β-galactosidase[345], trypsin[314,346-348], chymotrypsin[319], leucine aminopeptidase[336], ribonuclease[331], hexokinase[345,349], and streptokinase[277].

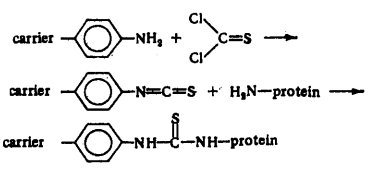
The carbodi-imides employed in peptide synthesis are good condensing agents. The reaction takes place in two stages, addition of the agent to a carboxy-group being followed by formation of a peptide link with elimination of a disubstituted urea:



This reaction can be used to form intra- and inter-molecular amide bonds[360], and enables an immobilised enzyme to be obtained in the absence of a carrier (e.g. the immobilisation of aminoacylase[53]). In most cases carbodi-imides are used to condense carboxy-groups of the carrier with amino-groups of the enzyme. In this way glutamate dehydrogenase[351], peroxidase[352,353], chymotrypsin[351], pronase[354], asparaginase[276], and acetylcholinesterase[112] have been immobilised on carboxymethylcellulose; glutamate dehydrogenase[351], chymotrypsin[351], and pronase[355] on dextran; glucose 6-phosphate dehydrogenase[146], glutamate dehydrogenase[351], β-galactosidase[155], pullulanase[356], trypsin[155], chymotrypsin[351], and citrate synthetase[159] on acrylic polymers; and trypsin[290] on nylon.

Several compounds having mobile halogen atoms—in particular bromo- and iodo-acetyl derivatives, acid chlorides, fluoronitrophenyl compounds, and cyanuryl halides (triazinyl trichlorides, Procion dyes)—have been used for immobilisation. They are able to react with amines and mercapto, hydroxy, and imidazole groups. Fluorophenyl-containing polymers have served for the immobilisation of alcohol dehydrogenase[357,358], invertase[358,359], amylases[357,358,360-362], pepsin[357,358], papain[360-362], alkaline phosphatase[273], and aminoacylase[205]. Triazinyl halides have been used for the immobilisation of enzymes mainly on aminoethylated celluloses, as well as on other polysaccharides. Insoluble preparations have been obtained in this way from glucose oxidase[363], lactate dehydrogenase[364], glucoamylase[363,365,366], dextranase[363], α-galactosidase[363], β-galactosidase[367,368], invertase[369], hyaluronidase[370], trypsin[363,371], chymotrypsin[189,372,373], papain[263], penicillinamidase[363,374,375], acetylcholinesterase[112,376], alkaline phosphatase[363], ribonuclease[363], pyruvate kinase[363,368,377], and creatine phosphokinase[363]. Derivatives of iodo- and bromo-acetic acids and also iodoalkyl esters have effected the immobilisation of chymotrypsin[378,379], trypsin[380], thrombin[381], pronase[355], glucoamylase[341,382], aminoacylase[53,383], penicillinamidase[275], urease[380], aldolase[384], and streptokinase[277]. The action of ethyl chloroformate has immobilised pepsin[385], trypsin[289], chymotrypsin[289], and ficin[289]. Penicillinamidase[106,275] and alkaline proteinase[386] have been attached to acid chlorides of carboxylated cation-exchange resins. Among inorganic compounds sulphuryl and thionyl chlorides have been used[387,388] to immobilise lactate dehydrogenase, invertase, pepsin, alkaline phosphatase, and threonine deaminase. New bonding agents of this type are transition-metal chlorides (in particular titanium tetrachloride[389,390]), by means of which glucose oxidase, uricase, glucoamylase, α-amylase, invertase, trypsin, urease, and glucose isomerase have been attached to various carriers, including yeast cells.

Various cyanates are quite often used to establish covalent bonds between protein and carrier. Among them we must first mention isothiocyanates, obtained by the action of thiocarbonyl chloride on amines:



Similarly, treatment with carbonyl chloride leads to the formation of isocyanate groups. Insoluble derivatives of glucose oxidase[391], catalase[201], various amylases[222, 282,361,392,393], proteinases[358,361,393,394], and lipase[201] have been obtained by these procedures. Isocyanides[319,395] and cyanates[396] are employed considerably more rarely for immobilisation.

Among the less widely used methods for the covalent fixation of enzymes is the application of 2-ethyl-5-phenylisoxazole-3-sulphonate[276,397-401] to the immobilisation of trypsin and chymotrypsin, as well as asparaginase[276], apyrase[399], deoxyribonuclease[399], and choline esterase[399]. β-D-Glucosidase, α-amylase, glucoamylase, and trypsin have been immobilised on cellulose carbonate[402]. Reaction with compounds containing epoxy-groups has been used to immobilise certain proteinases[403]. Several enzymes have been immobilised on Enzacryls containing thiolactam and thiol groups[221,284]. Commercial preparations of insoluble enzymes have been produced by the above methods[404-410].

5. Isolation of Enzymes by means of Membranes

Repeated application of enzymes is achieved also by isolating the enzyme solution by means of membranes whose pores are impermeable to protein macromolecules but permeable to the substrate and the reaction products. This is accomplished by microencapsulation, in which polymeric envelopes are formed around the enzyme solution, by producing artifical fibres containing minute droplets of the enzyme solution, and by enclosing the enzyme solution between membranes on an electrode surface. The application of enzymes in a reaction vessel with ultrafiltration of the reaction mixture through a membrane which retains protein macromolecules might have been included in this type of isolation. In the last case a solution of the substrate is introduced into the reaction vessel, omitting the membrane, and the enzyme can act on macromolecular substrates provided that the products are of low molecular weight.

Since in these systems the enzymes retain a certain mobility in solution, isolation of this type is difficult to relate completely to our problem of immobilisation. In view of the similarity between the methods of practical application of microencapsulated enzymes—in particular those enclosed in fibres—and of molecularly immobilised enzymes, we shall mention some of the relevant work and give a list of products obtained in this way (Table 1).

Table 1. List of immobilised enzymes.

No.	Enzyme	Ref.
1	Alcohol dehydrogenase	143, 204, 214, 357, 406
2	Acetaldehyde dehydrogenase	421
3	Glycerophosphate dehydrogenase	406
4	Lactate dehydrogenase	113, 137, 143, 144, 217, 388, 406, 411
5	Glycerate dehydrogenase	39, 40—42
6	Malate dehydrogenase	38, 217, 406
7	Isocitrate dehydrogenase	309, 310
8	Glucose 6-phosphate dehydrogenase	43, 82, 145, 146, 345, 406
9	Steroid dehydrogenase	179
10	Glucose oxidase	34, 35, 56, 57, 129, 135, 136, 137, 139, 175, 182, 183, 186, 200, 232, 246, 254, 259, 280, 306, 343, 363, 390, 391, 406, 408, 409, 420
11	Glyceraldehyde phosphate dehydrogenase	406
12	Xanthin oxidase	377
13	Glutamate dehydrogenase	351
14	L-Amino-acid oxidase	140—142, 187
15	D-Amino-acid oxidase	143, 147, 298
16	NAD transhydrogenase	311
17	Nitrite reductase	421
18	Urate oxidase	246, 255, 390
19	Catalase	32, 41, 42, 56, 77, 88, 104, 121, 122, 144, 187, 188, 202, 229, 231, 263, 298, 343, 411, 416, 420

Table 1 (continued).

No.	Enzyme	Ref.
20	Peroxidase	120, 129, 148, 186, 232, 258, 259, 352, 353, 405, 406, 409
21	Cytochrome-c	36, 37, 258, 405, 409, 121, 122, 308, 344
23	Protocatechuate 3,4-dioxygenase	312
24	Polyphenol oxidase	422
25	Luciferase	281
26	Lactoperoxidase	307
27	β-Tyrosinase	419
28	α-Glucan phosphorylase	338
29	Dextransucrase	103
30	Galactosyl transferase	423
31	Nucleoside-ribosyl transferase	350
32	Aminotransferase	420
33	Hexokinase	40, 41, 42, 44, 77, 146, 149, 298, 338, 345, 349, 377, 406, 419
34	Creatine kinase	363
35	Phosphoglycerate mutase	406
36	NAD pyrophosphorylase	71
37	Polynucleotide phosphorylase	342
38	Thiocyanase	423
39	Lipase	51, 201, 299, 301, 411
40	Acetylcholesterase	89, 112, 120, 129, 335, 376
41	Cholinesterase	121, 122, 124—126, 162, 335
42	Glycerol dehydratase	87
43	Acid phosphatase	40—42, 51, 77, 164, 259, 408
44	Alkaline phosphatase	40—42, 78, 122, 164, 165, 186, 191, 192, 273, 363, 388, 404, 408
45	Phosphatase	65, 66
46	Phosphomonoesterase	109
47	Phosphodiesterase	404
48	Deoxyribonuclease	81, 404
49	Nuclease	330, 332, 334
50	α-Amylase	85, 86, 131, 150, 203, 216, 217, 222, 223, 260, 261, 282, 389, 390, 393, 405, 406
51	β-Amylase	150, 217, 222, 358
52	Glucoamylase	34, 58, 59, 76, 90, 91, 105, 132, 151, 152, 200, 216, 261, 279, 306, 341, 363, 365, 366, 389, 390, 404
53	Maltase	416
54	Diastase	204, 301, 357, 361, 362
55	Cellulase	80, 298, 301
56	Dextralase	363
57	Lysozyme	60, 128, 232, 236
58	Neuraminidase	56, 406
59	β-Glucosidase	156, 157, 216, 298, 397
60	α-Galactosidase	363
61	β-Galactosidase	96, 158, 345, 367, 419, 420
62	Invertase	29, 30, 56, 89, 153—155, 262, 416, 419, 420
63	Naringinase	302
64	Pullulanase	218, 261, 301
65	Ribonuclease	46, 51, 52, 110, 114, 156, 204, 219, 232, 259, 272, 287, 328, 329, 331, 333, 334, 363, 404—409, 419, 420
66	Leucine aminopeptidase	73, 324, 325, 405
67	Aminopeptidase	326, 393
68	Carboxypeptidase	204, 218, 242, 243, 244, 326, 406, 408, 420
69	Iminopeptidase	72
70	Alkaline protease	49, 186, 228, 299, 386
71	Bacterial protease	198, 228
72	Neutral protease	299
73	Pepsin	31, 95, 204, 251, 299, 320, 321, 357, 358, 385, 387, 393
74	Kallikrein	144
75	Trypsin	46, 47, 61, 111, 119, 121, 128, 133, 144, 150, 158, 159, 182, 186, 289, 206, 207, 212, 213, 216, 228, 232, 234, 246, 248, 250, 258, 260, 269, 283, 286, 289, 290, 292, 293—298, 304, 313, 314, 316, 346—348, 358, 363, 371, 380, 389, 390, 393, 401, 404—410
76	Papain	48, 140, 148, 150, 155, 181, 184—186, 189, 207, 215, 227, 236, 238—241, 260, 278, 300, 304, 316, 346, 361, 363, 394, 397, 405—410, 420
77	Chymotrypsin	5, 41, 61—63, 112, 128, 144, 150, 182, 207, 219, 233, 236—238, 246, 252, 259, 264—267, 286, 297, 305, 315, 316, 319, 351, 358, 373, 378, 393, 395, 397, 398, 401, 405—410
78	Elastase	323
79	Cathepsin	224
80	Ficin	106, 186, 219, 270, 289, 300, 406, 407, 409
81	Thrombin	206, 208, 220 381,
82	Plasmin	47, 211
83	Rennin	252, 322
84	Bromelain	300, 407, 409
85	Pronase	107, 190, 209, 271, 355, 406
86	Subtilisin	64, 297, 405—407
87	Asparaginase	27, 108, 147, 230, 256—277, 288, 298, 301, 406
88	Aminoacylase	51—53, 74, 92—95, 101, 102, 163, 205, 285, 383
89	Urease	31, 32, 67, 68, 69, 122, 126, 129, 160, 161, 186, 193, 210, 230, 246, 254, 255, 286, 301, 380, 390, 405, 406, 411, 413, 414, 416, 420
90	Penicillinamidase	53, 70, 75, 106, 274, 336, 363, 374, 375, 419
91	Arginase	420
92	Adenosine deaminase	225, 226
93	Pyrophosphatase	298
94	Adenosine triphosphatase	83
95	Adenosine triphosphate deaminase	98
96	Adenosine triphosphate dihydrolase	166
97	Apyrase	83, 271
98	Orsellin decarboxylase	159
99	Arginine decarboxylase	143, 196
100	Cysteinesulphinate decarboxylase	143, 195
101	Oxynitrile lyase	145
102	Aldolase	149, 150, 167, 168, 253, 337, 384, 406, 419
103	Carbonic anhydrase	182, 183, 246, 317, 412, 417
104	Enolase	167—169
105	Hyaluronate lyase	370
106	Threonine deaminase	388
107	Aspartase	170
108	Glucose isomerase	99, 172, 416, 419

Table 1 (continued).

No.	Enzyme	Ref.
109	Glucose phosphate isomerase	149, 406
110	Triose 3-phosphate mutase	406
111	Phosphoglycerate phosphomutase	41, 42, 40, 77, 145, 167, 168, 171
112	Tryptophan synthetase	419
113	Isoleucine-tRNA synthetase	340
114	RNA synthetase	84
115	Histidine-tRNA synthetase	339
116	Citrate synthetase	159, 173
117	Prostaglandin synthetase	121, 122
118	Injectase	174

Inclusion in microcapsules has been applied mainly to urease[230,411-415], and also to lipase[411], maltase[416], glucose isomerase[416], carbonic anhydrase[317,412,417], catalase[411,418], and asparaginase[230]. By dispersing an aqueous solution of one or more enzymes in a solution of a linear polymer in an organic solvent, various enzymically active fibres and cloths have been obtained, which are able to retain such activity for a long time[419,420].

In order to facilitate the finding of references on the immobilisation of any individual enzyme, Table 1 gives a list of the immobilised enzymes known at the present time, their sequence corresponding to the generally accepted classification of enzymes.

III. EFFECT OF IMMOBILISATION ON THE PROPERTIES OF ENZYMES

1. General Description of Changes

It can be concluded from all the accumulated experimental results that immobilisation produces no fundamental changes in the catalytic properties of enzymes. Furthermore, even the quantitative parameters of their action—the catalytic constants, activation energies, optimum pH and temperature—quite often undergo no significant change. Henceforward, therefore, we shall consider only those cases in which the properties of the immobilised enzyme differ from its original properties.

In examining the experimental differences in properties between soluble and insoluble enzymes, we must bear in mind that the molecules of an immobilised enzyme function in a microenvironment which may differ considerably from the macroenvironment, i.e. that the medium may differ in composition inside and outside a particle of a heterogeneous enzymic catalyst. For this reason the International Commission has recommended that the experimental kinetic characteristics of immobilised enzymes should be qualified as "apparent".

We propose to discuss the kinetics of immobilised enzymes, and hence the production of the observed kinetic changes, at several levels (Table 2). Changes in enzymic kinetics at the molecular level (No. 5) are of greatest interest to theoretical enzymology, of course, but study of the kinetics of enzymes at this level requires that perturbations at levels 1—4 be taken into account.

In principle it is easiest to eliminate the effect of the apparatus, for which purpose we must operate at sufficiently low degrees of conversion of the substrate. The necessity must then be emphasised of verifying experimentally that the reaction velocity is independent of the degree of conversion. Our own experimental results have shown that, when the enzyme is inhibited by

reaction products, non-linearity arises even when only a few percent of the substrate has been converted. Development of the kinetics of apparatus with immobilised enzymes is of immense value for the introduction of heterogeneous enzymic catalysis into technical processes, and several theoretical and experimental papers have been devoted to this problem. Lack of space prevents discussion of all this work here, and the Reviewer prefers to refer only to a few of the most recent and interesting publications[424-429].

Table 2. Changes in kinetic properties of immobilised enzymes at various levels.

No.	Kinetic level	Causes of changes	Nature of effect	Conditions for maximum changes
1	Apparatus	conc. gradients along apparatus; variation in concn. during operation	dynamic: depends on activity of enzyme prep.	thorough conversion of substrate, especially when a product is an activator
2	Material	concn. gradients at interface of soln. with enzymically active material	as above	high moduli $\kappa = E/\rho\beta c^*$
3	Particle	concn. gradients through enzymically active material	as above	high moduli $\lambda = R^2E/D^*$
4	Matrix	effect of matrix on activity coeff. of solutes; partition of substrate and activator between soln. and matrix	static: independent of activity of gel	charged matrix; hydrophobic matrix when substrate hydrophobic
5	Molecule	direct action of matrix on conformation of protein macromolecule and on active centre	as above	not generalised

*E = activity of enzyme preparation; ρ = specific surface of material; β = mass-transfer coefficient; R = radius (half-thickness) of material; D = diffusion coefficient of substrate (product) in the grain.

By solving numerically the appropriate equations following from the mass-transfer balance at the surface and within the particle we have shown[430] that the mass-transfer resistance at the interface does not affect the form of the Michaelis–Menten equation, but increases the apparent value of K_m. The main parameter determining the concentration drop in the mass-transfer layer, and responsible also for the increase in the apparent K_m, is the modulus

$$\varkappa = \frac{E}{\rho \cdot \beta \cdot c} \quad , \tag{4.1}$$

where E is the enzymic activity of the product, ρ the specific surface of the material, β the mass-transfer coefficient, and c the concentration of the substrate in the solution. When $\kappa \leqslant 0.1$, the mass-transfer resistance can be neglected. Values of $\kappa \geqslant 10$, on the other hand, correspond to processes which are completely controlled by external diffusion, i.e. to infinite K_m.

Rony[431] has described the kinetics in a multilayer material in the presence of mass-transfer resistance. The kinetics of mass transfer in an enzymically active membrane has been described also for the presence of an electrostatic potential[432], for inhibition of the reaction by a product[433], and for a membrane with two consecutive reactions[434].

Disregarding external diffusion, we can describe the kinetics of reactions in a particle (membrane) in a steady state by the general equation

$$\operatorname{div}(D \cdot \operatorname{grad} c) = g(c) \, , \tag{4.2}$$

where D is the diffusion coefficient of the product within the material, and $g(c)$ a function describing the dependence of reaction velocity on substrate concentration. The concrete form of this equation and hence the possibility of its analytical solution depend on the geometry, the material, and the function $g(c)$. It is of practical importance to solve Eqn. (4.2) for an infinite sheet (membrane), for a sphere, and in certain cases also for an infinite cylinder (fibre). In the case of a membrane, solution presents no difficulty for various forms of kinetic equation. Among the many papers giving solutions of this equation, mention must be made of that by Moo-Young and Kobayashi[435], who give a general solution for certain of the most often encountered forms of the function $g(c)$.

For a sphere Eqn. (4.2) becomes

$$\frac{d^2c}{dr^2} + \frac{2}{r} \cdot \frac{dc}{dr} = \frac{1}{D} g(c) \tag{4.3}$$

and can be solved analytically only for reactions of zero or the first kinetic order: only an approximate solution is available for real enzyme kinetics. In the case of Michaelis–Menten kinetics better approximate solutions of the same equation were obtained by Blum and Jenden[436], and subsequently developed by O'Sullivan[437]. Murray[438] solved the same equation by a single-perturbation method. The paper mentioned above[435] gives approximate solutions of Eqn. (4.3) for several forms of the function $g(c)$, and exact numerical solutions for Michaelis–Menten kinetics have been obtained by Keller[439] and by Kěstner[440,441].

From all the approximate and numerical solutions it may be concluded that the form of the fundamental kinetic equation is unaffected by either internal or external diffusion, but the apparent value of K_m increases. In this case the diffusion resistance may be measured by the dimensionless modulus

$$\lambda = R \sqrt{\frac{E}{K_m \cdot D}} \quad , \tag{4.3'}$$

where R is the radius of the grain, and K_m the Michaelis constant for the immobilised enzyme. To a first approximation the apparent K_m varies linearly with λ:

$$K_{m(\text{app.})} = K_m (1 + 0.018 \cdot \lambda) \, , \tag{4.4}$$

in which 0.018 is a coefficient determined from the numerical solutions. Thus diffusion resistance at the surface and inside the material itself leads to an increase in the apparent K_m. The smallest difference between observed and actual values of K_m is ensured by the lowest activity and minimum linear dimensions of the material. Increasing the diffusion coefficient by controlling the pore size and raising the mass-transfer coefficient by stirring assists the achievement of this aim.

Interaction of solutes with the matrix of an immobilised enzyme may lead to considerable changes in the concentration of the solutes within the carrier. A typical example is the variation in the effective hydrogen-ion concentration in an electrically charged matrix. The change in the effective pH is given by

$$\Delta \text{pH} = 0.43 \cdot e\psi/kT, \tag{4.5}$$

where ϵ is the charge on the proton, ψ the electrostatic potential in the matrix, k Boltzmann's constant, and T the

absolute temperature. A similar equation describes the variation of the concentration of an electrically charged substrate in the matrix. The applicability of the above equation has been shown by Goldman, e.g. in his review[7]. Agreement between calculated and experimental shifts in pH has been found[119] for trypsin trapped in silica gel.

The crowding of a hydrophobic substrate into a comparatively hydrophobic matrix has also been confirmed experimentally[129,442], but a quantitative description of this phenomenon is lacking. Laurent[443] examined the effect of a polymer medium on the activity coefficients of enzyme, substrate, and enzyme–substrate complex, which may produce a change in the apparent value of K_m.

Thus the microenvironment of the molecules of an immobilised enzyme is formed under the influence of various factors, which are quite often difficult to assess quantitatively.

2. Change in Activity and Stability of Enzymes

The main purpose of obtaining immobilised enzymes is to increase the integral activity of the enzyme defined by the total quantity of product obtained. The effectiveness of immobilisation η_{imm} is given by the ratio of the integral activities of the insoluble derivatives and of the initial enzyme:

$$\eta_{imm} = \frac{P_{imm}}{P_{sol}} \quad , \tag{4.6}$$

where P_{imm} is the quantity of product formed by the insoluble enzyme under practical conditions, and P_{sol} the corresponding quantity for the soluble enzyme.

We shall suppose that P_{sol} is determined mainly by the quantity of enzyme employed A_{sol} and the duration of the reaction t_{sol}. The latter is governed by the practical requirements of completing the reaction within acceptable periods. On the assumption that the activity of the soluble enzyme does not diminish significantly under the operating conditions during the period t_{sol}, we obtain for the effectiveness the formula

$$\eta_{imm} = \frac{A_{imm}}{A_{sol}} \cdot \frac{1}{t_{sol}} \int_0^{t_{imm}} [1 - f(t)]\, dt \quad , \tag{4.7}$$

where A_{imm} is the initial activity of the immobilised enzyme, t_{imm} its time of operation determined by its stability, and $f(t)$ the rate of inactivation of the immobilised enzyme under the working conditions.

The ratio A_{imm}/A_{sol} determines the retention of activity on immobilisation (or the "activity yield" of immobilisation), and will henceforward be denoted by γ. The remaining part of Eqn. (4.7)—the integral coefficient of prolongation of the action of the enzyme—is denoted by I_{pr}:

$$I_{pr} = \frac{1}{t_{sol}} \int_0^{t_{imm}} [1 - f(t)]\, dt \quad . \tag{4.8}$$

Equation (4.7) thus simplifies to

$$\eta = \gamma \cdot I_{pr} \quad .$$

The quantity I_{pr} is evaluated from two fairly arbitrary values of t_{sol} and t_{imm}, and can hardly be determined accurately. Immobilisation is regarded as advisable in practice for values of I_{pr} exceeding unity.

The coefficients γ can be regarded as the product of the coefficients α and β of immobilisation of the enzyme and development of activity:

$$\gamma = \alpha \cdot \beta = \frac{B_{imm}}{B_{sol}} \cdot \frac{E_{imm}}{E_{sol}} \quad , \tag{4.9}$$

where B_{sol} is the initial quantity of enzymic protein, B_{imm} the quantity of protein in the preparation obtained, E_{sol} the specific activity of the soluble enzyme, and E_{imm} the observed specific activity of the immobilised enzyme. The enzymic protein remaining in the reaction mixture or in the wash-waters can hardly be utilised, so that there is no need to practice to separate the coefficient γ into two components. However, such an approach is quite often used in elucidating the nature of immobilisation processes.

Complete bonding of a protein, when $\alpha = 1$, is well known in ion-exchange sorption, but α is considerably less than unity in most of the methods described for obtaining immobilised enzymes. The actual values of α depend significantly on the conditions of immobilisation, and it is extremely difficult to make any generalisations. In some cases, especially with adsorption, an enzyme washes out for weeks, which prevents accurate determination of α.

The coefficient β is also almost always smaller than unity, but an increase in enzymic activity has been demonstrated quite reliably in several researches[39,42,69,72,78,95,391,444]. An increase is often observed when enzymes are adsorbed, the activity sometimes increasing dozens of times[42,444]. This is fully consistent with the considerable conformational changes in a native protein detected by various methods on adsorption, which in other cases leads to almost zero values of β. Nor is the nature of such a phenomenon as the enhanced activity of trypsin on freezing or coagulation of its solutions entirely clear. These processes for enhancing enzymic activity have been patented[445,446].

An interesting example of an increase in the total activity of a jointly immobilised three-enzyme system has been reported by Mattiasson and Mosbach[345]. The increase is attributed to facilitation of the transfer of the product of the first reaction to molecules of the enzymes which effect subsequent stages.

The diminution in specific activity of enzymes on fixation may be due to chemical modification of certain groups in the active centre, shielding of the enzyme molecule or of its active centre from access by the substrate, and change in conformation of the protein macromolecule. Undesirable modification of the active centre on covalent immobilisation can be diminished by preliminary formation of a complex of the enzyme with an inhibitor, which is subsequently rinsed out of the preparation. The presence of shielding is proved by a difference in the activity of the preparation towards substrates of low and of high molecular weight. A linear decrease in observed activity with increase in the logarithm of the molecular weight of the substrate has been shown for certain immobilised enzymes[107,109]. The existence of this "sieve effect" has been demonstrated also by the restoration of the original activity on solubilisation of the matrix[313]. To eliminate undesirable effects of the matrix on the enzyme molecule it is advisable to effect attachment through an "extension bridge" or "arm" of 6–10 methylene groups[113,178,258,447-449]. Carriers with ligands immobilised "on the arm" are most suitable for use as affinity sorbents.

The reasons for the well known increase in stability of enzymes on immobilisation have been summarised by Zaborsky[450]. They are indirect, such as shielding of the enzymes from the action of lytic micro-organisms and elimination of autolysis (or proteolysis by proteinase impurities), owing to separation of the enzyme molecules on the carrier. These factors may partly explain the prolonged retention of enzymic activity, but the enhancement of resistance to the short-lived action of denaturing factors indicates the operation of molecular mechanisms of stabilisation. It is most often reported that immobilised enzymes resist the action of high temperatures[87,120,152,166,173,198,217,219,226,256,270,281,285,350,376,383].

It is interesting that Surovtsev et al.[265] have shown the presence of two fractions differing in thermal stability in an immobilised enzyme. However, other workers have reported a worsening of the temperature stability of enzymes[185,225,281,433,451-453]. Nevertheless, on the whole an increase in lability of enzymes is rarely encountered on immobilisation.

Extremely long periods of operation or retention of activity during storage have been reported for immobilised enzymes. A column of a gel containing invertase, for example, functioned for between 18 months and 3 years[419,454,455]. Specimens of certain covalently bound dehydrogenases have been used for more than a thousand analytical determinations[217].

It has been quite often reported that immobilised enzymes are less liable to be inhibited[120,249,452,456]. It is astonishing that they retain their activity in 4–8 M solutions of urea and other reagents which rupture hydrogen bonds[101,203,314,347]. The protective action may depend on the nature of the matrix: the immobilisation of trypsin on cyanogen bromide-Sephadex, for example, protects the enzyme from the action of urea, but bonding to agarose by the same method has no protective effect[347]. According to several workers[101,314] urea may increase the vulnerability of a substrate to attack by an enzyme, and may thus even increase the effectiveness of the latter. If a denaturing agent leads to a loss of enzymic activity, the bonds between the protein molecule and the matrix may help to restore the native three-dimensional structure[113,249,309,326,457].

Deoxyribonuclease immobilised on glass is able to develop its activity in the absence of the bivalent cations required by the soluble enzymes[465,458].

Immobilisation protects enzymes also from oxidation and denaturation on exposure to γ-rays[202].

3. Effect of Immobilisation on Fundamental Characteristics of Enzymes

Differences in the substrate specificity of immobilised and soluble enzymes can be explained by differences in the accessibility of the enzyme molecule to substrates of different molecular weights. This is true, for example, for proteolytic enzymes[107,209,219,268,294]. Such differences enable other peptide fragments to be obtained by means of immobilised proteinases than by the action of the soluble enzymes, and hence yield additional information in establishing the primary structure of proteins[294]. Immobilised amylases do not act on amylopectin[152], but form more products of low molecular weight from starch[459]. Immobilised luciferase is more sensitive to variation in the molecular weight of synthetic substrates[281]. Immobilisation of dextransucrase eliminates the factor controlling the type of glucosidic bonds formed, and therefore leads to more strongly branched products[103].

The increase in the Michaelis constant predicted by theory is observed in many cases. Increases by factors of 2–10 are found with creatine phosphotransferase[460], apyrase[274], cholinesterase[376], lactase[461], phosphomonoesterase[109], and glucoamylase[279] covalently fixed on cellulose. The same effect is observed with lipoxygenase attached to Sephadex[308], with adsorbed invertase[452] and glucoamylase[59], and also with many enzymes enclosed in microcellular fibres[419]. Phosphatase in a collodion membrane shows increases in K_m by factors up to 350.[433] For unknown reasons lyophilisation increases the apparent K_m of immobilised lactase[461]. When immobilised enzymes are used in a column, increasing the rate of flow of the substrate diminishes K_m,[5,256,452,462] in good agreement with the hypothesis that the apparent K_m depends on the conditions of mass transfer. Decreases of 90% or more are observed with glucose oxidase[391], succinate dehydrogenase[39], trypsin[292], bromelain[463], cholinesterase[129], and penicillinamidase[374]. This phenomenon can in principle also be explained by concentration of the substrate into the matrix. In particular, a 90% decrease in K_m is observed with bromelain covalently bound to carboxymethylcellulose only at low ionic strengths, whereas at high ionic strengths, when interaction between the substrate and the carboxy-groups of the carrier is suppressed, insoluble and soluble enzymes have the same Michaelis constant.

It is interesting that an improvement in thermal stability on immobilisation is sometimes accompanied by a fall in the temperature optimum of the enzyme[90,188,383,452]. However, the optimum temperature usually rises[169]. The apparent activation energy of an enzymic reaction most often remains unchanged, but increases[391] or decreases[169,383] have been shown in some cases. A change in form of the Arrhenius plot may occur[169].

The change in the pH dependence of enzyme activity depends on the carrier used. The optimum pH has become more acid with protocatechate dioxygenase[312], trypsin[292], chymotrypsin[63], invertase[89], urease[193], and penicillinamidase[374]; and more alkaline with lipoxygenase[306,344], trypsin[119,292], chymotrypsin[267,313], elastase[323], and invertase[188,369]. The shifts in the optimum pH are usually 0.5–1.0, and seldom reach 2. They are explained by the difference between the local pH of the microenvironment of the active centre of the enzyme and the pH measured in the bulk of the solution. This produces a change in the measured apparent values of pK_a for ionisation of the functional groups in the enzyme. The local microenvironmental pH is influenced by the charge on the matrix, the change in the charge on the substrate on coversion into the products, diffusion of substrate and product, change in the total charge of the protein on immobilisation, etc. The variation in the optimum pH of a two-enzyme system can be explained by the cooperative action of the enzymes[306].

Furthermore, immobilisation quite often produces a change in the form of the pH dependence. Broadening of the bell-shaped curve is observed with adsorbed succinate dehydrogenase[39], covalently bound acetylcholinesterase[194], pronase[190], enolase[169], adenosine deaminase[226], and also with many enzymes enclosed in cellular fibres[419]. Narrowing of the bell is observed with adsorbed glucoamylase[90] and with covalently bound papain[300], invertase[464], asparaginase[256], and penicillinamidase[374]. A detailed analysis of the reasons for the variation in the pH dependence will be found in the review by Goldman and his coauthors[7].

IV. APPLICATION OF IMMOBILISED ENZYMES

1. Use in Technical Processes

Most papers on immobilised enzymes are concerned with the preparation of heterogeneous enzymic catalysts for use in industrial technology. General aspects of the introduction of enzymic catalysis, prospects for its development, and possible difficulties are discussed in several reviews and symposia[17,19,465-469]. In the present Review we shall disregard specific aspects of the technical application of immobilised enzymes, and give only the principles underlying their use.

Processes in which immobilised enzymes are employed can be classified according to their purpose—(*a*) preparation of a required product as a pure substance or as a component of a mixture, (*b*) removal of an undesirable impurity from production or from industrial wastes, (*c*) chemical conversion of one optical isomer to facilitate resolution of a racemic mixture, or (*d*) concentration or isolation of a required substance by specific sorption. Table 3 gives examples of specific proposals for the application of immobilised enzymes. It includes only those suggestions which have been subjected to at least preliminary testing on a laboratory scale: it omits those for which such testing is lacking.

According to the Reviewer's information, processes for the separation of racemic amino-acids and for the production of 6-aminopenicillanic acid have been introduced on an industrial scale. In view of the comparatively high cost of immobilised enzymes we may expect in the near future the introduction firstly of processes in which expensive products—medicinals and biochemical reagents—are manufactured. The following stage may be large-scale processes in the food and chemical industries.

2. Application in Laboratory Investigations and in Medicine

Immobilised enzymes are being increasingly widely used in fundamental biochemical research as models of subcellular structures and for the study of steric effects on enzyme kinetics. Working models of active transfer have been produced by means of enzyme membranes[486,487]. Brown et al.[487] have effected the active transfer of glucose in a membrane containing hexokinase and phosphatase, and termed the phenomenon "vector catalysis". Certain other researches[281,327] can be regarded as an approach to the production of model biological systems.

The application of immobilised enzymes in practical analysis is also being extended. Several reviews have appeared on this topic[3,21,488-490]. Analytical applications of enzymes can be divided into three groups—(*a*) affinity chromatography, (*b*) determination of substrates in flow-type systems with optical transducers or by means of enzyme electrodes, and (*c*) determination of enzyme inhibitors.

Very many individual papers have been devoted to affinity chromatography, several reviews have been written[21,26,491,492], and Cherkasov has recently published a review in this journal[28]. Here only a few references are given to work in which an immobilised enzyme has been used as affinity adsorbent[291,346,485,493,494].

The use of enzyme electrodes offers a convenient method for determining substrates. They are made from a specific electrochemical transducer, whose sensitive surface is covered with a membrane containing the enzyme[235]. Enzyme electrodes are divided into two groups according to the principle on which they act, i.e. to the nature of the substance determined: (*a*) the product is determined; (*b*) the decrease in the diffusion of the substrate through the enzyme membrane is determined. Data on enzyme electrodes are given in Table 4. In most cases, however, the stability of such electrodes is inadequate, and they are not manufactured by industry, probably for this reason.

Table 3. Proposals for the introduction of enzyme catalysis into industrial technology.

Enzyme	Initial substance or mixture	Product and effect	Reference
	preparation of required product		
Amylase	starch	glucose, glucose syrup	34, 85, 282, 365, 470-473
Invertase	sucrose	invert syrup	89, 369, 441, 454, 455, 474
Proteinase	milk	curdled milk for cheese product	252, 322, 475, 476
Penicillinamidase	benzylpenicillin	6-aminopenicillanic acid	8, 31, 70, 336, 363, 374, 477, 478
Glucose oxidase	glucose	gluconic acid	7
Glucose isomerase	glucose	invert syrup	172, 479
Steroid dehydrogenase	cortisol	prednisolone	179
Oxynitrilase	benzaldehyde	mandelonitrile	100
Polynucleotide phosphorylase	mononucleotides	oligonucleotides, polynucleotides	342, 428
Laevansucrase	sucrose	laevans	103
Adenylate kinase	acetyl phosphate; adenosine diphosphate	adenosine triphosphate	480
NAD pyrophosphorylase		nicotinamide-adenine dinucleotide	71
	removal of undesirable impurities		
β-Galactosidase	milk, whey	hydrolysis of difficultly soluble and assimilable lactose	481, 482, 483
Protease	beer	hydrolysis of proteins which cause cloudiness	225, 423
Protease	antibiotics	hydrolysis of immunogenic protein impurities	355
Naringinase	citrus joices	removal of bitter taste of naringin	302
	resolution of racemic mixtures		
Aminoacylase	acetylated DL-amino-acids	free L-amino-acids and acetyl-D-amino acids	94, 102, 383, 484
	concentration by specific sorption		
Proteases	treated stock	natural protease inhibitors	144, 291, 346, 485

Substrates can be determined also in a system comprising measuring devices, a column of an immobilised enzyme, and a flow-type colorimeter (or fluorometer). The column can be replaced by a tube with the enzyme attached to its inner surface[217,200]. Such systems have been assembled for determining glucose (by means of glucose oxidase[136,137,254]), urea (by means of urease[210,254,255]), uric acid (by means of urate oxidase[254]), and ethanol and lactic and malic acids (by means of the appropriate dehydrogenases[217]).

Fundamentally similar types of equipment are used for determining enzyme inhibitors. Especially high sensitivity is achieved when fluorogenic substrates are used. This method has been employed to determine organophosphorus compounds which inhibit immobilised cholinesterase[126,142,268,500]. Besides high sensitivity, it has the further substantial advantage that, in contrast to chemical

methods of analysis, in which substances are determined by means of their functional groups, enzymic analysis enables toxic substances to be determined from their biological action, which consists precisely in the inhibition of certain key enzymes.

Another application of immobilised enzymes is to controlled proteolysis in determining the primary structure of proteins[159,224,501]. The electrophoretograms of certain enzymes can be developed by applying to the test strip a polyacrylamide sheet in which have been immobilised the enzymes and substrates required for the development[145]. Thus a film containing glucose 6-phosphate dehydrogenase is used to develop phosphoglucomutase, and a film containing these two enzymes to develop pyrophosphorylase.

Table 4. Principles of the action of enzyme electrodes.

Compound determined	Enzyme in membrane	Species determined by transducers	References
Glucose	glucose oxidase	O_2	135, 280, 495, 496
Urea	urease	NH_4^+	142, 161, 497, 498
Glutamine	glutaminase	NH_4^+	466
Asparagine	asparaginase	NH_4^+	147
L-Amino-acids	L-amino-oxidase	NH_4^+	140–142, 499
D-Amino-acids	D-amino-oxidase	NH_4^+	147
Ethanol	alcohol oxidase	H_2O_2	491
Amygdalin	β-glucosidase	CN^-	156, 157

The therapeutic effect of the parenteral introduction of soluble enzymes has been known for a long time. Among the many applications of enzyme therapy the greatest attention has recently been attracted by the treatment of certain malignant growths with asparaginase. But the success of enzyme therapy is very often brought to naught by the rapid decomposition of the enzyme in the living organism and because of the serious immunological reactions caused by the added enzyme as a foreign protein. A way to overcome these obstacles is to replace native enzymes by insoluble or soluble derivatives[502]. Immobilised enzymes can be introduced into the bloodstream, of course, only when their particle size does not exceed a few micrometres. In particular, the use of microencapsulated enzymes is recommended for these purposes. The effectiveness of encapsulated asparaginase[242,276,503,504], catalase[418,505], and streptokinase[277] has already been demonstrated by animal experiments. The injected enzymes possessed negligible immunogenicity and greater stability. But it is not yet clear how the organism will react to the prolonged introduction of considerable quantities of a polymeric carrier of the enzyme. It may therefore be advisable to use biodegradable polysaccharide carriers.

A fundamentally different way of using immobilised enzymes for the controlled variation of blood composition consists in passing the blood through an enzyme column outside the organism. It has been recommended, for example, that the cumbersome and expensive dialysis equipment of the "artificial kidney" should be replaced by a small column and immobilised urease[129,414,458]. The column should contain also a sorbent to bind the ammonia formed.

Many polymeric materials on contact with blood cause haemolysis, which is harmful to the human organism, and extremely dangerous thrombosis. In order to obtain improved implantation materials it has been recommended that polymers should be produced with proteolytic enzymes or proteins attached to them[151]. Materials of this type have been used for the treatment of burns and wounds[446].

The above examples show the possibilities of the use of immobilised enzymes in medical practice. However, the realisation of these possibilities is evidently still more complicated than the modification of technical processes or the establishment of new analytical methods.

NOTE ADDED IN PROOF

While the Review was being prepared for press the number of papers and patents on immobilised enzymes almost doubled, but it was impossible to include this material in the Review. Several symposia have also been held on this topic, among which it is necessary to mention the First All-Union Symposium on the Preparation and Application of Immobilised Enzymes[506] (held in Tallinn in May 1974).

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Principal Practical Applications of Ferrocene and Its Derivatives

A.N.Nesmeyanov and N.S.Kochetkova

A little more than 20 years have elapsed since the discovery of ferrocene (dicyclopentadienyliron) and during this period its chemistry has developed quite extensively. The present authors have seen the beginning of practical studies on the applications of ferrocene and its compounds.
The review does not deal with the applications of ferrocene-containing polymers.
The bibliography includes 81 references.

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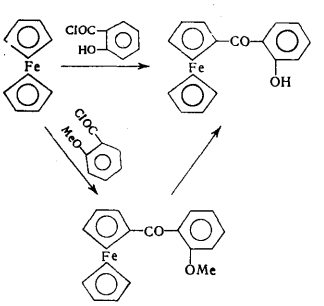
I. INTRODUCTION

The practical applications of ferrocene and its derivatives[1-4] can be grouped in the following main classes: absorbers of different types of radiation, including cosmic rays, regulators of combustion processes, highly effective non-toxic medicinal substances, components of various redox systems, and certain others.

At the present time many different ferrocene derivatives can be obtained in amounts necessary for practical applications. The wide assortment of commercial ferrocene derivatives which are available, for example, in the USA, is indicated by the advertisements of the American firm Research Organic Inorganic Chemical Corporation[5]. Ferrocene homologues, mono- and di-acylferrocenes, ferrocenecarboxylic acids, and many other compounds are quoted as available to a prospective buyer. The possibility of carrying out classical organic reactions with ferrocene[1-4] and the possibility of employing normal chemical apparatus give rise to the hope that the industrial chemistry of ferrocene derivatives will develop in the immediate future on the widest possible scale. A brief survey of the principal practical applications of ferrocene and its derivatives is given below.

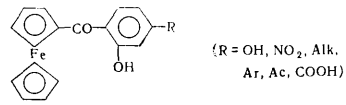
II. RADIATION ABSORBERS: AGENTS ENHANCING THERMAL STABILITY AND LIGHT RESISTANCE

Many aroylferrocene derivatives containing OH groups and other substituents in the *ortho*- or *para*-position of the aromatic ring proved to be effective inhibitors of the light-induced ageing of polymers. The best of these—*o*-hydroxybenzoylferrocene—was obtained by the present authors[6] from salicyl chloride and by Schaaf[7] from methoxysalicyl chloride with subsequent replacement of the methoxy-group by the hydroxy-group:



An interesting report has been published[8] according to which polymers containing *o*-hydroxybenzoylferrocene can be used to coat space ships to protect them from various types of radiation. The Table shows that the best effect is achieved when the inhibitor is introduced into a melamine-alkyd resin. The authors suggest that the action of this inhibitor is associated with its capacity to absorb radiation strongly in the range 200—500 nm; possibly the stabilising role is ensured not only by the ferrocene moiety of the molecule but also by the *o*-ketophenol residue, since agents enhancing light resistance, consisting of derivatives of benzoylbenzene and salicylic acid, are generally known. The replacement of one of the benzene rings of benzoylbenzene by the ferrocene residue enhances the inhibiting capacity of these substances.

Substituted *o*-hydroxybenzoylferrocenes with the substituent in the *para*-position are used to stabilise polyolefins[9].



(R = OH, NO_2, Alk, Ar, Ac, COOH)

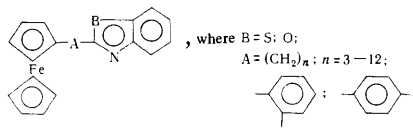
Products obtained by the condensation of ferrocene with ethyl methyl ketone[10] and many others[11] have also been proposed.

Agents enhancing the light resistance of polymers.

Polymeric resin	Inhibitor	Expt. PE*
Melamine-alkyd	1% 2-hydroxybenzoylferrocene	5000
Melamine-formaldehyde	5% 2-methoxybenzoylferrocene	375
Polyvinylbutyral	5% 2-hydroxybenzoylferrocene	320
Melamine-modified polyvinylbutyral	5% 2-hydroxybenzoylferrocene	275
Melamine-alkyd	1% dibenzoylferrocene	260
Silicone-alkyd	1% 2-hydroxybenzoylferrocene	200
Silicone-alkyd	5% 2-hydroxybenzoylferrocene	200
Silicone-alkyd	5% dibenzoylferrocene	200
Melamine-formaldehyde	5% 2-hydroxy-4-methoxybenzoylferrocene	154
Melamine-formaldehyde	5% dibenzoylferrocene	160

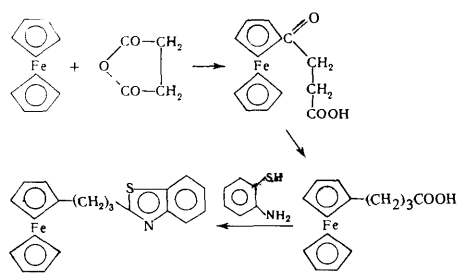
* PE are relative units of the efficiency of the ultraviolet light absorber, expressing its capacity to inhibit the decomposition of polymeric materials.

Heterocyclic ferrocene derivatives can be used as bleaching agents in the textile industry and as scintillators. For example, a number of patents[12] deal with compounds having the general formula



, where B = S; O;
$A = (CH_2)_n$; $n = 3-12$;

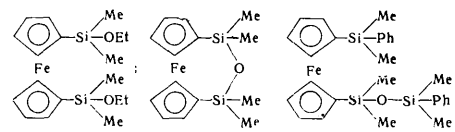
An example of the synthesis of one of them—1-ferrocenyl-3-benzothiazolylpropane—is given below:



The compounds indicated in Rei's Patent[12] include substituted naphthothiazoles, naphthoxazoles, anthrothiazoles, and anthroxazoles.

Stabilisers of another type are ferrocene derivatives of a number of elements. For example, tetraferrocenyl derivatives of Group IV elements are used as stabilisers (antioxidants)[13].

Organosilicon derivatives of ferrocene are used to enhance the thermal stability of organosilicon polymers[14].



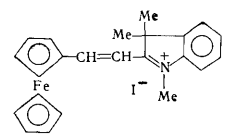
In their presence organosilicon materials withstand longer heating without appreciable signs of decomposition. A number of reports on this field were published recently[15-18].

III. FERROCENE DYES

1. Cyanine and Indolenine Dyes

Substances capable of absorbing light in the far visible region are of greatest interest among cyanine dyes: compounds of this kind are effective sensitisers, increasing the sensitivity of photographic materials with respect to light at longer wavelengths. These dyes contain as a rule fairly long polymethine chains and their stability in air is low; the period during which photographic materials based on them are serviceable does not amount to years, as is usually the case, but to days and even hours. These factors present considerable difficulties both in the synthesis and in the application of photographic materials of this kind. The introduction of a ferrocene chromophore into the molecule of a cyanine dye results in an appreciable bathochromic shift of the absorption bands in their spectra, which leads to new prospects for the development of the chemistry of ferrocene-containing organic sensitisers.

Titov et al. synthesised a green indolenine dye[19]:

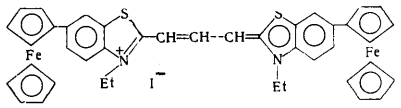


Possibly the α-ferrocenylcarbon atom of the conjugated chain plays the role of the second positively charged atom in the conjugated system, as was shown in studies by Nesmeyanov, Sazonova, and Postnov[20-22].

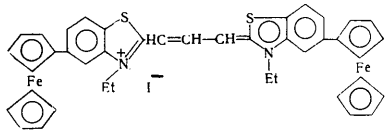
The interest in dyes of this type (sensitisers for light-sensitive layers) is illustrated by French and American patents[23,24].

Cyanine dyes (thiacarbocyanines) containing a ferrocenyl substituent in the benzene ring of benzothiazole and also dyes containing such a substituent in the main chain are known. These are blue-green substances, the spectra of

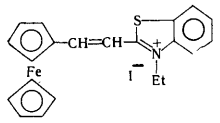
whose solutions contain absorption bands in the visible region (600–610 nm).[25]



λ = 608 nm;



λ = 592 nm;

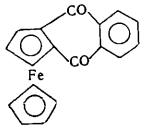


λ = 601 nm.

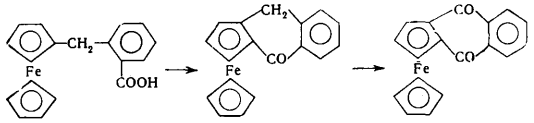
A negative reproduction material based on unsubstituted or substituted ferrocene has also been mentioned[26].

2. Ferrocene anthraquinone

Another type of ferrocene-containing dyes are compounds of the ferrocene anthraquinone series: here the anthraquinone molecule is modified by replacing one benzene ring by one cyclopentadiene ring of the ferrocene system:



Such compounds have been synthesised by Vil'chevskaya and the present authors[27–29] by the cyclisation of *o*-carboxybenzylferrocene with polyphosphoric acid,

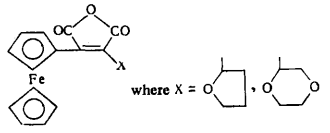


followed by oxidation using activated manganese dioxide. These compounds dye wool, silk, and artificial fabrics, giving various pink and brown shades without the use of a mordant, which is of great interest in the last instance.

3. Other Dyes

A United States patent[30] describes yellow pigments consisting of products of the condensation of ferrocene with phthalic anhydride which are insoluble and infusible up to 360°C.

Unusual compounds, described in a patent[31], were obtained by the condensation of ferrocene with maleic anhydride in tetrahydrofuran, dioxane, and other solvents in the presence of peroxides:



Possibly a polyrecombination reaction, similar to that achieved by Korshak and Sosin[32], takes place in this case.

It is interesting that the above substances have been patented not only as inks soluble in organic solvents but also as anticorrosion agents, pesticides, fungicides, and even as antidetonators.

IV. COMBUSTION REGULATORS (ANTIKNOCK-, ANTIFOULING-, AND ANTISMOKE-AGENTS, AND COMBUSTION CATALYSTS)

There is a fairly extensive, mainly patent literature on these applications of ferrocene and its derivatives. It is noteworthy that antismoke[33], antifouling and antiknock[34], and catalytic properties[34–37] are characteristic of the same compounds.

Various classes of organic derivatives of ferrocene have been mentioned in patents: ferrocene[34,35], ferrocene homologues[39–41], vinylferrocene[42], cyclopentenylferrocene[42], carbinols[35], formylferrocene[35], alkenylferrocenes[36,38], ferrocenecarboxylic acid[35], and certain other compounds[35]. Apart from data on individual compounds, mixtures with two and more components have been described[36]. For example, mixtures of ferrocene or its homologues with cyclopentadienylnitrosylnickel containing 85–50% $C_{10}H_8R_2Fe$ (where R = H, Me, or Et) and 15–50% C_5H_5NiNO and a mixture of ferrocene with cyclopentadienylthallium[38] are used as antidetonators. However, so far ferrocene and its derivatives have not yet been generally recognised as antiknock agents. The reason for this is that they all suffer from a common disadvantage—the *deposition* of iron(III) oxide as the combustion product on the components of the engine and primarily on the sparking plugs of a carburator engine greatly impairs the working parameters and accelerates the wear of such components[41].

Fuel compositions based on nitrocellulose with added ferrocene (1–2%), which exhibit a high plasticity[43], and also compositions containing 30–70% of ferrocene, benzoylferrocene, or dibenzoylferrocene in the presence of nitric acid[44] have been proposed in British patents.

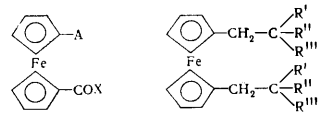
Pyrotechnic compositions based on triferrocenylphosphine and mercury nitrate have been obtained[45].

V. MEDICINAL SUBSTANCES

Iron enters into the composition of haemoglobin—the basis of the vital activity of the organism. For this reason various inorganic iron preparations were used previously to treat diseases associated with iron deficiency in the organism. However, most of these are relatively inefficient and have many side effects (irritation of the gastrointestinal tract and others).

Ferrocene derivatives proved to be much more effective and relatively non-toxic medicinal substances.

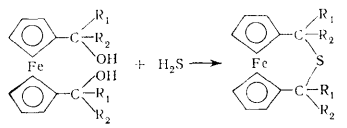
Ferrocene homologues described in patents possess anti-anaemic properties[46–48]. Homologues containing secondary and tertiary alkyl and cyclohexyl groups joined to ferrocene via a methylene unit have been obtained from the corresponding ketones:



(A = H or COX)
(X = s- or t-alkyl or C_6H_{12})

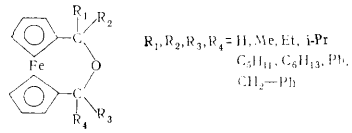
Homologues with the same alkyl substituents linked directly via a secondary or tertiary carbon atom to the cyclopentadiene ring have been obtained by the direct alkylation of ferrocene[49]. These are thick reddish liquids, which are introduced into the organism in the form of capsules, oil emulsions, and other medicinal forms; the application of ferrocene derivatives together with anticoagulants (nitro-compounds, tetrahydrofuran, and others) has also been mentioned in a patent[48].

Ethers and thioethers derived from ferrocene have been proposed in the USA for the same purposes. For example thioepoxyferrocene[50] obtained by the reaction of carbinols with hydrogen sulphide,



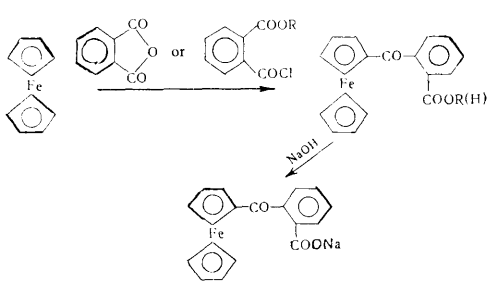
and a number of other compounds[51,52] have been suggested.

Epoxyferrocene[53,54], which combines simultaneously anti-anaemic and anticoagulant activities in the organism, has been recommended:



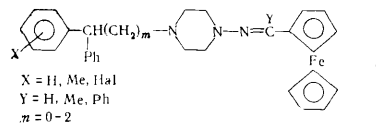
A characteristic feature of the ferrocene derivatives listed above is their insolubility in water. Possibly this is why they require the simultaneous employment of anticoagulants, very toxic compounds such as nitro-derivatives, tetrahydrofuran, and others being recommended.

Until recently medicinal preparations derived from ferrocene were unknown in the world market. The first such preparation is *"ferrocerone"*, which was synthesised in the USSR. It is the sodium salt of *o*-carboxybenzoylferrocene and was developed by Vil'chevskaya and Palitsyn together with ourselves at the Leningrad Institute of Haematology and Blood Transfusion[55-61]. It was synthesised from ferrocene and the half-ester half-chloride of phthalic acid and also from ferrocene and phthalic anhydride[58,59] according to the following scheme:

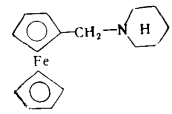


Ferrocerone is soluble in water, is non-toxic, and is readily assimilated by the organism; it exhibits a wide therapeutic spectrum. It can be used to treat various forms of iron deficiency anaemia[55,57], a severe infection of the nasopharynx[56], and others. Ferrocerone is manufactured in the form of tablets and is administered orally, which is very convenient for the patient, particularly when the gastrointestinal tract is affected.

Ferrocene derivatives have not been recommended solely for the treatment of various iron deficiency diseases. It has been suggested that many other diseases be treated with ferrocene derivatives. For example, an antiulcer preparation has been recommended[62]:



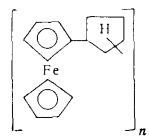
The physiological activity of aminoferrocene derivatives[63] having the composition



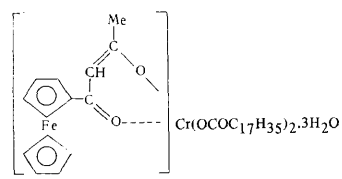
has also been briefly mentioned.

VI. ELECTRON-EXCHANGE RESINS AND OTHER REDOX SYSTEMS

The capacity of ferrocene to undergo reversible oxidation-reduction made possible the practical application of this system in various redox processes. The first example of organoiron electron-exchange resins was polyferrocenylcyclopentene, which we obtained by the decomposition of ferrocene in the presence of aluminium chloride[64,65]:



This oligomer is insoluble in water. In oxidation by potassium dichromate in the presence of sulphuric acid the capacity of this redox resin under static conditions proved to be 2.00—2.38 milliequivalents per gm. of air-dry resin. It was reduced with ascorbic acid. The cycle was repeated three times without appreciable effect on the capacity. At the present time the chemistry of ferrocene-containing polymeric redox resins has developed fairly extensively[66-71]. A ferrocene electrode[72-76] as well as ferrocene-containing antistatic agents are known. A mixed chromium chelate salt derived from ferrocenoylacetone,



has been proposed as an antistatic agent[77,78]. The possible applications of organometallic compounds in electronics are described in a monograph[79].

Thus the known practical applications of ferrocene and its derivatives can be grouped in a number of classes. In one of them the applications are based on the ability of ferrocene and its derivatives to absorb various types of radiation. A ferrocene chromophore imparts a bright

colour ranging from yellow-orange to blue-green and as a rule these products are firmly fixed on various materials, including synthetic fabrics. All this makes it possible to employ ferrocene derivatives as dyes of a new type and also as photographic materials and light sensitisers.

Another important application is based on the ability of ferrocene and its derivatives to regulate various combustion processes. This leads to the possibility of using them as antismoke, antifouling, and antidetonation agents and also as combustion catalysts.

Iron is a component of the organism important for its vital activity. A deficiency of this element leads to severe illnesses. The low toxicity of ferrocene and its derivatives and their ability to treat diseases associated with iron deficiency in the organism as well as many other ailments gives rise to the third important practical application—medicinal preparations based on ferrocene derivatives.

Ferrocene is capable of undergoing reversible oxidation–reduction under mild conditions. As a result of this property, ferrocene derivatives sparingly soluble in water have been proposed as electron-exchange resins (redox resins) and also as other redox systems.

In conclusion of this brief review, we may mention that cyclopentadienyl and other derivatives of almost all transition and non-transition metals are now known. Many of these compounds are quite stable in air and there are easy methods for their synthesis.

Thus there are very many possible practical applications of these compounds in a wide variety of fields[80,81].

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Ferrocenophanes

G.B.Shul'pin and M.I.Rybinskaya

The review deals with unusual cyclophanes of the ferrocene series, which are known as ferrocenophanes. The methods of synthesis of ferrocenophane systems are described and the dependence of their properties and structures on the type and length of the bridge is discussed. Special attention has been devoted to the employment of ferrocenophane models for the solution of a number of theoretical problems in ferrocene chemistry. The stereochemistry and practical applications of ferrocenophanes are discussed. Other organometallic analogues of cyclophanes, only a limited number of examples of which are so far known, are also described. The literature up to 1973 inclusive has been covered.
The bibliography includes 231 references.

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I. INTRODUCTION

Ferrocenophanes are ferrocenes in which the two cyclopentadienyl rings are linked by a bridge consisting of several carbon atoms or atoms of other elements. However, the name ferrocenophane is also sometimes given to compounds in which the carbon atoms of the same cyclopentadienyl ring are linked by a bridge. The properties of such compounds differ little from those of disubstituted homoannular ferrocenes and are not dealt with in the present review.

Attempts to synthesise the ferrocenophane system were undertaken soon after the discovery of ferrocene since, it was evident that a bridge between the two rings should introduce interesting modifications into the properties of the molecule. The first ferrocenophane was synthesised in 1957 and since then studies in this field are continually attracting attention, since ferrocenophanes proved to be useful models for the investigation of the structural, stereochemical, and certain theoretical problems. The synthesis of ferrocenophanes with a single bridge has developed fairly widely so that the simplest of them are quite readily available and have been tested for practical purposes. On the other hand, the synthesis of ferrocenophanes with a number of bridges presents considerable difficulties.

The study of the properties of ferrocenophanes has shown that among them compounds with small bridges are particularly interesting. Such ferrocenes do not simply combine the characteristics of ferrocenes and cyclophanes, the properties of both being transformed in a specific manner. In contrast to ferrocenophanes, the analogous compounds with other transition metals (titanium, cobalt, nickel, and chromium) are so far represented only by isolated examples. They too are discussed in the present review.

The only previous review on ferrocenophanes[1] deals with the literature up to 1966, but since then many new ferrocenophanes have been synthesised and the range of interest shown in this field has greatly expanded; there is therefore no doubt about the need for a new review. We may note that isolated data on ferrocenophanes for the period 1964–1972 may be found in annual reviews of literature on ferrocene[2-10].

According to the proposed nomenclature[1,11], all ferrocenophanes can be divided into two groups. The first includes compounds where within the limits of one ferrocene nucleus the rings are linked by one or several bridges. Derivatives where two or more ferrocene nuclei are linked by chains of atoms, so that each ferrocene fragment constitutes as it were a bridge in relation to the other, may be assigned to the second group. For compounds of the first type, the length of the bridge is represented by a number in square brackets or by several numbers in square brackets if there are several bridges. The positions of the bridges are indicated by numbers in round brackets. The numbering begins with the longest bridge, proceeds along the bridge and completely around the ring, and then along the next bridge (in order of decreasing length of the bridges). The heteroatoms are designated by a number indicating their position in the bridge. For compounds of the second type, a set of numbers indicating the lengths of all the bridges joining the ferrocene nuclei is indicated within a single set of square brackets. A new nomenclature, common to all phanes (cyclophanes and metallocenophanes), was proposed recently[12].

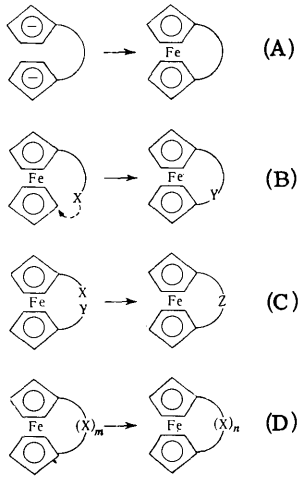
II. METHODS OF SYNTHESIS OF FERROCENOPHANE SYSTEMS†

There are several fundamental approaches to the synthesis of ferrocenophanes. The first makes it possible to obtain a ferrocenophane together with the synthesis of the

† A. A. Pogrebnyak, a Diploma student at Moscow State University, took part in writing this chapter.

ferrocene nucleus and may be called the direct method (see Scheme 1, A).

Scheme 1



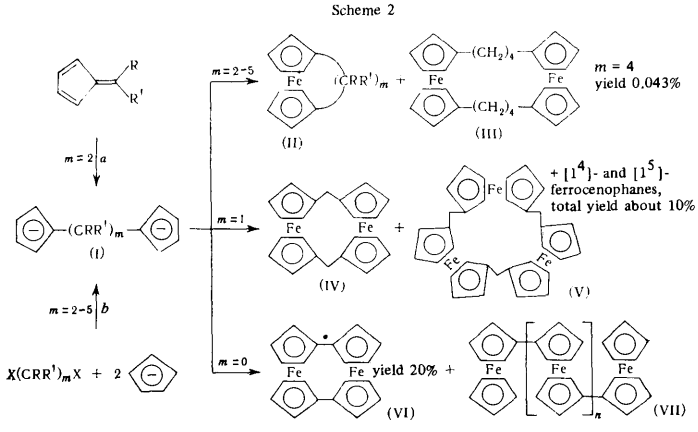
Another method consists of intramolecular substitution in the second cyclopentadienyl (CPD) ring; a group entering into the composition of a substituent in the first ring (B) is then involved in the substitution. In the third method the bridge may be formed by the closure of two heteroannular substituents (C). Finally there is a possibility of a transition from [*m*]- to [*n*]-ferrocenophanes ($m < n$ or $m > n$) by the expansion or contraction of the bridge (D). In addition other special methods used in specific instances are also known.

Naturally each of the fundamental approaches described has many different versions. In the present review all the methods are classified according to these four fundamental types.

A. DIRECT SYNTHESIS

Direct synthesis is understood as the formation of the ferrocenophane system from dicyclopentadienide dianions of type I (Scheme 2) where both cyclopentadienyl rings are linked by a bridge beforehand. In this case ferrocenophanes are obtained by the same method as the usual ferrocenes (the reaction is most often carried out in the presence of anhydrous $FeCl_2$).

Scheme 2



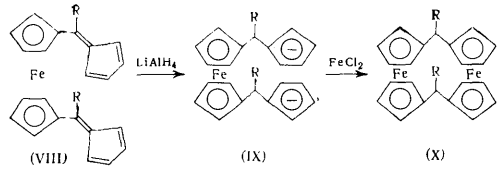
Type (I) dianions are usually obtained by the reaction of the cyclopentadienide anion with the corresponding dihalogeno-compounds (Scheme 2, method *b*). Thus the reaction of the cyclopentadienide anion with $\alpha\omega$-dihalogenoalkanes ($m = 2-5$) yields hydrocarbons in which the two cyclopentadiene rings are linked by a chain of methylene units and which are converted into the dianions (I) after appropriate treatment. The reaction of (I) with $FeCl_2$ makes it possible to synthesise bridged ferrocenes but the yields in this process are very low (with the exception of the case where $m = 2$) and therefore only the synthesis of [2] ferrocenophane is of preparative importance. Naturally the yields of [*m*] ferrocenophanes fall sharply with increase of chain length (Table 1), while the amount of polymeric products increases.

Table 1. Type (II) ferrocenophanes.

No.	*m*	R	R′	Method of synthesis	Yield, %	M.p. (b.p.), °C	Refs.
1	2	CH_3	CH_3	*a*	low	168—169	13,14,16
2	2	CH_3	$CH(CH_3)_2$	*a*		(150—160/1.2)	14
3	2	CH_3	$CH_2CH(CH_3)_2$	*a*		(170—180/2—4)	14
4	2	CH_3	$CH(C_2H_5)(CH_2)_3CH_3$	*a*		(113—123/5)	14
5	2	CH_3	C_6H_5	*a*		(138—165/3—5)	14
6	2	H	H	*b*	50	104—107	15,16
7	3	H	H	*b*	2.5	106—107	17
8	4	H	H	*b*	0.053	58—59	17
9	5	H	H	*b*	0.025	61—62	17

A convenient method for the preparation of dianions with $m = 2$ consists of the interaction of fulvenes with sodium (Scheme 2, method *a*). A whole series of [2] ferrocenophanes containing various substituents in the bridge (Table 1), particularly the widely investigated 1,1,2,2-tetramethyl[2]ferrocenophane, have been synthesised by this procedure.

For $m = 1$ [dianion (I) is obtained from methylene dihalide and the cyclopentadienide anion], the reaction does not lead to [1] ferrocenophane, since the unduly large strain and the mutual inclination of the rings must have an effect on the molecule of this compound; the product is a mixture of [1^n]ferrocenophanes, the lowest members of which are (IV) and (V) (Scheme 2)[18-20]. The molecular weights of all these compounds have been determined mass-spectrometrically. The dianion (IX), which can also be obtained from difulvene (VIII) on treatment with $LiAlH_4$, is formed as an intermediate in this reaction. The interaction of (IX) with $FeCl_2$ yields [1,1]ferrocenophane (X).[21]



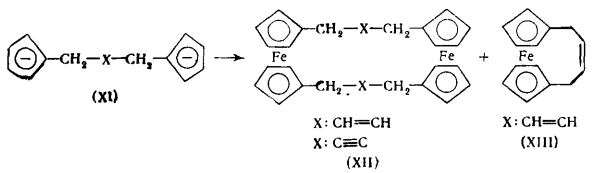
When $m = 0$, the reaction of the dicyclopentadienide dianion (I) with $FeCl_2$ in tetrahydrofuran (THF) gives [0,0]ferrocenophane (VI) together with the polymeric polyferrocenyl (VII).[22]

[4,4]Ferrocenophanes containing double and triple bonds in the bridges [compounds (XII)] have been obtained recently[19]. When *trans*-1,4-dichlorobut-2-ene is used as

the starting material, the monomeric derivative (XIII) is formed in addition to (XII). It is interesting that the ^{1}H NMR spectra indicate a *cis*-disposition of the methylene groups of the bridge relative to the double bond (the spin–spin splitting of the olefinic protons is 10.4 Hz).

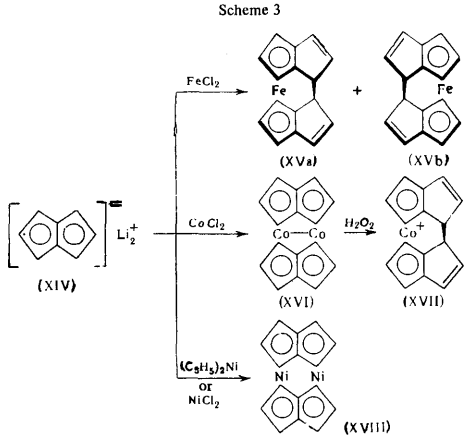
Ferrocenophanes containing silicon atoms in the bridge have been obtained from the corresponding dianions, for example from $[C_5H_5(CH_3)_2SiSi(CH_3)_2C_5H_5]^{2-}$.[23,24]

The direct method has also been used for the synthesis of titanocenophane. The reaction of the dianion (I) ($m = 1$, R = R′ = H) with $TiCl_4$ gave a 30% yield of 1,1′-methylenetitanocene dichloride[19]. The cyclopentadiene rings in this compound are inclined relative to one another, but the non-bridged initial titanocene dichloride has the same structure and therefore the introduction of the monomethylene bridge does not distort the geometry of the molecule, in contrast to [1]ferrocenophane (which has still not been synthesised). Bridged derivatives of titanocene with a silicon or germanium atom in the bridge have been recently synthesised by a similar procedure[25].



Several different bridged metallocene derivatives have been synthesised by Katz and coworkers[26,27] using the dianion (XIV) (Scheme 3).

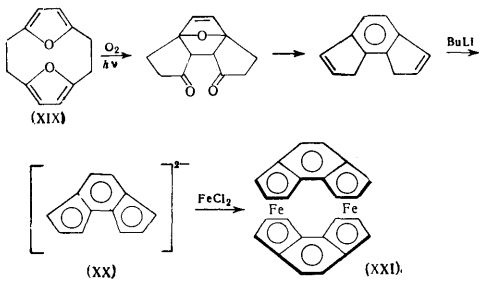
Scheme 3



The structures of compound (XV)[28] and (XVII) are similar to that of "bis-(π-azulene)iron"[29,30] (see below).

The two cyclopentadienide anions from which [*m*,*n*]-ferrocenophanes are obtained may be linked not by one but by two chains[31] and by condensed benzene [the dianion (XX)][32] or naphthalene[33] rings. The dianion (XX), obtained by the photochemical oxidation of furanocyclophane (XIX), gives rise to the interesting ferrocenophane (XXI) on treatment with $FeCl_2$.[32] The corresponding nickel compound was obtained similarly[34]. A dicobalt derivative analogous to the ferrocenophane (VI) has been synthesised recently[35].

A single instance of the synthesis of bisarenemetal π-complexes, in which two benzene rings are linked by a bridge, is known. The reaction of *trans*-stilbene with $CrCl_3$ in the presence of triethylaluminium results in the formation of 1,1′-tetramethylene-βγ-diphenylbisbenzenechromium, which has been isolated as the iodide salt. Its pyrolysis yields 1,2,3,4-tetraphenylbutane, which confirms the proposed structure[36].



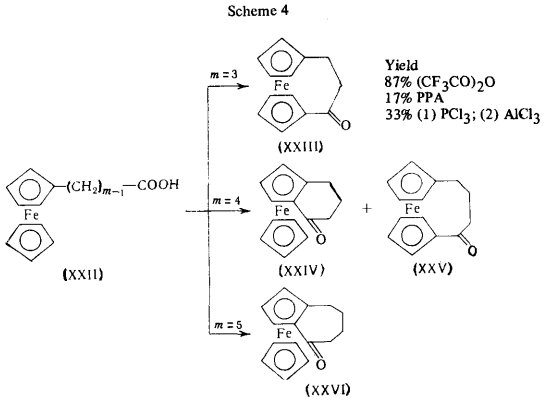
B. INTRAMOLECULAR SUBSTITUTION IN THE CYCLOPENTADIENE RING

This procedure has many different versions and leads both to ferrocenophanes containing a purely hydrocarbon bridge and to [*m*,*n*]ferrocenophanes. The intramolecular cyclisation of ferrocenylpropionic acids, whereby [3]ferrocenophanes can be obtained, has been developed in greatest detail[37–72].

1. Intramolecular Acylation

Rinehart and Curby obtained the first ferrocenophane (XXIII)[37] by the cyclisation of β-ferrocenylpropionic acid (XXII) in the presence of polyphosphoric acid (PPA). However, it was found that the method has a very limited applicability and is suitable only for the synthesis of [3]ferrocenophanes[39,40]. Thus, whereas the cyclisation of γ-ferrocenylbutyric acid still gives a small yield of the corresponding [4]ferrocenophan-1-one[41], acids with a longer methylene chain yield exclusively products of homoannular cyclisation or polymers (Scheme 4)[42–46].

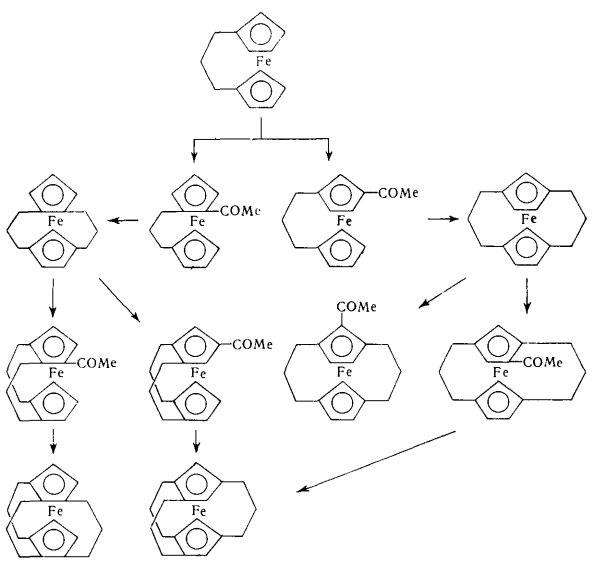
Scheme 4



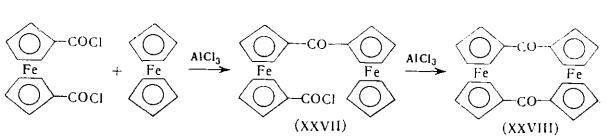
The reaction does not proceed via a heteroannular mechanism in all cases, even for $m = 3$. Thus, when there is a fairly bulky substituent in the cyclopentadiene ring or in the propionic acid chain, a considerable amount of the homoacylation product is formed[47–51]. Nevertheless [3]ferrocenophanes have been obtained mainly by this

method hitherto. The initial β-ferrocenylpropionic acid (XXII, $m = 3$) can be conveniently synthesised from acetylferrocene[39] or ferrocenealdehyde[47,52-54] according to the following schemes respectively: $FcCOCH_3 \rightarrow FcCOCH_2COOC_2H_5 \rightarrow FcCH_2CH_2COOH$ or $FcCHO \rightarrow FcCH=CHCOOH \rightarrow FcCH_2CH_2COOH$. The [3]ferrocenophan-1-one obtained by the cyclisation of β-ferrocenylpropionic acid is readily reduced to [3]ferrocenophane by a mixture of $LiAlH_4$ and $AlCl_3$.[55] By consecutive application of the above stages and of reduction, Rinehart et al.[47] obtained ferrocenophanes with two and three bridges. One of the possible syntheses is illustrated in Scheme 5. [3]Ferrocenophanes with a number of bridges were obtained similarly by Schlögl and coworkers[53,56-58]. Two-bridge ferrocenophanes containing three-, four-, and five-membered bridges in various combinations have been described[59-61]. It is noteworthy that the synthesis of multibridge ferrocenophanes consists of many stages and is very laborious. French chemists have made a detailed study of the cyclisation of substituted β-ferrocenylpropionic acid[45,46,48-51,62-72].

Scheme 5



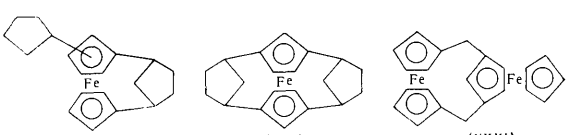
The synthesis of [1,1]ferrocenophanes (XXVIII) by the Friedel–Crafts reaction is closely related to the cyclisation of aliphatic ω-ferrocenyl acids discussed above[73,74]. This reaction proceeds via the formation of the intermediate (XXVII)[75], whose geometry promotes electrophilic attack on the second ring. Compound (XXVIII) has also been obtained from ferrocenecarboxylic acid chloride[76]. The cyclisation of *o*-carboxybenzeneferrocene [probably *o*-carboxybenzoylferrocene [Ed. of Translation)] does not lead to ferrocenophanes[43,44].



(XXVII) (XXVIII)

2. Other Examples of Substitution in the Cyclopentadiene Ring

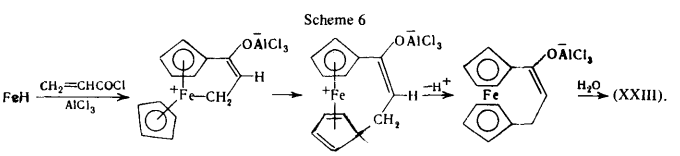
Bridged ferrocenes can be formed not only in intramolecular acylation but also in the heteroannular alkylation of ferrocene by olefins. The ferrocene molecule is cleaved by hydrogen fluoride[77] or phosphoric acid[78] with liberation of cyclopentadiene, which then alkylates other ferrocene molecules. In the simultaneous intramolecular alkylation of both rings the product is a ferrocenophane which can also be obtained by the reaction of ferrocene with anhydrous $AlCl_3$ in benzene[79] or in methylene dichloride[80], or by treating ferrocene with zinc chloride[81,82]. Apart from the ferrocene with a single bridge, the derivative (XXIX) and the ferrocene (XXX) with two bridges are also formed[83]. The structures of these compounds have been demonstrated by chemical methods and by ^1H NMR[83]. By alkylating ferrocene with methylene dichloride, Neuse and coworkers obtained the ferrocenophane (XXXI) together with polymeric products[80]. Apart from other products, the reaction of ferrocene with formaldehyde in the presence of acids gives the ferrocenophane (IV).[84]



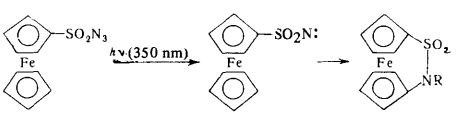
(XXIX) (XXX) (XXXI)

An interesting and synthetically important reaction was recently described by Turbitt and Watts[85]. When ferrocene reacts with acryloyl chloride, [3]ferrocenophan-1-one (XXIII) and propionylferrocene are formed, the ratio of the products depending on the reaction temperature. When the reaction is carried out at −78°C, compound (XXIII) is obtained in 40–60% yield. The sequence of stages leading to (XXIII) proposed by the authors is illustrated in Scheme 6.

Scheme 6



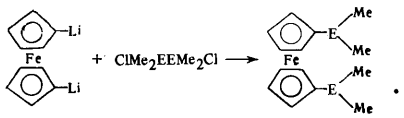
The nitrene (XXIII) formed when compound (XXXII) is irradiated in benzene attacks the second ring, giving the ferrocenophane (XXXIV) with two heteroatoms in the bridge[86]:



(XXXII) (XXXIII) (XXXIV)

Organometallic and halogeno-derivatives of ferrocene have been used to synthesise ferrocenophanes. Thus several bridged compounds containing silicon or germanium atoms in the bridge [for example (XXXVI) with E = Si or Ge] have been obtained by the reaction[23,87] of 1,1-dilithioferrocene (XXXV) with the corresponding dichlorides.

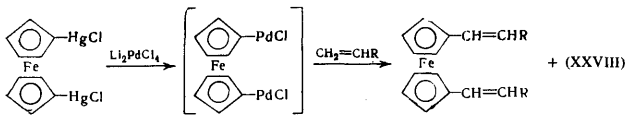
Some of these ferrocenophanes have also been obtained by the direct method (A).



(XXXV) (XXXVI)

The interesting 1,2,3-trithia[3]ferrocenophane is formed when compound (XXXV) reacts with sulphur[88]. Treatment of dibenzylferrocenylacetonitrile with butyllithium leads to the substitution of one of the hydrogen atoms of the free cyclopentadiene ring by lithium, and, after intramolecular attack on the CN group, 1-aza-3,3-dibenzyl[3]ferrocenophan-1-ene is formed[89]. [0,0]Ferrocenophane (VI) has been obtained by the reaction of (XXXV) with cobalt chloride, or of 1,1'-diodoferrocene with copper[90], or by heating a mercury derivative of ferrocene with silver[91]. A copper derivative of 1-bromo-1'-ethynylferrocene was also used to synthesise [2,2]ferrocenophane-1,13-diyne[92]. In a study of the addition of ferrocene to olefins in the presence of palladium salts, Kasahara et al. observed the formation of [0,0]ferrocenophane (VI).[93] When this reaction is carried out in the presence of carbon monoxide, [1,1]ferrocenophane-1,12-dione (XXVIII) is formed[94] (Scheme 7).

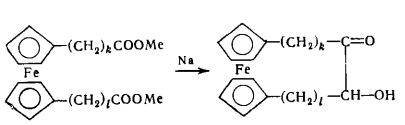
Scheme 7



C. CYCLISATION INVOLVING TWO HETEROANNULAR SUBSTITUENTS IN THE FERROCENE NUCLEUS

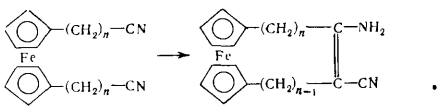
1. Cyclisation of 1,1'-Disubstituted Alkylferrocenes with ω-Functional Groups

The acyloin cyclisation developed by Schlögl and Seiler[95,96] is a universal method for the preparation of ferrocenophanes with a bridge of any length. In this procedure a 1,1'-di-(ω-methoxycarbonylalkyl)ferrocene (XXXVII) is condensed in the presence of finely divided sodium in boiling xylene. Acyloin [m]ferrocenophanes with m = 4, 6, 8, 9, or 10 have been obtained. Tnis method is less suitable for the synthesis of ferrocenophanes with an odd number of carbon atcms in the bridge, since in this case the required starting materials are the asymmetric diesters (XXXVII, $k \neq l$), which are difficult to obtain.



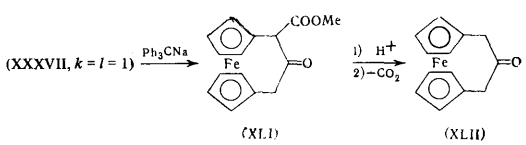
(XXXVII) (XXXVIII)

The cyclisation of the corresponding symmetrical dinitriles (XXXIX, n = 1, 2, 5, or 7)[97,98], which can be obtained by various methods[98-101], has been suggested for the synthesis of ferrocenophanes with an odd value of m. The sodio-derivative of N-methylaniline or (for n = 1) methylmagnesium iodide were used as catalysts. This method made it possible to synthesise macrocyclic [11]- and [15]-ferrocenophanes[98]:



(XXXIX) (XL)

The possibility of employing the Dieckmanncyclisation for synthesising ferrocenophanes has so far been demonstrated in only one instance[102]. Under the influence of triphenylmethylsodium, the diester (XXXVII, $k = l = 1$) is converted into the bridged ferrocene (XLI), which decarboxylates to the ketone (XLII) after hydrolysis:

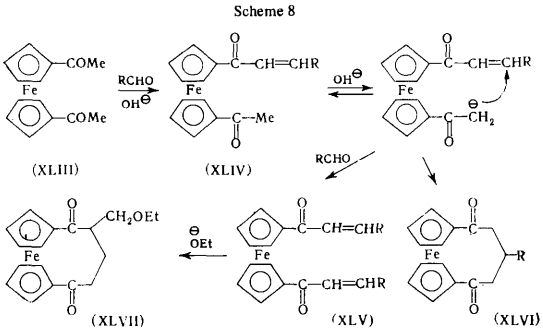


(XLI) (XLII)

2. Cyclisation with the Intermediate Formation of a Carbanion and Its Attack on a Double Bond

In 1960 Hauser and coworkers isolated two products after the reaction of 1,1'-diacetylferrocene (XLIII) with benzaldehyde in the presence of alkali: the red 1,1'-dicinnamoylferrocene (XLV, R = C_6H_5) and a yellow product to which the structure of a bridged diketone (XLVI, R = C_6H_5) was attributed (Scheme 8).[103] The ratio of the products depends on the amount of benzaldehyde introduced into the reaction. Thus, when 1 mole of benzaldehyde per mole of (XLIII) is used, the yield of (XLV) is 6–13% and the yield of the ferrocenophane (XLVI) is fairly high (66–68%).

Scheme 8



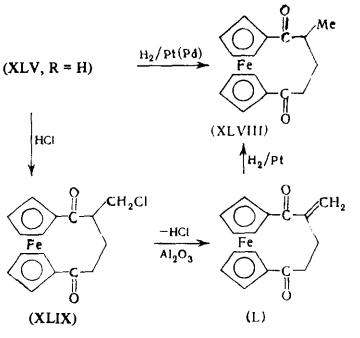
With increase of the amount of aldehyde to 6 moles, the yield of (XLVI) falls to 5% and the amount of (XLV) increases to 75%. Furdik et al. soon showed that not only benzaldehyde but also other aromatic[104-106] and aliphatic aldehydes[107] can be used in this reaction. It was found that, for aliphatic aldehydes and m-nitrobenzaldehyde, the yields of ferrocenophanes are significantly lower (about 10%) and that only the dicinnamoyl derivatives (XLV) are formed in the reactions with o- and p-nitrobenzaldehydes. The condensation also occurs under the influence of acid catalysts[108].

The formation of ferrocenophanes from various 1,1-diacylferrocenes was investigated in later studies[109-111].

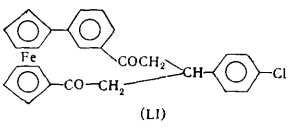
The ferrocenophane (XLVI, R = H) has also been obtained from 1-acetyl-1′-acryloylferrocene (XLIV, R = H)[112,113] or from 1-acetyl-1′-β-chloropropionylferrocene[114], which confirms the scheme proposed for the formation of the ferrocenophane. It was also found[115] that 1,1′-dicinnamoylferrocene (XLV, R = C_6H_5) undergoes retroaldol condensation under the influence of a base with formation of compound (XLIV, R = C_6H_5), which then condenses to (XLVI, R = C_6H_5) in 92% yield. Barr and Watts showed[113] that the reaction of 1,1′-diacetylferrocene with formaldehyde in aqueous ethanol solution of sodium hydroxide yields as the main product the ferrocenophane (XLVII), formed by the condensation of 1,1′-diacryloylferrocene (XLV, R = H).

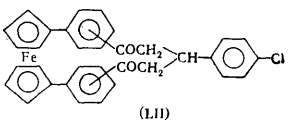
It is interesting that the catalytic hydrogenation of 1,1-diacryloylferrocene (XLV, R = H) over platinum or palladium leads to the formation of a new C–C bond and of the ferrocenophane (XLVIII). The same product was synthesised by the cyclisation of (XLV, R = H) under the influence of HCl with subsequent dehydrochlorination of the product (XLIX) to (L) and catalytic hydrogenation of the latter (Scheme 9).[116]

Scheme 9



An instance of the formation of 4,methyl[4]ferrocenophan-1-one by the intramolecular attack of the carbonion on the double bond of 1-acetyl-1′-isopropenylferrocene[117,118] is also known. Treatment of difulvene (VIII, R = CH_3) with sodamide leads to the formation of a ferrocenophane with a three-membered bridge[74,119]. Toma and Salisova recently employed the method involving addition to an activated double bond in order to synthesise ferrocenophanes with different bridge lengths[120,121]. 3-Phenylacyl[3]ferrocenophan-1-one, 2-(*p*-chlorophenyl)-1-cyano[4]ferrocenophan-1-one, and 3-(*p*-chlorophenyl)[7]ferrocenophane-1,5-dione were obtained in this way[120]. The method proved to be convenient for the synthesis of compounds (LI) and (LII).[121]



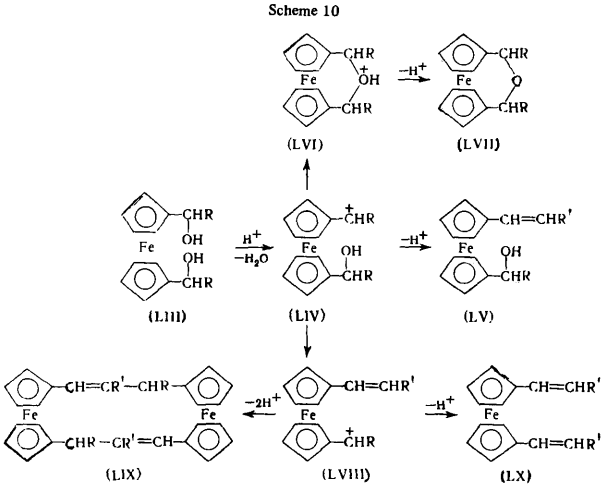


Finally one should note that the polymerisation of 1,1′-divinylferrocene[122] and 1,1′-di-isopropenylferrocene[123] yields high-molecular-weight products containing ferrocenophane rings.

3. Cyclisation with the Intermediate Formation of a Carbonium Ion

Cyclisation with the intermediate formation of a carbonium ion with the charge in the α-position relative to the ferrocene nucleus is widely used to synthesise [3]ferrocenophanes. The ease of formation of these carbonium ions is well known. Carbonium ions such as (LIV) (Scheme 10) are formed following the elimination of the hydroxy-group from α-ferrocenylmethanols (LIII) under the influence of acids. The reaction can proceed further in several ways. When R is not a powerful electron acceptor (R = alkyl, aryl, or hydrogen), the next stage involves attack by the hydroxyl of the α-carbonium centre with subsequent elimination of a proton from (LVI), which results in the formation of 2-oxa[3]ferrocenophane (LVII, R = Alkyl, aryl, or H)[13,124-135]. When R′ in the β-position relative to the ferrocene ring is a powerful electron acceptor, for example CN or $COOC_2H_5$ (then R = CH_2CN or $CH_2COOC_2H_5$), the carbonium ion (LIV) eliminates a proton from the β-position particularly easily and is converted into the olefin (LV), which then gives rise to the diolefin (LX) via the same mechanism[98,101]. Species of the type of (LVIII) can dimerise following intermolecular attack by the carbonium ion on the double bond with formation of the ferrocenophane (LIX, R = CH_3, R′ = H).[133] We may note that intramolecular attack on the double bond, leading to [3]ferrocenophane, is also possible.

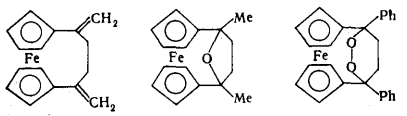
Scheme 10



The α-carbonium ion can also be formed by the hydrolysis of the quaternary salt $N^+Me_3I^-$, which has in fact been used in the synthesis of 2-oxa[3]ferrocenophane[129,133,135].

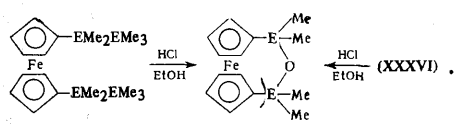
Hisatome and Yamakawa[136] found recently that, on treatment with HCl in benzene, 1,1′-di-(α-hydroxyisopropyl)ferrocene undergoes an unusual condensation leading to the [4]ferrocenophanes (LXI) and (LXII) apart from the uncylised ferrocenes. The analogous reaction of 1,1′-di-(α-hydroxy-α-phenylethyl)ferrocene yielded[137] a series of [4]ferrocenophanes, including the peroxide (LVIII) whose structure was confirmed mass-spectrometrically. The acid-catalysed dimerisation of 2-ferrocenylpropene

results in the formation of a [3]ferrocenophane containing the ferrocenyl group in the 1-position[138].



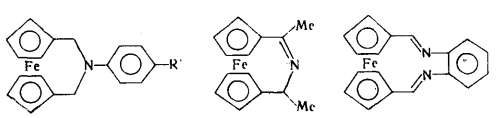
(LXI) (LXII) (LXIII)

Hydrolysis or alcoholysis of various 1,1′-disubstituted ferrocenes whose substituents consist of silicon or germanium atoms has been used to synthesise the corresponding ferrocenophanes with an oxygen atom in the bridge[24,139-142]. Thus Kumada et al.[141] obtained the bridged ethers (LXV) from both uncylised ferrocene (LXIV) and from the ferrocenophane (XXXVI, E = Si or Ge):



(LXIV) (LXV) (XXXVI).

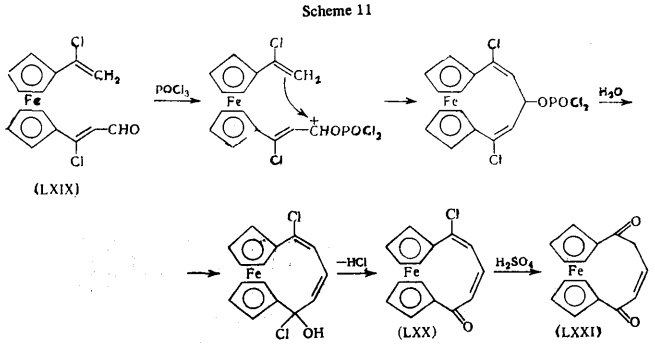
The dicarbinol (LIII, R = H) was used[143,144] to obtain 2-aryl-2-aza[3]ferrocenophanes (LXVI), which are formed when (LIII) is treated with aryl isocyanates (R′ = H, OCH_3, or NO_2). It is noteworthy that another three-membered ferrocenophane (LXVII) with a nitrogen atom in the bridge was synthesised by the reduction of 1,1′-diacetylferrocene monoxime[145]. Condensation of ferrocene-1,1′-dialdehyde with *o*-phenylenediamine[146] resulted in a product to which the authors attributed the structure (LXVIII). The condensation of ferrocene-1,1′-dicarboxylic acid dichloride with hydrazine leads to a polymer in which [3]ferrocenophane rings were detected[147].



(LXVI) (LXVII) (LXVIII)

The reaction of the $\alpha\beta$-unsaturated aldehyde (LXIX) with $POCl_3$ in dimethylformamide leads[148] to the bridged dienone (LXX), which can be converted into compound (LXXI) by treatment with sulphuric acid[113]. A mechanism has been proposed for the formation of the ferrocenophane (LXX) (Scheme 11)[116]:

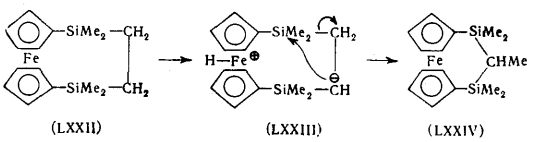
Scheme 11



(LXIX) (LXX) (LXXI)

D. EXPANSION AND CONTRACTION OF THE BRIDGE

Ferrocenophanes can be obtained from other ferrocenophanes with longer or shorter bridges. Thus the reaction of [3]ferrocenophan-1-one (XXIII) with diazomethane results[54] in the expansion of the bridge and the formation of two [4]ferrocenophanes containing carbonyl groups in the 1- and 2-positions. Both ketones can be reduced to [4]ferrocenophane by a mixture of $LiAlH_4$ and $AlCl_3$ or by the Wolff–Kishner method. 1-Aza[4]ferrocenophane has been obtained by the Beckmann rearrangement from [3]-ferrocenophan-1-one[149]. An instance of bridge contraction and conversion from [4]- to [3]-ferrocenophanes is known. On prolonged heating up to 380°C, compound (LXXII) is converted into (LXXIV).[150] The authors suggest that a proton is initially transferred from one of the methylene groups of the bridge to the iron atom with formation of the carbanion (LXXIII), which then rearranges to (LXXIV):

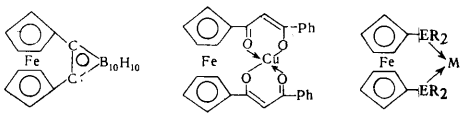


(LXXII) (LXXIII) (LXXIV).

E. OTHER METHODS OF SYNTHESIS

An unusual rearrangement with formation of the interesting [2]ferrocenophane (LXXV) containing a carborane ring in the bridge was described by Zakharkin et al.[151]

Certain 1,1′-disubstituted ferrocenes proved to be convenient bidentate ligands for the formation of complexes with various metals, for example (LXXVI)[152] and (LXXVII) with E = P or As, R = CH_3 or C_6H_5, and M = $Cr(CO)_4$, $Mo(CO)_4$, $W(CO)_4$, $Ni(CO)_2$, $Ni(CO)I_2$, PtX_2, or PdX_2 (X = halogen)[75,153,154].



(LXXV) (LXXVI) (LXXVII)

It is suggested that diacetylferrocene forms complexes with $AlCl_3$[155] and $SnCl_4$[156] in which the metal atom is coordinated to both carbonyl groups simultaneously. The hypothesis has been put forward that the blue compound formed when ferrocene and $AlCl_3$ are dissolved in carbon tetrachloride is a kind of ferrocenophane in which the two ferrocene rings are linked by two aluminium atoms[157]. The interaction of 1,1′-di(acetoacetyl)ferrocene with a nickel(II) salt resulted in the formation of a polynuclear ferrocenophane[158]. Finally the anhydride of ferrocene-1,1′-dicarboxylic acid is apparently a bridged dimer[159].

III. CHEMICAL PROPERTIES

A bridge of any length in ferrocenophanes gives rise to a definite steric hindrance to the approach of the attacking agent towards the cyclopentadiene rings and short bridges ($m = 2$) also distort the ferrocene structure, resulting in an inclination of the rings, to such an extent that the behaviour of ferrocenophanes of this kind differs qualitatively from that of non-bridged 1,1′-disubstituted ferrocenes. This can be illustrated by the following examples.

Whereas the reductive cleavage of ferrocene and its alkyl derivatives by lithium in propylamine results in the formation of the corresponding cyclopentadienes (yield from 45 to 77%), [3]ferrocenophane decomposes only partly under these conditions and [3][3](1,3)ferrocenophane is completely resistant to the reaction of lithium[160].

Table 2. The β/α ratio in the acetylation products[161].

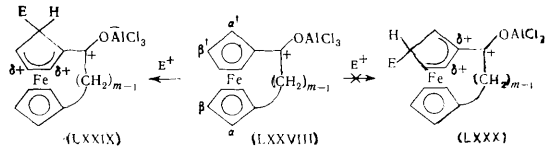
[3]Ferrocenophane	1.57
[4]Ferrocenophane	1.65
[5]Ferrocenophane	2.19
3-Phenyl[5]ferrocenophane	2.62
1,1'-Dimethylferrocene	1.95
1,1'-Diethylferrocene	2.88

Ferrocenophanes (with $m \geq 3$) behave similarly to 1,1'-dialkylferrocenes in reactions with electrophilic agents. Rinehart et al.,[47] Rosenblum et al.,[54] and Watts and coworkers[161-163], who made a detailed study of the acetylation of [m]ferrocenophanes, found that the ratio of the acetyl[m]ferrocenophane isomers $\beta/\alpha > 1$ and increases with the length of the bridge[161], i.e. a behaviour similar to that of 1,1'-dialkylferrocenes is observed (Table 2). However, molecular orbital calculations[164] lead to the expectation that the α-isomer should predominate. For this reason, the preferential formation of the β-isomer in the acetylation of [m]ferrocenophanes and 1,1'-dialkylferrocenes is explained by the dominant influence of steric factors. With $m = 4$ and particularly with $m = 5$, the bridge methylene groups hinder markedly the α-positions in the cyclopentadiene rings.

Table 3. The ratio of the products of the acetylation of [m]ferrocenophan-1-ones[163] [for the significance of the symbols see the structure (LXXVIII)].

m	β/α	α'/α	$(\alpha+\beta)/\alpha'$
3	4.2	0.6	9.5
4	1.2	0.5	4.5
5	0.8	0.01	170

The acetylation of acetylferrocene results in the formation of a small amount of the 1,2-diacetyl derivative (the 1,3-isomer was not found) in addition to the main product 1,1'-diacetylferrocene. Derivatives containing the acetyl group in the β'-position of the ring bound to the carbonyl group were also not found among the products of the acetylation of [m]ferrocenophan-1-ones[163] (Table 3). On the other hand, the amount of the α-substituted products (particularly with $m = 3$ or 4) is fairly appreciable. This finding was accounted for in the following way. The aluminium chloride used in the acetylation reaction forms a complex with the carbonyl group of [m]ferrocenophanone, which results in the formation of the strongly polarised structure (LXXVIII). If the rate-determining stage is the formation of the σ-complex (LXXIX) or (LXXX), the addition of the acetylium ion to the α'-position should predominate despite the steric hindrance, since in this case [structure (LXXIX)] the sites with a reduced electron density are more remote from the carbonium centre formed from the carbonyl group than in the β'-addition [structure (LXXX)]:

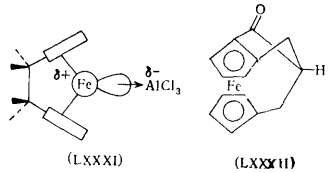


(LXXIX) (LXXVIII) (LXXX)

Thus the result is consistent with molecular orbital calculations and electronic factors presumably predominate in this case over steric factors. The sharp increase of the ratio β/α for $m = 3$ (cf. Table 2 and 3) was explained[163] on the basis of the *trans*-effect—the concept, which was adduced for the first time to account for the electronic effects in metallocenes. The diacetylation of [3]ferrocenophane has been described[61].

It is very remarkable that [2]ferrocenophane cannot be acetylated[14,16,161], whereas it is protonated at the iron atom significantly more readily than all other ferrocene derivatives[15,16]. This is shown by the disappearance of the 472 nm band ($\epsilon = 450$) from the [2]ferrocenophane spectrum after the addition of 0.1% sulphuric acid to the alcoholic solution[15,16]. The marked mutual inclination of the rings in this compound probably causes an electronic rearrangement in the molecule and withdrawal of electron density (of three filled non-bonding orbitals) from the side opposite to that of the bridge. This leads to a sharp increase of the basicity of the compound. The coordination of one of the electron pairs with $AlCl_3$ induces a flow of electron density from the rings to the iron atom, as a result of which the compound loses the capacity for electrophilic substitution [structure (LXXXI)][161].

A somewhat lower rate of solvolysis of 1-acetoxy[3]ferrocenophane compared with the corresponding non-bridged ferrocene derivatives has been observed, which has been attributed to some destabilisation of the α-carbonium centre in the ferrocenophane molecule, since in this case the cationic centre and the cyclopentadiene ring are non-coplanar[165].



(LXXXI) (LXXXII)

Several studies have been made on reactions involving the bridge, see for example Refs. 113, 116, 166, and 167. Some of these reactions were mentioned in the description of the methods of synthesis of ferrocenophanes. [3]Ferrocenophanes with a carbonyl group in the 1-position[168] or 2-position[169] were converted into tosylhydrazones from which the corresponding carbenes were generated. It was shown that the carbenes exist in the triplet state[169]. When the two tosylhydrazones were heated with sodium hydride, [3]ferrocenophan-1-ene was obtained. It is interesting that the reduction of ferrocenophane (LXXXII) gives rise only to the corresponding carbinol and the hydrocarbon could not be obtained[9,170].

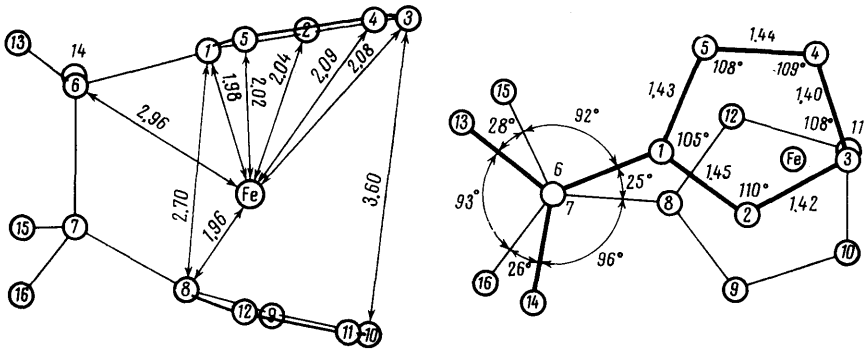


Figure 1.

IV. STUDIES BY PHYSICAL METHODS

A. Structural Studies

The structures and conformations of bridged ferrocenes were discussed theoretically in early investigations[171,172]. The determination of the crystal and molecular structures of 1,1,2,2-tetramethyl[2]ferrocenophane[173] showed that the two cyclopentadiene rings in this compound are inclined relative to one another at an angle of 23° and, in contrast to ferrocene, are staggered to the extent of only 9°. The strain in this system is shown by the fact that the dihedral angle in the bridge is only 26°. The bond lengths slightly exceed the normal values. The structure of this compound is illustrated in Fig. 1. We may note that, according to a calculation[174], the distortions in the structure accompanied by inclination of the rings by up to 45° should not be reflected in the metal–ring bond energy.

The mutual inclination of the cyclopentadiene rings in [3]ferrocenophan-1-one is naturally smaller than in the more strained [2]ferrocenophane, amounting to 8.8°.[175] Some of the experimental angles and bond lengths (Å) are indicated in Fig. 2. The second bridge in [3][3](1,3)ferrocenophane does not increase appreciably the mutual inclination of the rings (the angle is 9°).[176] The two cyclopentadiene rings in this molecule are in the eclipsed prismatic conformation. A virtually eclipsed conformation was also found in 1,2,3-trithia[3]ferrocenophane (the angle of ring inclination is 2.85°).[177] The crystal and molecular structures of [1,1,1]ferrocenophane[178] and the molecular structure of [1,1]ferrocenophane[179,180] have also been determined and the crystal lattice constants of the compounds (XLVI, R = thienyl)[181] and (LXXVII, E = As, R = CH_3, and M = NiI_2CO)[182] have been published.

X-Ray diffraction analysis of "bis-(π-azulene) iron" showed that this compound is a ferrocenophane in which the two seven-membered rings are non-planar and are linked via the *ortho*- and *para*-positions with formation of a two-membered bridge[29,30]. A similar structure was recently found for bis(pentalenyl)iron[28]. This compound exists in the form of two enantiomers (XVa and XVb).

B. The Study of Conformational Mobility

The cyclopentadiene rings in the ferrocene molecule are parallel and the barrier to their mutual rotation about the axis passing through the iron atom and the centre of the ring is very small (0.9 kcal mole^{-1} compared with 3.0 kcal mole^{-1} for rotation about the C–C axis in ethane)[183]. The introduction of a bridge into the ferrocene molecule precludes such rotation, but the mutual rotational oscillations of the rings persist and their amplitude should diminish with decrease of the length of the bridge. X-Ray diffraction analysis (see above) established that the cyclopentadiene rings are mutually inclined in [*m*]ferrocenophane molecules with fairly short bridges (*m* = 2 or 3).

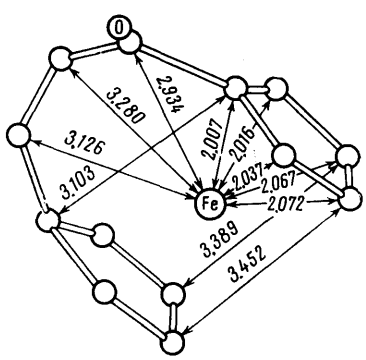


Figure 2.

Models have shown that with longer bridges the rings are parallel. The decrease of conformational mobility following the introduction of a bridge and particularly the mutual inclination of the rings are reflected in the spectroscopic characteristics of ferrocenophanes. Thus the sharp deformation of the [2]ferrocenophane molecule is reflected by the marked bathochromic shift of the "440 nm" band, associated‡ with the $A_{2g}(e_{2g} \rightarrow e_{2g}^*)$ transition[184], to 472 nm (Table 4). Its intensity increases at the same time. On the other hand, the displacement from conjugation of the carbonyl groups in the α-positions of the bridge

‡ Other assignments have also been made (see the paper of Barr and Watts[185] and the reference quoted therein).

leads to a hypsochromic shift of the above band. This effect has been observed in electronic spectra on passing from 1-acetyl-1′-methylferrocene to its bridged analogues—[3]- and [4]-ferrocenophan-1-ones[54]. The absorption maximum in the spectrum of the bridged [5]ferrocenophane-1,5-dione occurs at a lower wavelength (452 nm) than in the spectrum of the uncyclised and unstrained 1,1′-diacetylferrocene (460 nm).[186] Comparison of the electronic spectra of [3]ferrocenophane and [3]ferrocenophan-1-ene shows that there is virtually no conjugation of the double bond with the ferrocenyl fragment[168].

Table 4. Electronic spectroscopic data[15,185] [λmax (nm) and ϵ].

Compound	λ, nm	ϵ
Ferrocene	440	90
1,1′-Dimethylferrocene	437	100
1,1′-Di-(t-butyl)ferrocene	442	105
[2]Ferrocenophane	472	450
[3]Ferrocenophane	442	185
[4]Ferrocenophane	433	100
[5]Ferrocenophane	448	110
1,1′-Di(methoxymethyl)ferrocene	434	110
2-Oxa[3]ferrocenophane	443	220

Table 5 shows that an increase of the strain in the molecule and the displacement of the carbonyl group from conjugation with the cyclopentadiene ring as the length of the bridge is reduced are reflected in the infrared spectra [a shift of ν(C=O) towards higher frequencies].

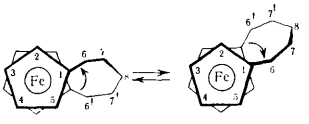
Table 5. The stretching vibration wave-numbers of the carbonyl group[54,113].

Compound	ν, cm^{-1}
[5]Ferrocenophan-1-one	1642
[5]Ferrocenophane-1,5-dione	1658
[4]Ferrocenophan-1-one	1647
[4]Ferrocenophan-2-one	1681
[3]Ferrocenophan-1-one	

The protons of the cyclopentadiene rings are shown in the ^{1}H NMR spectra of [m]ferrocenophanes[54,183,186] by multiplets, characteristic of an AA′BB′ system, resembling the corresponding signals in the spectra of 1,1′-disubstituted ferrocenes with electron-donating substituents[101]. Whereas in the spectrum of [4]ferrocenophane whose cyclopentadiene rings are parallel the signal of the above protons constitutes a fairly narrow singlet (40 MHz in C_6D_6), in the spectra of [3]- and particularly [2]-ferrocenophane, whose cyclopentadiene rings are inclined, the above signal splits into two triplets corresponding to the α- and β-protons. In the spectrum of the latter the spacing between the triplets reaches 0.54 p.p.m. The anomalous spectra of [2]- and [3]-ferrocenophanes were explained by the fact[183] that, owing to the mutual inclination of the rings, the orbitals of the lone electron pairs of the metal are rehybridised. The resulting asymmetric distribution of electron density in the space between the cyclopentadiene rings leads to different degrees of shielding of the α- and β-protons [structure (LXXXI)].

Detailed studies of the temperature variation of the ^{1}H NMR spectra of ferrocenophanes to investigate the conformational mobility of the molecules have not been made. It is only known that the methylene singlet in the spectrum of the [3]ferrocenophane is slightly broadened at −55°C[183] and the multiplet due to the cyclopentadiene protons of [5]ferrocenophane loses its fine structure at −110°C and at the same time shifts towards a high field[186]. The changes in the spectra of 1,2,3-trithia[3]ferrocenophane with increase of temperature indicate the mobility of this molecule[88].

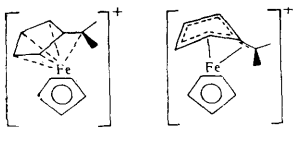
The ^{13}C NMR spectrum of [5]ferrocenophane was investigated recently[186]. The carbon atoms of the cyclopentadiene rings give rise to three signals with δ = 68.4 and 66.9 p.p.m. ($C_{2,5}$ and $C_{3,4}$) and 89.2 p.p.m. (C_1) relative to tetramethylsilane (in CH_2Cl_2 at +15°C). The bridge methylene groups give rise to three signals in the range δ = 22–26 p.p.m. Whereas one of these signals, probably associated with $C'_{6,6}$, does not change its position when the temperature is altered (in the range between −70° and +70°C), the other two signals shift appreciably to a lower field with increase of temperature. This change in the spectrum may be caused by the conformational transitions (LXXXIIIa) ⇌ (LXXXIIIb) due to the mutual rotation of the cyclopentadiene rings and the inversion of the bridge. The change in the contributions of the conformational populations as the temperature is altered leads to a significant change in the average anisotropic screening of the C_7 and C_8 nuclei in the inhomogeneous magnetic field[187] due to the ferrocene rings. The ^{13}C NMR spectrum of [5]ferrocenophane-1,5-dione may indicate a lower conformational mobility of the molecule[186].



(LXXXIIIa) (LXXXIIIb)

C. Application of Ferrocenophanes in the Study of α-Ferrocenylcarbonium and Ferricenium Ions

The problem of the structure of α-ferrocenylcarbonium ions has been solved with the aid of ferrocenophanes. To account for the unusual stability of α-ferrocenylcarbonium ions, two fundamental alternative structures, (LXXXIV) and (LXXXV), were proposed. In the first the cyclopentadiene ring with the α-carbonium centre assumes a fulvenoid configuration and is displaced relative to the iron atom, while in the second the cyclopentadiene ring is deformed and the carbonium centre approaches the iron atom.

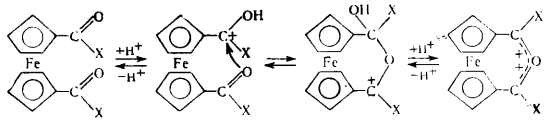


(LXXXIV) (LXXXV)

If structure (LXXXIV) is correct, the introduction of a bridge in the α- or β-position with respect to the carbonium ion centre should prevent the displacement of the

cyclopentadiene ligand, whereas a bridge of this kind cannot interfere with the deformation of the ring. [3]- and [4]-Ferrocenophanes with the $-\overset{+}{C}H_2$, $-CH\overset{+}{C}H_3$, or $-\overset{+}{C}(CH_3)_2$ cationic centre in the α- or β-positions with respect to the bridge have been obtained[188-192]. It was found that these compounds are no less stable than the cations without a bridge and that the ^{1}H NMR spectra of ferrocenophanes with a carbonium ion centre resemble those of the corresponding 1,1′-dialkylferrocenes with a cationic centre in the α- or β-position with respect to the alkyl substituent. On this basis, preference was given to structure (LXXXV). Japanese workers investigated the ^{1}H NMR spectra[3] of [3]- and [4]-ferrocenophane carbonium ions[191] in which the positive charge arises at the α- or β-carbon atom of the bridge. The authors believe that the spectra reflect the molecular deformations arising in consequence of the interaction of the positive charge both with the π electrons of the cyclopentadiene rings and with the iron atom.

In a study of ^{1}H NMR spectra the formation of the bridged dications (LXXXVII) in solutions of 1,1′-diacylferrocenes (LXXXVI) in strong acids was postulated[193]. When [5]ferrocenophane-1,5-dione is dissolved in concentrated sulphuric acid, a carbonium ion is formed, which is reflected[194] in the ^{13}C NMR spectrum. Comparison of the ^{13}C NMR spectra of mono- and 1,1′-di-acylferrocenes in protic acids[194] also indicates the possible formation of the bridged ion (LXXXVII).



(LXXXVI) (LXXXVII)

Bitterwolf and Ling[195] showed that in a strongly acid medium ($BF_3.H_2O$) biferrocenyl, diferrocenylmethane, and 1,2-diferrocenylethane are readily protonated as both iron atoms, which is reflected in the ^{1}H NMR spectra. However, in contrast to ferrocene, the solute is then oxidised, the rate of oxidation increasing with decrease in the length of the chain joining the two ferrocene fragments. The oxidation of [1,1]ferrocenophane is very rapid and is accompanied by the liberation of one mole of hydrogen. The hydrogen atoms in the specific conformation of the diprotonated [1,1]ferrocenophane (Fig. 3) probably approach one another and a chemical bond is formed between them, which leads to the elimination of hydrogen. The iron atoms are then oxidised.

[0,0]Ferrocenophane can be oxidised at one of the iron atoms with formation of ferricenium picrate or fluoroborate. An intense absorption, consisting of a double band at 1550 nm (ϵ = 2100) and 1140 nm, was observed in the electronic spectrum of this compound[22,196]. The position of this band and its molar extinction coefficient are independent of the solvent and concentration, which enabled the authors to assign this absorption to an intramolecular electron transfer between the two iron atoms. [1,1]Ferrocenophane gives rise to a picrate which absorbs at 780 nm[22]. In both cases the band undergoes a sharp hypsochromic shift relative to its position in the spectrum of ferrocenylferricenium picrate (1900 nm, ϵ = 551).[197]

D. Other Studies

It has been established that the two bands in the region of 1000 and 1100 cm^{-1}, characteristic of the vibrations of the unsubstituted cyclopentadiene rings, are absent from the infrared spectra of ferrocenophanes, but almost always occur in the spectra of mono- or homopoly-substituted ferrocenes. This feature can be used to establish whether the intramolecular cyclisation reaction is homoannular or heteroannular (see Scheme 4).

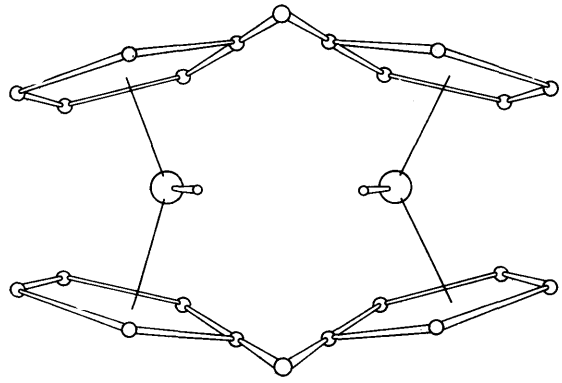


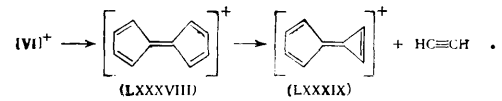
Figure 3.

The dipole moments of [m]ferrocenophanes have been measured[198] and have been found to decrease in the following sequence: Me_4[2]§ > [3] > [4] > [5] (1.00, 0.85, 0.81, and 0.76 D respectively), owing to the increase of the mobility of the molecule with increase in the length of the bridge. It is interesting that the dipole moments of β-acetyl[m]ferrocenophanes (m = 3, 4, or 5) are equal to the sums of the dipole moments of acetylferrocene and the corresponding [m]ferrocenophane. This finding was explained by the hyperconjugation between the methylene and carbonyl groups in the $CH_3CO-C_5H_3-CH_2-$system. The polarographic behaviour of various ferrocenophanes has been studied[199,200] and their magnetic susceptibilities have been measured[200]. It was found that [m]ferrocenophanes are oxidised electrochemically more readily than ferrocene and are comparable in this respect to 1,1′-dialkylferrocenes[199]. Under these conditions, [2]ferrocenophane decomposes, since the ferricenium cation formed is unstable. The magnetic anisotropy of the carbonyl group in 2-acetyl[3]ferrocenophane has been discussed[201].

Unfortunately systematic and detailed mass-spectrometric studies on ferrocenophanes have not been made[202,203]. The spectra of [5]ferrocenophanes, like those of the majority of the ferrocene derivatives, are characterised by an intense molecular ion peak. The fragmentation of this ion for the simplest [5]ferrocenophane is accompanied by the loss of CH_3, C_2H_5, C_3H_5, and C_4H_7. When the bridge contains an α-carbonyl group, CO is the first to be eliminated[113]. Very intense M^+ and M^{2+} peaks were observed in the spectrum of [3][3](1,3)ferrocenophane. The fragmentation of the molecular ion involves the loss of methyl, acetylene, ethylene, and propene with subsequent decomposition of the ions formed[204]. The mass spectra of [1,1]-ferrocenophanes have been described[21,202,205]. Apart from the most intense M^+, M^{2+}, and Fe^+ peaks,

§ 1,1,2,2-Tetramethyl[2]ferrocenophane.

the [0,0]ferrocenophane spectrum shows small peaks with m/e 128 and 102, which may be due to the (LXXXVIII) and (LXXXIX) ions respectively[90]. The spectra of [2,2]ferrocenophane-1,13-diyne[92] and 1-hydroxy[3]ferrocenophane[206] have been published. The formation of an ion corresponding to the ferrocenophane (LXX) was noted in the fragmentation of the dicarbinols (LIII)[206]:

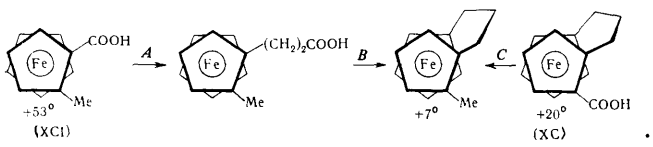


V. THE STEREOCHEMISTRY OF FERROCENOPHANES

The configurational and conformational studies on metallocenes, particularly on [3]ferrocenophanes, have been reviewed by Schlögl[207,208].

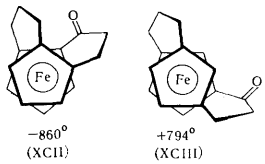
Monosubstituted [m]ferrocenophanes, as well as homoannular disubstituted ferrocenes, should exist in the form of two optical isomers. Detailed stereochemical studies have so far been made only on [3]ferrocenophanes. The key compound for the determination of the absolute configurations of these derivatives is [3]ferrocenophane-α'-carboxylic acid (XC), the absolute configuration of which was established by a correlation with methylferrocene-α-carboxylic acid (XCI), as shown in Scheme 12. The transformations were carried out as follows: Stage A involves the transformations COOH → CHO → CH = CHCOOH → CH_2CH_2COOH, stage B involves cyclisation with the aid of $(CF_3CO)_2O$ and reduction by a mixture of $LiAlH_4$ and $AlCl_3$, and stage C involves reduction by the same mixture. The absolute configuration of the acid (XCI) had been established previously[209]. Similar studies have been made also for ferrocenophanes containing substituents in the β-position[210]. Apart from chemical correlations, the Horeau method of kinetic resolution was used to establish the configuration of [3]ferrocenocarboxylic acids by the interaction of their anhydrides with (-)-α-phenylethylamine[210].

Scheme 12



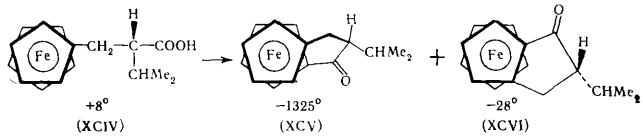
The doubly bridged ketone (XCII) was synthesised by a series of consecutive transformations from the acid (XC) obtained by the resolution of the racemate with (-)-α-phenylethylamine. The β-derivative (CXIII) was obtained similarly[210].

The intramolecular cyclisation of 1-(β-carboxypropyl)-1′-methylferrocene yielded the corresponding α- and β-methyl[3]ferrocenophanones with the oxo-group in the bridge. Each ketone was resolved into its optical isomers by the formation of methylhydrazones[210].

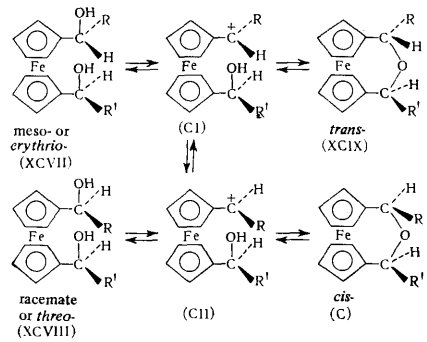


The study of the circular dichroism (CD) of optically active homo-disubstituted ferrocenes and [3]ferrocenophane substituted in the α-position of the ring led to conclusions concerning the preferred conformations of the substituents or the bridge[208,211]. The study of the dipole moments and the temperature variation of the circular dichroism of α- and β-substituted (in the cyclopentadiene ring relative to the bridge) [3]ferrocenophanes showed that the activation energy for the inversion of the bridge is significantly higher for the α-derivative, as was to be expected, and this results in the existence of a preferred bridge conformation[211]. Moreover, on passing from [3]ferrocenophanes α-substituted in the cyclopentadiene ring to the β-substituted derivatives, a decrease of the amplitude of the Cotton effect may be noted and in certain cases the sign of the curves is reversed[212].

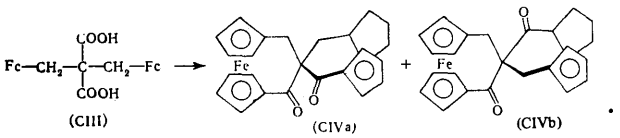
The chirality of the ferrocenophane molecule may be caused by the introduction of a substituent not only in one of the rings, as in the above discussion, but can arise also when an asymmetric centre is introduced into the bridge. The cyclisation of the optically active acids $FcCH_2CHRCOOH$, leading to ketones with hetero- and homo-bridges, which also exhibit optical activity [for example compounds (XCV) and (XCVI)], has been described[48,49].



A careful study of the stereochemistry of the 1,1′-diol⇌2-oxa[3]ferrocenophane interconversions was made by Yamakawa and Hisatome[213]. 1,1′-Di-(α-hydroxyalkyl)ferrocenes can exist in the *meso*-form (*erythro*- if R ≠ R′) (XCVII) and as the racemate of two optical isomers (*threo*- when R ≠ R′) (XCVIII). The resolution into the *meso*-form and the racemate was achieved by 7–8 recrystallisation of the product obtained by the reduction of the corresponding diacylferrocene. On treatment with dilute HCl, the mixture of compounds (XCVII) and (XCVIII) is converted into a mixture of the *cis*- and *trans*-isomers of the ferrocenophane, (C) and (XCIX) respectively, which can be separated chromatographically. The ferrocenophanes (XCIX) and (C) are converted reversibly into the diols (XCVII) and (XCVIII) on treatment with acid alumina. It is significant that the interconversions are stereospecific. The relative amounts of the products in the (XCVII) ⇌ (XCIX) and (XCVIII) ⇌ (C) interconversions have been determined but small amounts of another isomer are also obtained in these processes owing to the equilibrium (CI) ⇌ (CII) between the two forms of the intermediate carbonium ion.

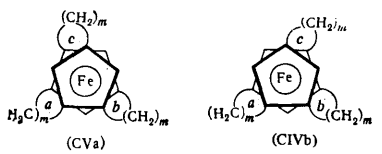


When the acid (CIII) was treated with $(CF_3CO)_2O$, a mixture of stereoisomeric spiranes (CIV) was obtained[214] and was resolved by chromatography on partly acetylated cellulose[215].



(CIII) (CIVa) (CIVb)

Optical isomerism of a new type may be expected for the ferrocenophanes (CV, $m = 4$ or 5) with three bridges, which have not yet been synthesised. Models show that such ferrocenophanes with fairly long bridges can exist in the antiprismatic configuration. The introduction of two bridges (a and b) restricts the mutual rotational oscillations of the rings, while the third bridge (c), which has rotated to the left or to the right, should result in the formation of two enantiomers—(CVa) and (CVb) respectively.



(CVa) (CIVb)

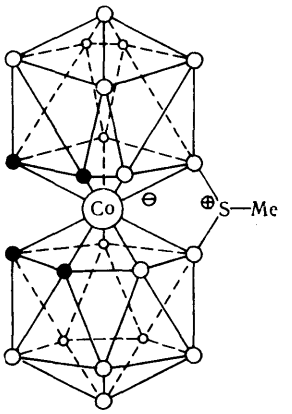
VI. APPLICATIONS

The use of ferrocenophane models for the solution of certain theoretical problems and the synthesis of polymers containing ferrocenophane fragments was mentioned above.

It has been suggested that [2]ferrocenophanes (Table 1, Nos. 1–5) be used as additives to epoxy-resins and silicones[14]. It was found recently that [3]ferrocenophanes with silicon and oxygen atoms in the bridge are effective inhibitors of the oxidation of polyorganosiloxanes[216,217]. Bridged cyclic ethers[218–221] and thioethers[218] exhibit biological activity and can be used in the treatment of diseases associated with iron deficiency in the organism. Derivatives of [3]ferrocenophan-1-one[167,222] and also 1-aza[4]ferrocenophane[149] exhibit a similar activity. These compounds have proved useful also as additives to fuel. It has been suggested that 2-aza[3]ferrocenophane be used in macromolecular chemistry. The dicarbinol formed on reduction of 3-phenyl[5]ferrocenophane-1,5-dione was converted into a bridged ether and thioether, which can be used as pesticides, dyes, fuel additives, and medicinal preparations for the treatment of iron-deficiency diseases[223]. Like titanocene dichloride, 1,1′-methylenetitanocene dichloride can be used for the fixation of molecular nitrogen and also as a cocatalyst in the polymerisation of olefins[19].

ADDENDUM

Japanese workers described recently the synthesis of bridged bicyclic ferrocenes with two nitrogen atoms in the bridge by the reaction of the 1,1′-diacetylferrocene–$AlCl_3$ complex with o-phenylenediamine[224]. French chemists continued the study of the stereochemistry of substituted [3]ferrocenophanes[225]. Plešek et al.[226] synthesised the interesting bridged carborane derivative (CVI).



(CVI)

Turbitt and Watts made special use of ferrocenophane models in a detailed study of α-ferrocenylcarbonium ions[227]. Continuing the investigation of ferrocenophanes by ^{13}C NMR, Nesmeyanov et al.[228] obtained the spectra of certain [3]ferrocenophanes and the carbonium ion formed when [3]ferrocenophan-1-one is dissolved in CF_3COOH. The introduction of the phenyl substituent in the 3-position of the bridge of [5]ferrocenophane results in the non-equivalence of all five carbon atoms of the cyclopentadiene ring owing to the diastereotopy (and the anisochronic properties) of the nuclei within each of the two pair $C_{(2)} - C_{(5)}$ and $C_{(3)} - C_{(4)}$ arising following the introduction of the substituent[228]. This effect was observed previously for non-bridged mono-substituted ferrocenes containing a chiral centre in the substituent[229–231].

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Organophosphorus Complexones†

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Organophosphorus complexones are a new group of highly effective complex-forming compounds capable of binding metal ions in aqueous media. The principal trends in the development of studies on the synthesis and properties of organophosphorus complexones are discussed and methods for the modification of their structures and their most interesting applications are indicated.
The bibliography includes 130 references.

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I. INTRODUCTION

Progress in many branches of science and engineering is to a large extent associated with the development of the chemistry of coordination compounds with polydentate ligands, among which complexones occupy one of the leading places. The chemistry of complexones opens up virtually unlimited possibilities for the modification of the properties of cations, which creates vast prospects for their extensive application. However, the inadequate assortment of these compounds has limited the range of their applications. Until recently, these ligands were used mainly only in analytical chemistry as titrating and masking agents. Virtually the only available and widely used complexone was ethylenediaminetetra-acetic acid, the possible applications of which are extremely limited[1,2].

The development of modern engineering and of the national economy places new tasks before science. A number of important problems of this kind, such as the cleaning of thermal power engineering equipment, the separation of elements with similar properties, the treatment of plant chlorosis, the elimination of incorporated metals from the organism, the metallation of dielectric materials, and the stabilisation and catalysis of complex systems can be solved successfully by employing complexones. However, the complexone-type ligands used in the solution of these problems must possess in each individual case a set of properties ensuring their optimal applicability. For this reason, it was necessary to create a large assortment of complexones with a wide range of complex-forming properties and in the first place complex-forming agents capable of giving rise to complexes with maximum stability over a wide pH range, from strongly acid to strongly alkaline media, and also selectively acting compounds with a specific set of properties. The first of these problems is solved by combining in the structure of the complexone the highly basic nitrogen atoms with polydentate salt-forming groups. The solution of the second problem involves much greater difficulties, since it is necessary to chelate selectively metal ions with similar physical and chemical properties, dimensions, steric configurations, and, what is most important, similar tendencies towards complex formation. The difficulties are aggravated also by the fact that, by virtue of their polydentate nature and in most cases the flexibility of their steric configuration which permits a multiplicity of conformations with deformation of the bond angles and lengths within certain limits, complexones become very readily adapted to the geometrical requirements of the cations.

A higher selectivity in chelate formation, particularly for polydentate compounds, can be achieved only by synthesising a special reagent taking into account the complete set of properties of the internal ligand contour and the cation and also the postulated structure of the chelate to be formed. The change in the electronic states at the sites responsible for coordination and the rigidity of the system is also important.

The ligand molecule with the specified properties should be synthesised on the basis of the known correlation between the structure of the ligand and its properties, the theory of the action of complexones (by varying the number of their binding sites), the nature of the electron-donating atoms and their immediate environment, the stereochemistry of the molecule as a whole, the number of rings formed and their dimensions, the rigidity of the system, and the distribution of electron density among the sites responsible for coordination.

One of the fundamentally new and promising ways of the specific synthesis of a complexone molecule involves the incorporation in the latter of aminoalkylphosphonic acid groups[2-4]. The specificity of the chelating agent containing a phosphonic acid group is determined primarily by its stereochemistry, which differs from that of the carboxy-group. The phosphonate ion is almost tetrahedral (distorted tetrahedron) with a threefold symmetry axis. The carboxylate ion is planar with a planar symmetry. The valence angles and bond lengths are also different.

π-Bonding between the oxygen and phosphorus atoms is much weaker than between oxygen and carbon atoms in the carboxy-group. The polarisability of the P–O bonds in

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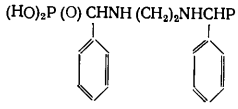
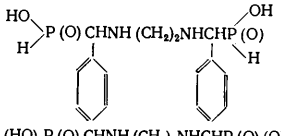
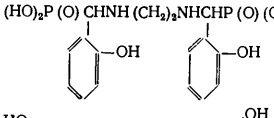
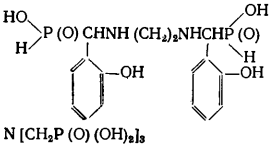
the phosphoryl group is greater than that of the C–O bond in the carboxy-group. For this reason, on the one hand the inductive effect plays a major role in phosphonic acid compounds and on the other the phosphonic acid group is highly nucleophilic. In the presence of the two hydroxy-groups of the phosphonic acid which are potentially capable of coordination, the stereochemistry of such complexones allowed an *a priori* assumption that the higher stability of their chelates is a result of the possible formation of additional rings and led to the expectation that they will be selective with respect to cations with an enhanced coordination capacity and high electrostatic characteristics.

Although the properties of aminoalkylenephosphonic acids were first reported by Schwarzenbach and coworkers as early as 1949,[5] the interesting and extremely specific properties of organophosphorus complexones were not discovered either in that investigation or in later studies by Martell and coworkers[6-9] dealing with the phosphorus analogues of the familiar complexone ethylenediamine-tetra-acetic acid (EDTA). Only comprehensive investigations using potentiometric, polarographic, infrared spectroscopic, NMR, and ESR methods, carried out mainly by Soviet investigators, led to the discovery of the specificity of the interaction of phosphorus-containing complexones with the cations of elements in various Groups of Mendeleev's Table[2-4,10-16].

The present review does not claim to cover completely the literature on organophosphorus complexones, since its aim is to characterise the principal trends of the developments in this field. At the start of studies on

Table 1. Complexones and their abbreviated designations.

Acid	Formula	Abbreviation	Refs.
Ethylenediamine-*NN'*-di-(methylenephosphonic)	$(HO)_2P(O)CH_2NH(CH_2)_2NHCH_2P(O)(OH)_2$	EDDMPO	14, 18, 26
Ethylenediamine-*NN'*-bis-(dimethylmethylene-phosphonic)	$(HO)_2P(O)C(CH_3)_2NH(CH_2)_2NHC(CH_3)_2P(O)(OH)_2$	EDBDMPO	18
Oxybisethylenediamine-*NN'*-bis(dimethylmethylene-phosphonic)	$(HO)_2P(O)C(CH_3)_2NH(CH_2)_2O(CH_2)_2NHC(CH_3)_2P(O)(OH)_2$	OEDBDMPO	19
Thiobisethylenediamine-*NN'*-bis(dimethylmethylene-phosphonic	$[(HO)_2P(O)C(CH_3)_2NH(CH_2)_2]_2S$	TEDBDMPO	20
Diethylenetriamine-*NN'*-bis-(dimethylmethylenephos-phonic)	$[(HO)_2P(O)C(CH_3)_2NH(CH_2)_2]_2NH$	DETBDMPO	19
Pentamethylenediamine-*NN'*-bis(dimethylmethylene-phosphonic)	$(HO)_2P(O)C(CH_3)_2NH(CH_2)_5NHC(CH_3)_2P(O)(OH)_2$	PMDBDMPO	20
N-(2-Hydroxyethyl)ethylene-diamine-*NN'N'*-tri(methylene-phosphonic)	$(HO)_2P(O)CH_2N(CH_2)_2N[CH_2P(O)(OH)_2]_2$ CH_2CH_2OH	HEEDTMPO	33
Ethylenediamine-*NNN'N'*tetra-methylenephosphonic)	$[(HO)_2P(O)CH_2]_2N(CH)_2N[CH_2P(O)(OH)_2]_2$	EDTMPO	6, 14, 26
Diethylenetriamine-*NNN'-N'N''*-penta(methylenephosphonic)	$[(HO)_2P(O)CH_2]_2N(CH_2)_2N(CH_2)_2N[CH_2P(O)(OH)_2]_2$ $CH_2P(O)(OH)_2$	DETPMPO	22
Ethylenediamine-*NN'*-diacetic-*NN'*-di(methylenephosphonic)	$(HO)_2P(O)CH_2$ $HOOCCH_2$ $N(CH_2)_2N$ $CH_2P(O)(OH)_2$ CH_2COOH	EDDADMPO	9, 18
Ethylenediamine-*NN'*-di(phenyl-methylenephosphonic)	$(HO)_2P(O)CHNH(CH_2)_2NHCHP(O)(OH)_2$ 	EDDPMPO	18
Ethylendiamine-*NN'*-di(phenyl-methylenephosphonous)		EDDPMPOS	34
Ethylenediamine-*NN'*-di(*o*-hydroxy-phenylmethylenephosphonic)	$(HO)_2P(O)CHNH(CH_2)_2NHCHP(O)(OH)_2$ 	EDDHPMPO	34
Ethylenediamine-*NN'*-di(*o*-hydroxy-phenylmethylenephosphonous)		EDDHPMPOS	34
Nitrilotri(methylphosphonic)	$N[CH_2P(O)(OH)_2]_3$	NTP	21
Ethylenediamine-*NNN'N'*-tetra-acetic	$(HOOCH_2C)_2N(CH_2)_2N(CH_2COOH)_2$	EDTA	
Nitrilotriacetic	$N(CH_2COOH)_3$	NTA	
Diethylenetriamine-*NNN'N'N''*-penta-acetic	$(HOOCH_2C)_2N(CH_2)_2N(CH_2)_2N(CH_2COOH)_2$ CH_2COOH	DTPA	

organophosphorus complexones, polyaminopolyphosphonic acids were difficult to obtain. For this reason, a special series of studies were made to develop convenient methods for the synthesis of compounds of this type.

They were based on the principle of the synthesis of α-aminoalkylphosphonic acids discovered by Kabachnik and Medved' at the beginning of the 1950s, which consists of the simultaneous or consecutive treatment of an amine and an oxo-compound by phosphorus(III) derivatives capable of existing in the form of two tautomers [3,17-22].

In the synthesis of alkylenediaminediphosphonic and alkylenediaminepolyphosphonic acids the amine is the corresponding diamine (usually ethylenediamine) and the oxo-compounds are aldehydes or ketones or the Schiff bases prepared beforehand from the diamine and the oxo-compound.

The phosphorus-containing component can be any derivative of phosphorous, phosphonous, or hypophosphorous acid. Esters, for example dialkyl phosphites or phosphonites, are used in the two-stage synthesis; the ester group is subsequently hydrolysed. In the single-stage synthesis (a modification of the method of Moedritzer and Irani[21]) phosphorous acid is employed. In the synthesis of ethylenediaminedi(alkylenephosphonous) acid we employed hypophosphorous acid as the phosphorus-containing component.

There is now a possibility of obtaining the following principal types of organophosphorus complexones by the above methods which have a wide range of applicability.

(1) Alkylenepolyaminebis[dialkyl(arylalkyl)methylenephosphonic] acids:

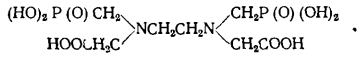
$$(HO)_2P(O)C(R'R'')NH[CH_2-X-CH_2]_nCH_2NHC(R'R'')P(O)(OH)_2$$

R', R''=H, Alk, Ar; $n = 0,1$; X=O, NH, S, CH_2 .

(2) Alkylenepolyaminepoly(alkylenephosphonic) acids, for example:

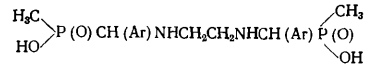
$$[(HO)_2P(O)CH_2]_2NCH_2CH_2N[CH_2P(O)(OH)_2]_2 .$$

(3) Alkylenediaminediaceticdi(alkylenephosphonic) acids:



(4) Alkylenediaminedi(arylmethylenephosphonous) acids:

(5) Alkylenediaminedi(arylmethylenephosphinic) acids:



As a result it became possible to synthesise and investigate a series of compounds the structure of which includes phosphonic, phosphonous, and phosphinic acid fragments, fully phosphorylated derivatives of polyamines, complexones with heteroatoms and aromatic groups, and complexones containing simultaneously carboxy- and phosphono-groups or phosphono- and hydroxy-groups.

Some of the complexones synthesised and the abbreviations used to designate them are listed in Table 1, which also includes references to their syntheses. The last three acids in Table 1, the widely familiar carboxyl-containing complexones, are included for comparison.

II. DISSOCIATION OF AMINOPHOSPHONIC ACIDS

A betaine-like zwitter-ionic structure is characteristic of both aminocarboxylic acids and their phosphorus analogues but the basicity of the amino-group in aminophosphonic acids is higher than in aminocarboxylic acids (Table 2).

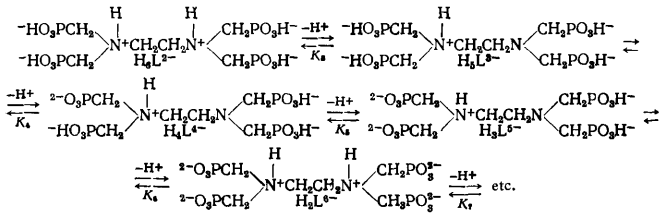
Table 2. Negative logarithms of the dissociation constants of phosphorus-containing complexones.

Designation	pK_1	pK_2	pK_3	pK_4	pK_5	pK_6	pK_7	pK_8	pK_9	pK_{10}
NTA	1.89	2.49	9.73							
NTP	0.3	1.5	4.64	5.88	7.3	12.1				
HMP*	1.7	2.0	5.1	6.45	10.98					
EDTA	2.00	2.76	6.16	10.26						
EDDMPO	4.61	5.72	8.02	10.47						
EDBDMPO	4.95	6.00	8.55	11.68						
OEDBDMPO	5.15	6.40	10.56	11.48						
TEDBDMPO	5.51	6.34	10.38	11.48						
DETBDMPO	5,39	6.55	10.40	11.20						
PMDBDMPO	5.77	6.13	11.0	>11						
HEEDTMPO	1.7	2.81	5.50	6.85	9.10	10.93				
EDTMPO	1.1	1.5	3.02	5.23	6.54	8.08	10.18	12.10		
DETPMPO	—	—	2.8	4.45	5.50	6.38	7.17	8.15	10.10	12.0
EDDADMPO	1.5	2.30	4.65	6.13	8.36	10.34				
EDDPMPO	4.18	5.56	7.44	9.69						
EDDPMPOS	4.32	7.58								
EDDHPMPO	4.37	5.41	6.64	8.77	9.94	11.19				
EDDHPMPOS	4,61	7.57	10.84	11.25						

*Hexamethylphosphoramide (Ed. of Translation).

The study of the deprotonation of polyaminopolyphosphonic acids showed[2-4,23,24] that the PO_3H_2 group dissociates at low pH. With increase of pH, the PO_3H^- groups dissociate and finally in the alkaline region the protons dissociate from the betaine nitrogen atoms. When the complexone molecule contains hydroxyphenyl groups, the phenolic hydroxyls are the last to dissociate at still higher pH than the betaine protons. In such cases stable hydrogen bonds may be formed.

In the course of more far-reaching studies on the mechanism of the acid dissociation of aminopolyphosphonic acids by infrared spectroscopy it was shown[25] that the dissociation of the third, fourth, and fifth protons from ethylenediaminetetra(methylenephosphonic) acid results in the formation of anionic forms in which protonated phosphono-groups are linked to one protonated and one non-protonated nitrogen atom, as shown below:



The presence of a deprotonated nitrogen atom in the anions H_5L^{3-}, H_4L^{4-}, and H_3L^{5-} suggests that metal–nitrogen bonds are more likely to be formed in acid complexes of EDTMPO.

It has been shown, also by infrared spectroscopy, that in the dissociation of ethylenediaminediaceticdi(methylenephosphonic) acid the species with protonated and deprotonated nitrogen atoms may exist in equilibrium. A similar view concerning the order of the dissociation of

protons in ethylenediaminemono(methylenephosphonic) and ethylenediaminedi(methylenephosphonic) acids was expressed by Uhlig and Achilles[28].

Comparison of the dissociation constants of aminophosphonic acids in the group under consideration with those of the analogous aminocarboxylic acids shows that the unusually high and close values of the last two dissociation constants, corresponding to the dissociation of the betaine protons, constitute a significant difference. In diphosphonic acid this is shown particularly clearly with increase of the length of the methylene chain joining the aminoalkylphosphonic acid groups; the difference between the last dissociation constants decreases to a factor of ten and less, which can be accounted for by the decrease of the inductive effect exerted by one amino-group on another.

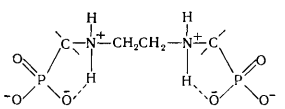
In tri-, tetra-, and penta-phosphonic acids the decrease of the mutual influence of the two positively charged nitrogen atoms is probably associated partly with the high charge of the anion and partly with the electrostatic binding (hydrogen bonding) of the betaine protons.

Table 2 shows that an increase of the number of iminomethylphosphonic acid groups initially increases the last two dissociation constants on passing from ethylenediaminedi(methylenephosphonic) acid to ethylenediaminetetra(methylenephosphonic) acid, but, on passing from the latter acid to diethylenetriaminepenta(methylenephosphonic) acid, the last two constants hardly change. This can be accounted for by an increase of the basicity of the nitrogen atom with the increasing negative charge in the molecule. Then, when the charge becomes large, the introduction of a new group alters it relatively little. A similar phenomenon has been observed in phosphates.

The combination of highly basic betaine nitrogen atoms and polydentate salt-forming groups in alkylenepolyaminepoly(alkylenephosphonic) acids leads to their deprotonation over a wide pH range, which extends the pH range in which complexes exist.

III. COMPLEXES WITH ALKALI METALS

All phosphorus-containing complexones form complexes on interaction with alkali metal cations. Thus ethylenediaminebis(dimethylmethylenephosphonic) acid forms the equimolar complexes



in the region corresponding to the dissociation of the betaine protons, i.e. at pH > 8 (K_{st} = 3.06 for LiX, 2.30 for NaX, < 1 for KX, and 3.37 for CsX). Their stability exceeds that of the corresponding EDTA complexes. We attribute this to the specific features of the effect of the phosphono-group and in particular to the involvement in complex formation of both oxygen atoms in the hydroxy-groups at the phosphorus atom. The participation of phosphono-groups of ethylenediaminebis(dimethylmethylenephosphonic) acid in coordination to alkali metals only at fairly high pH values can probably be explained by the necessity for the dissociation of the hydrogen bonds in the structure (see above) to liberate all the oxygen atoms of the phosphono-groups and also by the necessity to increase the overall negative charge of the molecule.

IV. COMPLEXES WITH ALKALINE EARTH METALS AND BERYLLIUM

Polyalkylenepolyaminepolyphosphonic acid containing not more than two phosphono-groups forms hardly any complexes with alkaline earth metals including calcium. An increase of the number of phosphono-groups and also their combination with carboxy-groups leads to the formation of stable complexes with alkaline earth metals, the logarithms of whose stability constants reach 8–9 (Table 3). Depending on the pH of the medium, complexes protonated to different extents are formed[2-4,12-14,27].

Table 3. Logarithms of the stability constants of the complexes MX.

Cation	EDBDMPO	EDDADMPO	EDTMPO	DETPMPO
Mg^{2+}	<2	8.54	8.63	6.40
Ca^{2+}	<2	9.02	9.33	7.11

The consecutive protonation of the normal complexes as the pH is reduced can be demonstrated for magnesium complexes of nitrilotrimethylphosphonic acid[12,13].

Table 4. Parameters of the infrared and NMR spectra of magnesium complexes of nitrilotri(methylphosphonic) acid.

Complex anion	ν(CH), cm^{-1} as	ν(CH), cm^{-1} s	ν(PO_3), cm^{-1}		δ_H, p.p.m.	$\delta_{^{31}P}$, p.p.m.
MgL^{4-}	2946					
	2877	2841	1099,1068	971	3.20	16.63
$MgHL^{3-}$	3000	2937	1106	973	2,83	7,65
MgH_2L^{2-}	2998	2946	1164,1103	971	2,76	7.20
MgH_3L^{-}	—	—	1167,1084	966	—	—
	2939					
L^{6-}	2845	2790	1083	969	3.45	17.67

The infrared spectrum of the solution of the normal complex $[MgL]^{4-}$ shows an increase in the symmetrical stretching vibration wavenumber ν(C–H) approximately by 50 cm^{-1} compared with the fully deprotonated free ligand. This is associated with the formation of a stable covalent Mg ← N bond. The formation of this bond is also confirmed by the chemical shifts to a high field of the proton doublet in the ^1H NMR spectra and the phosphorus triplet in the ^{31}P NMR spectra relative to the free ligand.

The bond between magnesium and oxygen atoms of the phosphono-groups is largely ionic, which is also indicated by the slight increase of the PO_3^- vibration frequency in the complex compared with the ligand.

When the first proton adds to the complex, the N–H bond is formed, this being accompanied by a characteristic increase of the C–H stretching vibration wavenumbers by 100 cm^{-1}. The second proton adds to an oxygen atom of one of the phosphono-groups, which is reflected by the appearance in the spectrum of the PO_3H^- band with a characteristic wavenumber of 1164 cm^{-1}. The third

proton adds to the second phosphono-group (the intensity of the 1164 cm^{-1} band then increases). All these conclusions are confirmed also by the ^{1}H and ^{31}P NMR spectra.

Table 5. Logarithms of the stability constants of polynuclear ethylenediaminebis(dimethylmethylenephosphonic) acid.

M^{2+}	$BeMH_2L$	$AlMH_2L$	$LaMH_2L$	$CdMH_2L$	M^{2+}	$BeMH_2L$	$AlMH_2L$	$LaMH_2L$	$CdMH_2L$
Mn	8.7	9.8	6.2	6.9	Ni	8.9	10.3	6.3	7.0
Fe	8.8	10.0	6.3	7.0	Cu	13.5	14.8	11.4	11.8
Co	8.9	10.1	6.3	7.0	Zn	10.1	11.3	7.2	7.8

The ability of these compounds to form stable mononuclear and dinuclear complexes with beryllium is particularly noteworthy[28-30]. The study of the mechanism of the complex formation process showed that it involves the interaction of beryllium with the phosphono-groups only; the nitrogen atoms of the iminoalkylphosphonic acid groups are not involved in complex formation. The free coordination sites in the complexes can be occupied by other cations with formation of polynuclear complexes having two coordination centres consisting of two different cations[28-31] (Table 5).

V. COMPLEXES WITH TRANSITION METALS

In the interaction with transition metals the specific features of phosphorus-containing complexones are shown primarily by the formation of stable hydrogen-bonded complexes, which is not characteristic of the carboxyl-containing prototypes. Among the normal complexes, those of copper are particularly stable (Table 6).

Thus the stability constant of the copper complex of ethylenediaminebis(dimethylmethylenephosphonic) acid (EDBDMPO, phosphicine) exceeds that of the corresponding EDTA complex by two powers of ten. The difference between the stabilities of the copper and other transition metal complexes is exceptionally large. Thus the stability of the phosphicine-copper complex exceeds those of the nickel and zinc complexes approximately by nine powers of ten (the stabilities of the corresponding EDTA complexes are similar). It has been established by ESR and electronic spectroscopy[11] that in the ground state of the copper(II) complex of ethylenediaminebis(dimethylmethylenephosphonic) acid the unpaired electron is in the $d_{x^2-y^2}$ orbital (the x and y axes are directed towards the electron-donating ligand atoms) and therefore the complex has the structure of an extended octahedron. The copper atom is linked to the two nitrogen atoms, which are located in the plane containing the unpaired electron and the other coordination sites are occupied by the oxygen atoms of the phosphono-groups. The bonds in the plane of the complex have an amount of covalent character typical for copper complexes.

Stable complexes with phosphorylated derivatives of polyamines are formed by readily hydrolysed elements: iron, aluminium, indium, gallium, titanium, and chromium. The high stability of their protonated complexes, in many cases exceeding the stability of the normal complexes of the corresponding aminopolycarboxylic acids, is remarkable.

The nature of these interactions can be illustrated using as an example the formation of aluminium nitrilotri(methylphosphonate). Aluminium forms two types of complexes with nitrilo(trimethylphosphonic) acid: sparingly soluble polynuclear compounds and soluble monoprotonated and normal compounds. In the region corresponding to the dissociation of the first three protons an insoluble compound is formed and is isolated as the hydrate $Al_3H_3L_2 \cdot 9H_2O$.

Table 6. Logarithms of the stability constants of transition metal complexes.

Complexone	Cu^{2+}	Ni^{2+}	Co^{2+}	Zn^{2+}	Mn^{2+}	Cd^{2+}
NTP	17.75	11.96	14.37	>16.37	10.20	11.55
EDBDMPO	8.83	3.84	3.84	4.31	3.57	
	20.35	11.23	11.19	13.38	8.00	
EDTMPO	11.14	9.12	8.51	9.90	6.99	8.81
	18.95	15.30	15.49	17.05	12.70	13.88
EDDADMPO	9.4	9.49			7.0	
	18.5	15.23	16.03	16.85	13.63	

Note. The numerals in the upper row refer to the $\lg K_{st}$ for the protonated complexes MH_2L and those in the lower row refer to the $\lg K_{st}$ for the normal complexes ML.

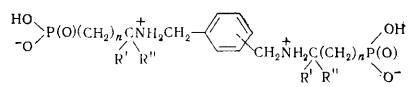
Infrared spectra show that in polynuclear compounds of this kind the bond between aluminium and nitrogen is weakened; evidently in this case the entire coordination capacity of aluminium is saturated by the oxygen atoms of the phosphono-groups. With increase of pH, the polynuclear complex gradually dissolves with formation of the soluble mononuclear complex AlH_2L^{2-} and its subsequent deprotonation and the formation of the stable normal mononuclear complex AlL^{3-}. In the presence of an excess of aluminium in the pH range 5–6 the sparingly soluble dinuclear complex Al_2L is formed and is isolated from solution as the hexahydrate. The study of the ^{1}H NMR spectra of the normal mononuclear complex showed the presence of the Al–N bond. The change of the chemical shifts relative to the fully deprotonated ligand reaches 0.28 p.p.m. The addition of an excess equivalent of alkali (pH 6.86–9.08) does not cause precipitation and no changes take place in the NMR spectra. A further increase of pH (9.1–10.7) leads to the appearance in the spectrum of two pairs of signals; one of these is intense and corresponds to the aluminium complex and the second, weak signal corresponds to the monoprotonated form of the ligand (HL). A further increase of pH leads to an increase of the intensities of the second pair of bands with their subsequent equalisation and is accompanied by the precipitation of aluminium hydroxide from solution.

In all probability the complex AlL^{3-} is present in solution in equilibrium with the monohydroxo-complex $[(AlOH)HL]^{3-}$, which is due to the great tendency of aluminium to form a bond with the water hydroxyl. This hypothesis is confirmed by the presence in the infrared spectrum of the solution of bands indicating the formation of a bond between nitrogen and a proton (N–H). The existence in the complexes of, as it were, a "disproportionated" water molecule is probably generally characteristic of compounds formed by readily hydrolysed cations.

The interaction of phosphorus-containing complexones with iron is unusual. Interpretation of the infrared, NMR, and ESR spectra and also of potentiometric data for iron complexes of carboxyl- and phosphorus-containing analogues leads to the conclusion that at low pH the interaction of the cation with the two groups of ligands proceeds via different mechanisms. Whereas carboxylated amines form very stable water-soluble normal 1 : 1 complexes with Fe^{3+}, phosphorylated amines give rise to protonated polynuclear water-insoluble complexes. Their inner sphere consists entirely of the oxygen atoms of the phosphono-groups. On passing to alkaline media, the stability of the nitrilotriacetic, EDTA, and other complexes with Fe^{3+} falls owing to the weakening of the bonds between the oxygen atoms of the carboxy-groups and the central ion caused by hydrolytic processes. Under these conditions, polynuclear complexes of phosphorylated amines are converted into normal soluble mononuclear and dinuclear complexes with formation of a thermodynamically favourable ring comprising M–N bonds [32].

Analysis of the ESR spectra of iron complexonates established the symmetry of the immediate environment of the central atom in these compounds. The compounds have a spectrum characteristic of Fe^{3+} in the high-spin state $^6A_1$—it consists of a single broad symmetrical line, which indicates hexagonal symmetry of the local environment of the iron ion; the splitting caused by the tetragonal or trigonal components of the crystal field is absent. These results are fully consistent with the determinations of the magnetic susceptibilities of these complexes (μ_{eff} = 5.86 Bohr magnetons, i.e. $s = 5/2$).

Table 7. Logarithms of the stability constants of the protonated complexes of xylylenediaminedialkylenephosphonic acids.



Position in ring	n	lg K_{st} for MH_2L complexes						
		R′	R″	Ni^{2+}	Cu^{2+}	Fe^{3+}	Dy^{3+}	UO_2^{2+}
m-	0	CH_3	CH_3	—	3.92	—	6.48	8.40
p-	0	CH_3	CH_3	—	<3	—	4.78	8.32
p-	1	H	H	—	4.08	—	6.17	9.4(ppt)
		EDBDMPO		3.84	8.33	>10	6.20	8.52

The introduction of a hydroxyl into the structure of the chelating agent increases the stability of the resulting compounds. *N*-(2-Hydroxyethyl)ethylenediaminetri(methylenephosphonic) acid prevents the hydrolysis of iron even when the complexes are boiled at pH > 12. [33]

Extremely stable highly coloured iron(III) and titanium(IV) complexes are formed by ethylenediaminedi-(*o*-hydroxyphenylmethylenephosphonic) and the corresponding phosphonous acids. However, the mechanisms of complex formation are different in the two cases: complexes with simultaneous participation in the coordination of all the electron-donating atoms may be formed with the phosphonous acid, while in the case of the phosphonic acid, where there is a greater number of binding sites, there is apparently competition between the oxygen atoms of the phosphono-group and the phenoxide ion [34,35].

The potential ability of aminoalkylphosphonic acids to increase the number of their binding sites by the inclusion of the oxygen atoms of the phosphono-groups favours the formation of complexes with the lanthanides, which have high coordination numbers and a high affinity for oxygen. Thus the stability of the protonated complexes of ethylenediaminebis(dimethylmethylenephosphonic) acid with the lanthanides is close to that of the corresponding normal ethylenediaminediacetic acid (EDDA) complexes and the stability of the protonated complexes of ethylenediaminediaceticdi(methylenephosphonic) acid exceeds that of the normal EDDA complexes by 6–7 powers of ten. A definite selectivity in the formation of complexes with individual lanthanides is observed.

The formation of complexes with the uranyl ion is interesting: the stability of its protonated complexes with phosphorylated polyamines is very high. The enhanced selectivity in relation to the lanthanides and the uranyl ion is promoted by the increased rigidity of the polymethylene chain joining the nitriloalkylphosphonic acid groups [36]. Thus xylylenediaminebis(dimethylmethylenephosphonic) acids, where the presence of the aromatic ring in the chain between the nitrogen atoms prevents the free rotation of the individual units and fixes the positions of the electron-donating atoms in space, proved to be effective only in relation to the large lanthanide and uranyl cations and to behave as weak complex-forming agents in relation to transition metals, including iron(III) (Table 7).

The difference between the pH ranges where polynuclear insoluble complexes of the above triply charged elements exist permitted the employment of organophosphorus complexones, particularly nitrilotri(methylenephosphonic) acid, as new selective reagents for gravimetric analysis [37].

Aluminium is deposited in the form of the polynuclear complex $Al_3H_3L_2.9H_2O$ from 0.1 *N* hydrochloric acid solutions. In this medium magnesium and alkaline earth metals altogether fail to form complexes. Certain transition metals, such as chromium, copper, and zinc, form less stable soluble complexes, so that their undesirable effect as well as the coprecipitation of transition metals can be eliminated by adding diethylenetriaminepenta-acetic acid as a masking agent (Table 8).

Table 8. Schemes for the possible determinations of metal cations in the presence of a number of elements.

Element determined	Conditions of determination	Elements not interfering with determination	Masking substance
Al	0,1 *M* HCl	Ni, Co, Cu, Zn, Cd, Mn, Cr, Fe, Ca, Mg, Sr, Ba	DTPA
Fe	2 *M* HCl	Ca, Mg, Sr, Ba, Be, Al, Ni, Co, Cu, Zn, Cd, Mn	—

The iron complexonate is stable even in 2 *N* hydrochloric acid, i.e. iron can be determined in the presence of the same elements as in the determination of aluminium. The possibility of determining iron in the presence of aluminium, whose complex decomposes in this medium, is most interesting. The difficulty of separating these metals and also of determining one metal in the presence of the other is generally known.

Our quantitative analytical methods can be successfully used in the analysis of polymetallic systems, in particular

in the analysis of various alloys and steels. Studies on these lines are being continued and the first successful results have already been obtained.

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The specific features of the activities shown by phosphorylated polyamine derivatives, distinguishing them from their carboxy-containing analogues, can be accounted for by the unusual structure of the internal ligand contour, caused by the increase of the number of electron-donating atoms by the inclusion of the oxygen atoms of the phosphono-groups, their high nucleophilicity, and their stereochemistry, which determines the geometry of the complex.

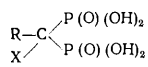
On this basis and experimental results, we postulated three most probable mechanisms for complex formation involving the phosphono-group[4,30,37]. The first mechanism presupposes the formation of a four-membered ring in which the metal ion is coordinated to the two oxygen atoms of the phosphono-group. Under these conditions, the metal can be coordinated in two ways. In the first way the metal ion is coordinated at the midpoint between the two oxygen atoms of each phosphono-group so that the ligand field has an approximately octahedral or tetrahedral coordination, but the oxygen atoms are not located at the vertices of the corresponding polyhedron, forming a new distorted polyhedron in which the coordination number of the metal is higher than usual. This hypothesis does not rule out the possibility of the formation by certain metal ions of complexes whose structure includes four-membered rings where the oxygen atoms of the phosphono-groups lie at the vertices of the polyhedra. Our approximate calculations showed that the strain in the rings with sp^2-hybridised oxygen atoms is insignificant.

The second mechanism presupposes the formation of an eight-membered ring where at least two metal ions are coordinated in turn to the four oxygen atoms of the two phosphono-groups. The complex can then be stabilised by internal hydrogen bonds formed by the coordinated water and the oxygen atoms of the phosphono-groups.

Finally the third type of coordination involves the formation of a network polymer in which the phosphono-group behaves as the tridentate moiety of the ligand. This type of coordination is characteristic, for example, of the insoluble polynuclear beryllium complex of nitrilotri(methylenephosphonic) acid. Three atoms of tetracoordinate beryllium close the ring within one complexone molecule. The remaining oxygen atoms are joined via the metal atoms to other similar molecules.

VI. HYDROXY- AND AMINO-ALKYLIDENEDIPHOSPHONIC ACIDS

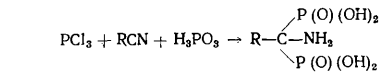
Our conclusion concerning the ability of phosphorylated complexones to form stable protonated complexes, based on the employment in the interaction with cations of only the electron-donating functions of the oxygen atoms in the phosphono-groups, constituted the basis for a detailed study of structurally simpler ligands containing a compact complex-forming group—half-substituted alkylidenediphosphonic acids with a hydroxy- or an amino-group at the carbon atom joined to two phosphono-groups. 1-Hydroxyalkylidenediphosphonic and 1-aminoalkylidenediphosphonic acids are compounds of this kind.



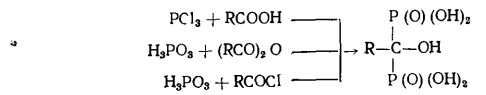
[X = OH or NH_2 and R = alkyl(C_1–C_{11}) or aryl].

Examples of this group of substances have been known for a long time. Thus hydroxyethylidenediphosphonic acid $CH_3C(OH)(PO_3H_2)_2$ has been known since the end of the previous century. During the last decade, many patents dealing with the methods of synthesis of substances of this type were published and various practical applications were suggested for them (see below), but quantitative studies on their complex-forming properties were carried out recently mainly by the present authors.

Aminoalkylidenediphosphonic acids were synthesised by the interaction of phosphorus trihalides with carboxylic acid nitriles in the presence of phosphorous acid[37,38]:

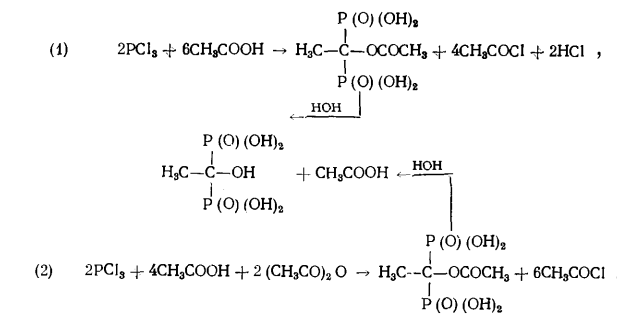


Hydroxyalkylidenediphosphonic acids were obtained by the acylation of phosphorous acid or phosphorus trichloride by carboxylic acids, their anhydrides, or halides[39–43]:



Among the compounds investigated, 1-hydroxyethylidenediphosphonic acid (HEDP) is at present of greatest practical interest. This is due to the ready availability of the starting material and the comparative simplicity of the synthesis, which have made industrial manufacture of this product a realistic proposition.

The reaction of phosphorus trichloride with acetic acid has been used to synthesise HEDP [reaction (1)]:



Together with acetoxyethylidenediphosphonic acid, which is readily hydrolysed to HEDP, acetyl chloride and hydrogen chloride are also produced in this reaction[42,43]. This permitted the joint industrial synthesis of HEDP and acetyl chloride. By the additional introduction of acetic anhydride into the reaction [reaction (2)], the maximum utilisation of the starting material is achieved and corrosive hydrogen chloride is virtually eliminated.

The complex-forming properties of α-substituted alkylidenediphosphonic acids are due to their structures[38,44]. The combination in one molecule of two highly acidic phosphono-groups and also of hydroxy- or amino-groups, which play the role of the basic centre in the molecule, enable these ligands to form stable complexes, not only normal but also protonated, with alkaline earth, transition, and lanthanide elements (Table 9), extending thereby the pH range corresponding to the existence of the complexes from acid to alkaline solutions. A unique property of HEDP is its ability to interact with cations in a strongly acid medium, up to 6 *N* nitric acid.

The steric configuration of their molecules enables α-substituted alkylidenediphosphonic acids to behave as tridentate ligands in coordination with a single cation despite

the presence of five electron-donating atoms and promotes the formation of very stable dinuclear complexes with both alkaline earth and transition metals. HEDP is known to form not only dinuclear but also polynuclear chain complexes with certain cations, in particular with calcium.

With aluminium, iron(III), thorium, and zirconium ions, the relatively low effective number of binding sites in HEDP, which cannot "saturate" the coordination capacity of the complex-forming ion, gives rise to the possibility of the formation of 1 : 2 metal : ligand complexes in the presence of an excess of HEDP, while in the presence of another ligand in the system mixed complexes may be formed. The frequent employment of HEDP in a mixture with other complex-forming agents is due to its ability to form such mixed complexes.

Table 9. Logarithms of the stability constants of alkylidenediphosphonic acid complexes.

	MDP			HEDP				ABDP			
	ML	M_2L	ML_2	ML	MHL	M_2L	ML_2	ML	MHL	M_2L	ML_2
Be^{2+}	—	19.1		16.5	13.4	25.7		16.2	10,4	23,4	
Al^{3+}	14.1		23.0	21.4	15.3	27.2	25.9	18.8	22,5		26.3
Fe^{3+}	19,9		26.6	21.6	16.2	29,1	25.2				
Ln^{3+}	12—13		20—22	18—20	15—16			16—17	11—12		22—24

Comparison of alkylidenediphosphonic acids with organophosphorus ligands containing a nitrogen atom in the alkylene chain linking the two phosphono-groups showed that the complex-forming capacity of alkylidenediphosphonic acids is not inferior, at any rate in the acid region, and in many instances actually superior to that of alkylenepolyamine-di(alkylenephosphonic) acids in which nitrogen is involved in coordination with the metals only after the betaine protons have been titrated.

Together with common properties determined by the presence of phosphono-groups, namely the preferential formation of complexes with cations having small (beryllium and iron) or large (alkaline earth metals) radii, the capacity to form stable complexes at acid pH, the tendency to form dinuclear complexes, etc., alkylidenediphosphonic acids have a number of characteristic features.

Thus alkylidenediphosphonic acids form fairly stable complexes with alkaline earth metals and very stable complexes with beryllium. Comparison of the stabilities of the complexes MHL of hydroxy- and amino-alkylidenediphosphonic acids with methylenediphosphonic acid (MDP) complexes ML, which have the same structure and are formed only via the coordination of the cation to the oxygen atoms of the phosphono-groups, shows that the stability constants of the complexes of substituted alkylidenediphosphonic acids with alkaline earth and certain transition metals differ little from the corresponding constants of the MDP complexes.

The stability constants of the protonated HEDP complexes of multicharged readily hydrolysed cations are higher than the constants of the corresponding normal MDP complexes, which is evidence for additional coordination of the hydroxy-group to these cations (Table 9).

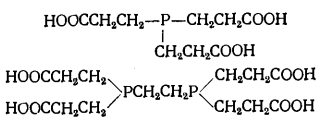
The higher stability of the normal complexes of these cations apparently indicates the involvement of the deprotonated hydroxy-group in complex formation. It is noteworthy that the stability constants of such HEDP complexes are higher than the constants of the corresponding aminobenzylidenediphosphonic acid (ABDP).

The stability of the normal HEDP complexes with iron(III), thorium, and uranium cations is particularly high. Apart from the high coordination capacity, the tendency to form coordinate bonds with oxygen is in this instance of primary importance.

The high capacity of these compounds to combine with metals and the selectivity of their action in relation to beryllium, aluminium, titanium, and thorium combined with their ready availability make them extremely promising ligands.

VII. COMPLEXONES WITH TERVALENT PHOSPHORUS

The specific features of the formation of complexes by organophosphorus complexones make possible the solution of many interesting problems. However, the problem relating to the formation of complexes in an aqueous medium of elements such as silver, mercury, vanadium, and molybdenum could not be solved with the aid of polyamine derivatives. We suggest that complexones in which tervalent phosphorus atoms instead of nitrogen atoms behave as electron-donating species are of interest in this respect[27,45].



The tendency of the above metals to stabilise the bonds with tervalent phosphorus atoms by the formation of an additional d_π bond (apart from the phosphorus–metal coordinate σ-bond), as a result of the transfer of an electron pair from the 4*d* orbitals of the above metals to the unfilled *d* orbitals of phosphorus which have similar energies, leads to the formation of stable complexes with these elements.

We have now investigated complexone analogues derived from phosphines, in which electron-donating phosphorus(III) atoms and acidic phosphono-groups are combined in the same molecule. These constitute a new type of promising ligands.

VIII. APPLICATIONS OF PHOSPHORUS-CONTAINING COMPLEXONES

The knowledge of the main physicochemical characteristics and of the specific features of the behaviour of phosphorus-containing complex-forming ligands suggests many potential applications of these substances in various branches of science and engineering.

Systematic study of the biological properties of alkylenebisnitrilodialkylphosphonic acids has led to the possibility of the employment of substances of this kind for the elimination from the organism of incorporated toxic metals and also has led to the discovery of their influence on the elimination of certain biologically important elements and on the state of metal complexes in the organism.

A biological investigation of organophosphorus complexones carried out at the Institute of Labour Hygiene and Professional Diseases of the Academy of Medical Sciences of the USSR revealed a unique property of this group of substances, namely virtual absence of toxicity.

The ability of alkylenebisnitrilodialkylphosphonic acids to form very stable complexes with copper leads to the elimination of copper from the organism and to the possibility of their use in the treatment of haepatocerebral dystrophy. The formation of stable water-soluble complexes with beryllium suggested that ethylenediaminebis-(dimethylmethylenephosphonic) acid ("phosphicine") can be used as an agent for accelerating the elimination of beryllium from the organism without affecting the calcium metabolism [3,46-48]. Experimental studies demonstrated the usefulness of phosphicine for the acceleration of the elimination of lead from the organism [3]. The efficiency of diethylenetriaminepenta(methylenephosphonic) acids in eliminating uranium has been discovered [49].

HEDP salts, particularly the sodium salt, are able to regulate the calcium content, which suggests their employment in the treatment of the imbalance of the calcium metabolism in the organism and to prevent or reduce the formation of stone, including dental calculus [50-57]. It has been shown that HEDP salts have an inhibiting effect on the deposition of calcium phosphate *in vitro* and *in vivo* in the aorta and in the kidneys of rats [58-60]; they retard osteoporosis [61].

HEDP salts increase the bactericidal activity of phenolic compounds, which suggests their employment in disinfectants, shampoos, mouth washes, tooth pastes, and many other similar products [62-64]. Ditin salts of HEDP have been suggested for the prophylaxis of dental caries [65].

In view of their high capacity for combination with metals, phosphorus-containing complexones may be recommended as effective agents for the dissolution of corrosive deposits and also for the etching of aluminium.

HEDP and its bivalent metal, cobalt, chromium, lead, nickel, and particularly zinc complexes inhibit the corrosion of aluminium, iron, copper, and alloys [66-73]. Metal diphosphonates are not hydrolysed, in contrast to the familiar corrosion inhibitors (polyphosphates) and are stable in the temperature range 20-300°C [71].

The HEDP complex of zinc (sodium or ammonium salt) has been proposed as an inhibitor of the corrosion of a copper surface and as an inhibitor of the corrosion of iron and its alloys [66,70]. It has been noted that the zinc complex is non-toxic [67,73], which makes it superior to the familiar inhibitors, for example chromates.

The employment of HEDP in the composition of alkaline etching solutions for aluminium and its alloys makes it possible to prevent completely the formation of hydrated alumina on the surfaces of the components in etching baths [74,75] and improves the quality of the varnishing of the aluminium surface; it is used as a reagent for the electrochemical deposition of metals [77-79].

The applications of complexones in electroplating led to the development of a highly effective process for the metallation of dielectric materials (which is extremely important for radioelectronics and space engineering) and of a fundamentally new technology for the deposition of metals on the surface of steels without the employment of toxic electrolytes. By varying the process conditions, a wide range of colours of various metallic and non-metallic materials was obtained [75].

Studies dealing with the employment of phosphorus-containing complexones in synthetic detergent and wetting agent compositions have developed particularly extensively in the last decade [80-92]. Hitherto sodium triphosphate has been used as the activating additive to synthetic wetting agents. Its disadvantages include a tendency to hydrolyse with conversion into insoluble orthophosphates, which are deposited on the surfaces of the reservoirs or the articles being treated. On the other hand, wetting agents containing organophosphorus ligands prevent the formation of insoluble deposits [93] and maintain the cleaning capacity of the solutions for a longer time than polyphosphates [94], improve the properties of anionic, non-ionic, and amholytic detergents [85], and in combination with surface-active agents synergise the wetting capacity of detergents [95-97].

Detergents containing HEDP are suitable for washing even in cold water [87].

Complexone salts are used as components of soap [97,98], including toilet soap. The addition of a mixture of HEDP and a polyaminopolycarboxylic acid, for example EDTA, to superfat soaps stabilises them [99] and permits the manufacture of soaps which are effective in hard water [100].

Hydroxyethylidenediphosphonic and nitrilotri(methylphosphonic) acids have been suggested as stabilisers for peroxide compounds; the efficiency of the additive is not lost even in the presence of considerable amounts of polyvalent cations [82,101-104]. The applications of HEDP in cosmetics are described in a number of publications [105,106].

To improve the contrast and colour purity in the treatment of monochrome and colour photographic reversal materials in acid and alkaline solutions, the employment of a tin complex of HEDP has been recommended [107].

The specific features of the action of the new complexones have opened up great possibilities also in the traditional field of the application of complexones, namely in analytical chemistry for effective and in certain instances also selective analytical determinations, which were impossible or difficult when EDTA was used. Alkylenepolyaminedi(alkylmethylenephosphonic) and polyalkylphosphonic acids can be used for the fractional determination of cations in combinations which are difficult to separate (copper-nickel, beryllium-alkaline earth metals, individual pairs of lanthanides, etc.). It has been suggested that ethylenediaminebis(dimethylmethylenephosphonic) acid be used as a highly sensitive titrant in the amperometric determination of beryllium in its alloys with magnesium and aluminium [108]. The quantitative deposition of zirconium by means of this acid in highly acid media can be used to determine zirconium and to separate it from associated elements. Ethylenediaminedi-(*o*-hydroxyphenylmethylenephosphonous) and ethylenediaminedi-(*o*-hydroxyphenylmethylenephosphinic) acids are highly sensitive selective reagents for titanium and tervalent iron [34,35,109]. HEDP has been suggested as a titrant in the complexometric determination of thorium [110].

Nitrilotri(methylphosphonic) acid is used in the determination of beryllium in the presence of alkaline earth and other elements [111].

The application of organophosphorus complexones as masking agents is noteworthy. Thus ethylenediamine-*NN'*-diacetic-*NN'*-di(methylenephosphonic) acid masks beryllium in the hydroxide precipitation reaction, this being the first instance of the masking of beryllium [112]; HEDP can be used as a masking and complex-forming agent for calcium [113-115], aluminium, and titanium [116], and polyvalent and heavy metals [117,118].

The differentiation of the stabilities and solubilities of protonated lanthanide complexes as a function of pH permits the chromatographic separation of yttrium, cerium, and other lanthanides with similar properties using eluent solutions of ethylenediaminebis(dimethylmethylenephosphonic), ethylenediaminetetra(methylenephosphonic), and hydroxyethylidenediphosphonic acids [119,120]. The use of HEDP for the re-extraction of protactinium [121] and also for the elimination of neptunium from plutonium

and the radiometric determination of neptunium in its preparations[122] have been described.

The ability of polyaminopolyphosphonic acids with a large number of binding sites and also of NTP and HEDP to bind alkaline earth metals in complexes permitted the application of these compounds as water softeners[123,124], to prevent the precipitation of calcium carbonate, sulphate, hydroxide, and phosphate in industrial equipment[125,126], and to remove scale formed previously[127].

In view of its ability to bind metal ions, HEDP can be used in the textile industry[128] to eliminate calcium and magnesium ions, which can give rise to undesirable tints on dying and can distort the colour of the fabric.

Phosphorus-containing complexones can be used in the chemical industry to remove admixtures of metal ions from the starting material.

Compounds of this kind can be used effectively in the petroleum and gas extraction industry. Thus it has been recommended that HEDP[129] be added to solutions of inorganic acid used to acidify boreholes and to impart greater fluidity to the liquid being extracted, which makes it possible to maintain in solution calcium, magnesium, and iron salts.

Phosphorus-containing complexones also found applications in agriculture[130]. Apart from the most important elements such as potassium and phosphorus, which are introduced into the soil, in many instances it is necessary to introduce also microelements—manganese, molybdenum, copper, and cobalt. However, when these elements are added to soil in the form of liquid phosphate fertilisers they are precipitated as insoluble complexes. The addition of a complex-forming agent such as HEDP eliminates this defect[55,115]. HEDP esters are used as pesticides in the fight against pests damaging agricultural crops[117]. Thus comprehensive studies of the properties of phosphorus-containing complexones and their salts have led to an unusually wide range of their possible applications, some of which have already been successfully realised in practice.

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Advances in the Synthesis and Manufacture of α-Aminoacids

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The review deals with the existing industrial chemical methods for the manufacture of aminoacids as well as new methods and new versions of the existing methods for their synthesis. Much attention has been devoted to methods of asymmetric synthesis of aminoacids, including homogeneous asymmetric hydrogenation. Enzymatic methods for the synthesis of certain aminoacids from chemical raw materials are examined. The literature of the last 7-8 years is mainly considered. The bibliography includes 385 references.

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I. INTRODUCTION

Together with the continuous search for new methods of synthesising aminoacids, during the last 7–8 years the existing methods have been investigated further and those which are most convenient for practical application have been selected and developed. This approach has been dictated by the colossal and rapidly growing need for aminoacids in various branches of the world's economy.

Major advances have been made in the field of asymmetric synthesis avoiding the need for the optical resolution of racemic aminoacids, which has been and still remains one of the greatest disadvantages of the chemical methods for the synthesis of aminoacids.

In terms of their biological value, aminoacids can be divided into two groups—non-essential aminoacids which the animal and human organism can synthesise at a sufficient rate to build up its own proteins and essential aminoacids which it cannot synthesise. The organism can obtain essential aminoacids only from outside in the form of food. If an essential aminoacid is missing from food or its amount is insufficient, the protein cannot be synthesised; this entails emaciation and death of the organism. For this reason, there is a need to balance the diet, i.e. to add the missing aminoacids to the less valuable [second class] proteins, which increases their nutrient value. Animal feed has been successfully balanced in animal husbandry by the addition of the missing methionine and lysine[1,2]. In the food industry grain products have not so far been balanced on a large scale by the addition of pure aminoacids, although this procedure does improve the nutrient properties of plant protein and hence increases the amount of first class protein suitable for use in food. The latter is particularly important, since a real possibility has arisen of meeting the rapidly growing requirements for food protein without altering the nature of the diet and organoleptic properties of the products[3,4]. Nevertheless at the present time the main consumption of aminoacids in the food industry comes from the employment of sodium glutamate as a powerful taste-improving agent. In many countries it is added to all products which are to be preserved, frozen, or stored for a long time; it is used in communal and domestic catering as a mixture with table salt[5,6]. Compositions imitating the taste and smell of food products are also made up of a mixture of aminoacids[3,7].

Aminoacids are also successfully employed in medicine. After severe operations, burns, and in other stress states, the human organism is unable to assimilate proteins in an amount necessary for regenerative processes, which impairs the state of the patient. In such cases aminoacid feeding is resorted to either in the usual way or by the introduction of a solution of aminoacids directly into the bloodstream. The excellent therapeutic effect achieved in such cases has given rise to a considerable requirement for aminoacid mixtures. Children suffering from phenylpyruvate oligophrenia are fed a mixture of aminoacids free from phenylalanine.

Table 1 (Belikov[1]).

Aminoacid	Amount manufactured, tonnes per year	Method of preparation
L-Glutamic acid	180000	Microbiol., chemical
DL-Methionine	32000	Chemical
L-Lysine	8000	Microbiol.
Glycine	2000	Chemical
L-Tryptophan	20	Chemical
L-Threonine	20	Microbiol., chemical

Certain individual aminoacids, both present in and absent from natural proteins, are employed in medicine. Thus methionine is used in the cirrhosis and fat infiltration of the liver, in dystrophy, and in atherosclerosis. Glutamic acid is mainly used in the treatment of diseases of the central nervous system: schizophrenia, epilepsy, psychoses, shock, etc. γ-Aminobutyric acid and its derivatives are widely used for these purposes. Until recently the only treatment for Parkinson's disease was surgical intervention in the region of the brain. An effective therapeutic agent—3,4-dihydroxyphenylalanine (DOPA) (plus its derivatives)—has now been found. The requirement for this aminoacid is very great.

Aminoacids are used as the starting materials for the synthesis of polypeptides, many of which are very active

physiologically, and also for the synthesis of other medicinal preparations.

Finally aminoacids have also found technical applications. When they are introduced into a polycondensation process, the resulting oligomers, while lacking the biological activity of proteins, nevertheless resemble them in structure and imitate some of their important physical properties. Artificial wool, silk, and leather are widely manufactured in this way, and are not inferior in their properties to the natural materials. The total world manufacture of aminoacids in 1972 is characterised approximately by the figures quoted in Table 1.

The relative contributions of aminoacids to various branches of the economy can be demonstrated using Japan as an example, where the manufacture of aminoacids has developed to the greatest extent:

The structure of the applications of aminoacids in Japan

Food industry	65%
Animal husbandry	18%
Medicine	15%
Others	2%

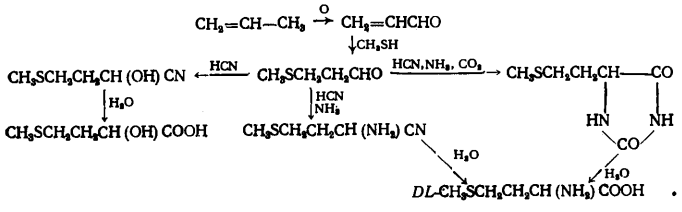
The world requirement for aminoacids increases by 10% annually[1].

II. INDUSTRIAL CHEMICAL SYNTHESES

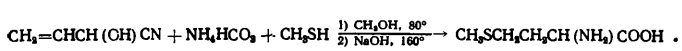
1. Methionine

The chemical synthesis of methionine, an aminoacid mainly consumed in poultry farming, has been most thoroughly developed[1,2,8]. Methionine is unique in its biological properties. Its L- and D-isomers are assimilated to equal extents by the organism. Moreover, the replacement of the amino-group by the hydroxy-group does not affect its nutrient properties. The hydroxy-analogue of methionine is manufactured in the USA. The manufacture of DL-methionine has begun in the USSR. It is also manufactured in the German Federal Republic, France, and Japan. The scale of the manufacture of methionine is greater than that of any other essential aminoacid[9].

The starting material for the synthesis is propene—a petroleum cracking product. Propene is oxidised to a acrolein, which is converted by a series of reactions into racemic methionine:



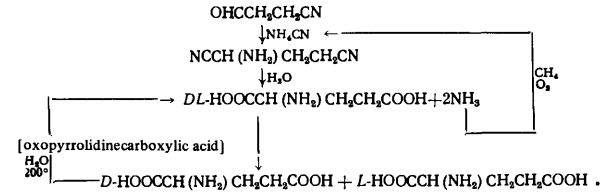
The sequence of reactions can be altered: cyanoallyl alcohol is initially obtained from acrolein and is then converted into highly pure DL-methionine in 80% yield[10]:



A number of other modifications and improvements of the basic process have been proposed[11-23].

2. Glutamic Acid

The raw material for the industrial manufacture of L-glutamic acid is acrylonitrile, obtained by the oxidative ammonolysis of propene. The reaction of acrylonitrile with carbon monoxide and hydrogen is carried out at an elevated temperature and pressure in the presence of $Co_2(CO)_8$ with formation of β-cyanopropionaldehyde, which also serves as the raw material in the synthesis of tryptophan. The subsequent reactions can be represented by the following scheme:

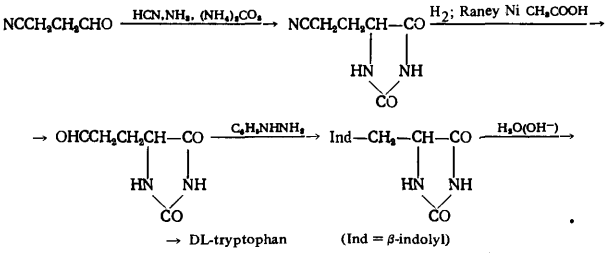


The racemic glutamic acid is resolved into its optical isomers by continuous selective crystallisation. This operation is based on the fact that the solubility of DL-glutamic acid in solutions of its salts (for example, its hydrochloride or its ammonium salt) is almost twice the solubility of the optical isomers. As a result, saturated solutions of DL-glutamic acid are supersaturated with respect to the optical isomers. The introduction of a seed of the L-isomer induces its crystallisation. The optical purity of the resulting L-glutamic acid is 95%.

After neutralisation, the monosodium salt of L-glutamic acid is obtained with an optical purity of 99.8%; it is used as an anabolic agent (to increase weight). The D-isomer of glutamic acid racemises at 200°C and is recycled[5,6]. The synthesis[24-40], cleavage[5,6,41,42], and racemisation[5,6,43] processes have been developed with careful allowance for possible complications, side reactions, and the possibility of the utilisation and reutilisation of the components and waste products of the synthesis. About 1200 tonnes of L-glutamic acid were obtained in Japan in 1972.[1]

3. Tryptophan

The industrial synthesis of tryptophan from β-cyanopropionaldehyde was achieved in Japan by the Ajinomoto Company[8,44-46]:



The overall yield of DL-tryptophan amounts to about 60%.[46] It is resolved into optical isomers also by the selective crystallisation of the ammonium[47] or zinc[48] salt of *N*-acetyl-DL-tryptophan, a procedure which is also used to purify DL-tryptophan[49-51].

4. Threonine

The synthesis of DL-threonine by the condensation of copper glycinate with acetaldehyde, which was proposed

in 1957,[52] proved to be the most convenient for the industrial manufacture from the standpoint of the raw material, yield, and economy. It is at present used in Japan[8]:

Copper glycinate + $CH_3CHO \xrightarrow{(OH^-)}$ "copper threoninate" →

→ DL-threonine complex (precipitate) + DL-allothreonine complex (solution)

↓

L-threonine + D-threonine.

The complex "copper threoninate" formed consists mainly of the DL-threonine complex. The DL-allothreonine complex obtained simultaneously is much more soluble in water, which makes it possible to separate the diastereoisomers by filtration[53-56]. Several versions of the synthesis have been developed on the basis of this scheme[57-60].

Selective crystallisation is used for the resolution of DL-threonine into optical isomers, as for glutamic acid[8]. The DL-allothreonine and D-threonine formed in the synthesis and after resolution into optical isomers are converted into L-threonine by a number of procedures. Thus L-threonine can be obtained from D-threonine by stereospecific reactions in which the formation of oxazoline derivatives plays an important role[61]. The same derivatives can be used to convert DL-allothreonine into DL-threonine[62,63]. Furthermore, the isomerisation of the copper complex of allothreonine in an alkaline medium in the presence of acetaldehyde leads to an equilibrium mixture of the allothreonine and threonine complexes, with the latter predominating[57,64]. Under these conditions, D-threonine may racemise into a mixture of DL-threonine and DL-allothreonine with inversion at both asymmetric atoms[8].

5. Glycine

In connection with the development of industrial methods for the synthesis of aminoacids by incorporating completed α-aminoacid fragments using glycine and its acyl derivatives, the requirement for these has increased. This is indicated by the large number of patents dealing with the development of new methods for the synthesis of glycine and its derivatives from available raw materials and also with the improvement of the existing methods.

The existing process for the manufacture of glycine from monochloroacetic acid and ammonia in the presence of hexamethylenetetramine and ammonium ions can be carried out continuously with a rational utilisation of the waste and a yield of 96.5%.[65-69] The interaction of monochloroacetic acid with the ammine complexes $[Cu(NH_3)_4]SO_4.H_2O$, $[Co(NH_3)_6](NO_3)_3$, $[Ni(NH_3)_6](NO_3)_2$, and $[Zn(NH_3)_4]SO_4.3H_2O$ yields the corresponding metal glycinates, which can be used in the synthesis of aminoacids[70].

Another process has been developed in which glycine is synthesised from formaldehyde, hydrogen cyanide, and ammonia (by the Strecker or Bucherer–Bergs methods)[71,72]. The resulting aminoacetonitrile can be converted into pure glycine via an oxazole derivative by the reaction with acetone[73]. Glycine can be obtained in 77% yield by the hydrolysis of hydantoin[74,75]. An 80–96% yield of glycine is obtained by the oxidation of acrylonitrile in the presence of tungstic acid or tungsten heteropolyacids[76]. Glycine synthesised by the oxidation of monoethanolamine in the presence of CuO and KOH is used in the synthesis of threonine[58]. *N*-Acylglycines can be obtained by treating hydroxymethyl and alkoxymethyl derivatives of various amides with carbon monoxide in 100% sulphuric acid:

$$\left.\begin{matrix}RCON(R')CH_2OH\\ RCON(R')CH_2OCH_3\end{matrix}\right\} \xrightarrow{H_2SO_4} [RCON(R')CH_2^{\oplus} \leftrightarrow RC\overset{\oplus}{O}N(R')=CH_2] \rightarrow$$

$$\xrightarrow{1)\ CO;\ 2)\ H_2O} RCON(R')CH_2COOH\ .$$

Usually R′ = H and the yields are between 20 and 88%.[77-79] Apart from their ready conversion into the free aminoacid, *N*-acylglycines can be used for the synthesis of peptides[80] and also as one of the components of the azlactone synthesis[81].

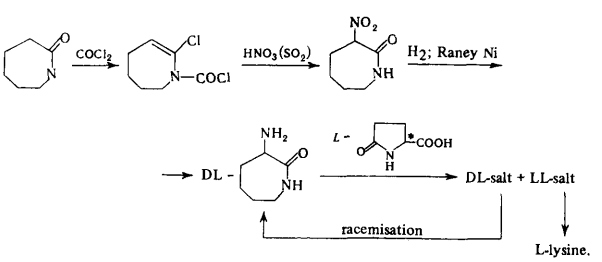
6. Aspartic Acid

DL-Aspartic acid is manufactured from ammonium fumarate or maleate, maleic anhydride being used as the starting material for the synthesis of the latter. A solution of ammonium maleate (or fumarate) in aqueous NH_4Cl with added ammonia (pH ~ 7.5) is heated for 75 min at 180°C. DL-Aspartic acid is isolated at the isoelectric point in 79% yield. The mother liquors and imino-$\alpha\alpha'$-disuccinic acid formed as a by-product are returned to the process[82]. Different versions of this synthesis have been described[83-89].

The method of asymmetric synthesis of L-aspartic acid from ammonium fumarate in a continuous process with the aid of microbial aspartase fixed in a polyacrylamide gel has been recommended for its industrial manufacture[90]. A 1 M solution of ammonium fumarate at pH 8.5 in the presence of $MnCl_2$ is passed through a 5 × 100 cm column filled with the carrier and the fixed enzyme at a rate of 160 ml h^{-1} at 37°C. After the usual treatment, pure crystalline L-aspartic acid is obtained in 95% yield. The enzyme retains its full activity for 7–8 days, but in the subsequent 22–23 days its activity falls to 25%.

7. Lysine

The chemical synthesis of lysine from ϵ-caprolactam has been achieved on an industrial scale in Holland[2,8]:



The resolution into isomers was carried out at the DL-α-aminocaprolactam stage by the crystallisation of the diastereoisomeric salt with L-pyroglutamic acid[2].

A number of patents deal with problems associated with the manufacture of lysine from ϵ-caprolactam. Methods have been described for the formation of α-halogeno-derivatives of ϵ-caprolactam[91,92], including those employing phosgene[93-96], and for their subsequent conversion into DL-lysine[97-100]. Procedures have been developed for the preparation and purification of α-amino-ϵ-caprolactam[101,102], for the resolution of the racemate[103-107], for the racemisation of optically active forms[108,109], and for hydrolysis with formation of lysine[110-117].

8. 3-(3,4-Dihydroxyphenyl)Alanine (DOPA)

Interest in 3,4-dihydroxyphenylalanine arose comparatively recently in connection with the observation of its therepeutic activity against one of the commonest severe nervous disorders in the elderly—Parkinson's disease[118]. Only the L-form has a therapeutic effect. The present requirement for this aminoacid is very great. L-DOPA is obtained by extraction with methanol from broad beans (*Vicia faba*): 1 kg of beans yields 18.7 g of L-DOPA.[119]

The development of a method for homogeneous asymmetric hydrogenation (see above) served as a basis for the experimental manufacture of L-DOPA. It is synthesised by the hydrogenation of 4-hydroxy-3-methoxyacetamidocinnamic acid, obtained by the azlactone synthesis from vanilline. The optical yield reaches 90%. Rhodium complexes with asymmetric *o*-anisylmethylcyclohexylphosphine are used as the catalyst[120-122]. This process is the first asymmetric chemical synthesis of an aminoacid on an industrial scale.

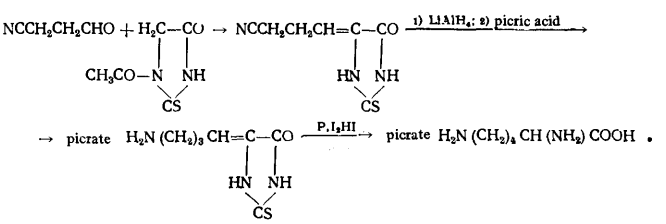
9. β-Alanine

The industrial synthesis of this important natural β-aminoacid[123] involves the addition of an excess of ammonia to acrylonitrile[124,125]. The process is carried out continuously, the yield of β-alanine exceeding 95%.[126] Acrylic acid[127,128] or acrolein[129] can be used instead of acrylonitrile. β-Alanine is used in the synthesis of pharmacological preparations, in particular of panthothenic acid[127] and also in the synthesis of polyamides[130].

III. METHODS FOR THE PREPARATION OF AMINOACIDS

1. From Unsaturated Compounds

Unsaturated compounds—acrylonitrile, acrolein, methyl acrylate, vinyl acetate, butadiene, ethylene, etc.—are widely used for the synthesis of aminoacids. The hydroformylation reaction constitutes a promising method for their conversion into aminoacids and has already been achieved on an industrial scale. The aldehydes or their derivatives obtained in this reaction are subsequently converted into aminoacids by the cyanohydrin or hydantoin syntheses. The industrial syntheses of L-glutamic acid and L-tryptophan from β-cyanopropionaldehyde, obtained by the hydroformylation of acrylonitrile[8], have already been discussed. An attempt has been made to employ this aldehyde also in the synthesis of lysine. It could not be condensed with hydantoin, hippuric acid, or rhodanine, but 1-acetyl-2-thiohydantoin proved to be suitable for this purpose. After the reduction of the condensation product with $LiAlH_4$ and hydrolysis, DL-lysine picrate was obtained in 18% yield with respect to β-cyanopropionaldehyde[131]:



The synthesis of *N*-acylaminoacids from aldehydes (or directly from olefins) and amides has been achieved with the aid of the hydroformylation reaction[132]:

$$RCHO + CH_3CONH_2 + CO \rightarrow RCH(NHCOCH_3)COOH.$$

Since the reaction of an aldehyde, amide, and carbon monoxide catalysed by $Co_2(CO)_8$ proceeds under conditions similar to those in the hydroformylation of olefins, a single-stage conversion of an olefin into an *N*-acylaminoacid is possible:

$$RCH=CH_2 + CH_3CONH_2 + 2CO + H_2 \rightarrow RCH_2CH_2CH(NHCOCH_3)COOH.$$

The reaction is carried out at 110–150°C, 150 atm of CO, and 50 atm of H_2 in 10–80 min. The solvents are dioxane, ethyl acetate, and acetic acid. *N*-Acetyl derivatives of the following aminoacids have been obtained in this way (the percentage yields are indicated in brackets): glycine (26), alanine (68), α-aminobutyric acid (46), valine (70), phenylalanine (56), α-amino-γ-cyanobutyric acid (58), the γ-monomethyl ester of glutamic acid (70), and methionine (64). Benzamide and the amide of lauric acid have been used in place of acetamide. The application of this method in the synthesis of acylglycines was discussed above[77-79]. Carbonylation of Schiff bases yields polypeptides and aminoacids:

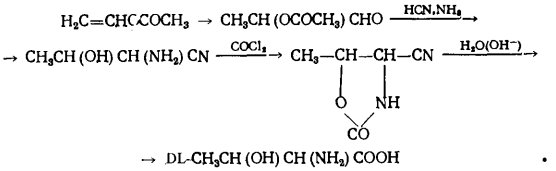
$$R'N=CHR + CO \rightarrow [R'NCH(R)CO-]_n \xrightarrow{H_2O} R'NHCH(R)COOH.$$

Alanine has been obtained in this way with R = CH_3 and R′ = H.[80]

DL-Glutamic acid can be synthesised in 88% yield from the dimethylacetal obtained by the hydroformylation of methyl acrylate in the presence of methanol[133]:

$$CH_2=CHCOOCH_3 \rightarrow (CH_3O)_2CHCH_2CH_2COOCH_3 \xrightarrow{HCN,\ H_2O} \rightarrow NCCH(OH)CH_2CH_2COOCH_3 \xrightarrow[2)\ H_2O(H^+)]{1)\ NH_4OH} DL\text{-}HOOCCH(NH_2)CH_2CH_2COOH.$$

An interesting synthesis of threonine from α-acetoxypropionaldehyde, obtained by oxo synthesis from vinyl acetate, has been described:



A mixture of 91% of DL-threonine and 9% of DL-allothreonine is obtained in 30% yield[134].

The diacetate derived from α-acetoxyacetaldehyde can be used in the synthesis of DL-serine:

$$H_2C=CHOCOCH_3 \xrightarrow{Br_2} CH_2BrCHBrOCOCH_3 \xrightarrow{(CH_3CO)_2O} CH_3OCOCH_2CH(OCOCH_3)_2 \xrightarrow{NaCN,NH_3} CH_3OCOCH_2CH(NH_2)CN \xrightarrow{H_2O(H^+)} CH_2(OH)CH(NH_2)COOH.$$

The yield of DL-serine is 78%.[135] DL-Serine can be obtained via hydantoin by treating the triacetate with NaCN and $(NH_4)_2CO_3$.[136] A mixture of DL-threonine and DL-allothreonine has been obtained in the same way from propenyl acetate in 64% yield[135].

DL-Glutamic acid is obtained by cyanohydrin synthesis from acrolein:

$$H_2C=CHCHO \xrightarrow{HCN,\ NH_3} [NCCH_2CH_2CH(NH_2)CN] \xrightarrow{H_2O(OH^-)} \rightarrow HOOCCH(NH_2)CH_2CH_2COOH.$$

Acrolein homologues can be used in the synthesis of glutamic acid homologues[137-139]. Various α-amino-β-hydroxyacids are obtained from αβ-unsaturated acids

via epoxy-compounds[140-146]. Thus *E*-crotonic acid yields DL-threonine[140]:

$$E\text{-}CH_3CH{=}CHCOOH \xrightarrow{H_2O_2;\ Na_2WO_4} trans\text{-}CH_3CH(O)CHCOOH \xrightarrow{HCl} \rightarrow erythro\text{-}CH_3CH(OH)CH(Cl)COOH \xrightarrow{NH_3} CH_3CH(OH)CH(NH_2)COOH .$$

The bromohydrin of crotonic acid can be converted into DL-threonine by reaction with urotropine[147] or by photochemical ammoniolysis[148]. These studies constitute a development of Carter's method[149,150].

DL-Methionine can also be obtained from crotonic acid. On treatment with C_2H_5OH and $(C_2H_5)_3N$, the acid chloride is converted into the ester with simultaneous migration of the double bond to the $\beta\gamma$-position; this is followed by the addition of CH_3SH, bromination with $P_2Br_2Cl_4$, amination, and hydrolysis. The yield of DL-methionine relative to crotonic acid is 32.5%.[151]

A number of intermediates formed in the synthesis of DL-serine from methyl acrylate or acrylonitrile have been described[152-155]. DL-Glutamic acid is obtained in 30% yield by the cyanoethylation of *N*-acylaminoacetonitriles[156] and also in 40% yields by the cyanoethylation of 2-phenyl-5-oxazolone (azlactone)[157]. Considerable amounts of β-alanine and DL-aspartic acid are obtained from the waste products in the manufacture of acrylonitrile by the oxidative ammonolysis of propene after a simple treatment[158]. The addition of dichloroacetic acid esters to butadiene yields $\alpha\epsilon$-dichlorohexenoic acid esters, which are converted by ammoniolysis, hydrogenation, and hydrolysis into DL-lysine[159,160]. Butadiene has been used to synthesise lysine via the nitro-derivative[161-164]. Various aminoacids can be obtained from the polychloroalkane formed in the telomerisation of ethylene with carbon tetrachloride[165] or trichloroacetic acid[166].

2. From Ketones

Monoaminomonocarboxylic acids can be obtained from methyl alkyl (or aryl alkyl) ketones in several ways via α-hydroxyiminoketones:

$$RCH_2COCH_3 \xrightarrow{R'ONO} RC(=NOH)COCH_3 \xrightarrow{NaBrO} RC(=NOH)COOH \xrightarrow[(A)]{H_2;\ Raney\ Ni;} RCH(NH_2)COOH$$

$$RC(=NOH)COCH_3 \xrightarrow{Zn/CH_3COOH} RCH(NHCOCH_3)COCH_3 \xrightarrow{O_2(HCl)} (C)$$

$$RC(=NOH)COCH_3 \xrightarrow{(C_2H_5O)_2SO_2} RC(=NOC_2H_5)COCH_3 \xrightarrow{NaClO} RC(=NOC_2H_5)COOH$$

$$(C) \xrightarrow{H_2;\ Pd/C} (B)$$

The following products were obtained [the method of preparation, R, and the percentage yield relative to the ketone (in brackets) are indicated]: *A*, $C_6H_5CH_2$ (53);[167] *B*, $C_6H_5CH_2$ (40);[168,169] *C*, $C_6H_5CH_2$ (-);[170] *A*, p-$CH_3OC_6H_4CH_2$ (46); *A*, 3,4-$CH_2O_2C_6H_3CH_2$ (45); *A*, C_6H_5 (44);[171] *B*, CH_3 (15);[168,169,172] *C*, CH_3 (80, with respect to the oxime)[170,173]; *B*, i-C_3H_7 (31—34.4);[168,169,172] *C*, i-C_3H_7 (-);[170] *B*, $CH_3(CH_2)_3$ (51—63);[172] *C*, s-C_4H_9 (-).[170,173]

In addition, the methylene group in methyl ketones can be halogenated, the halogen replaced by an amino-group, and the product oxidised by atmospheric oxygen. DL-Valine and DL-alanine have been obtained in this way[174]:

$$CH_3COCH_2R \xrightarrow{Br_2} CH_3COCHBrR \xrightarrow{NH_3;\ CH_3OH} [CH_3COCH(NH_2)R] \xrightarrow{O_2;\ HCl} \rightarrow DL\text{-}RCH(NH_2)COOH .$$

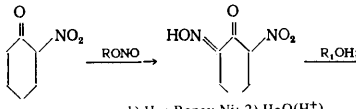
(R=CH_3; i-C_3H_7)

Acetylacetamide, obtained from diketen, is used as the starting material for the synthesis of a wide variety of aminoacids[175,176]:

$$CH_3COCH_2CONH_2 \xrightarrow{RBr} CH_3COCH(R)CONH_2 \xrightarrow{KOBr} CH_3COCH(R)NH_2 \xrightarrow{O_2} \rightarrow RCH(NH_2)COOH .$$

R- S-C_4H_9; i-C_4H_9; $C_6H_5CH_2$; $CH_3SCH_2CH_2$; $HOOCCH_2CH_2$.

The nitrosation of cyclic ketones is used in the synthesis of DL-lysine from cyclohexanone[177-179] and nitrocyclohexanone[180-184]:



$$\xrightarrow{R_1OH;\ NaOH} O_2N(CH_2)_4C(=NOH)COOR_1 \xrightarrow{1)\ H_2;\ Raney\ Ni;\ 2)\ H_2O(H^+)} H_2N(CH_2)_4CH(NH_2)COOH .$$

3. Carboxylation of Amines

Several studies have been made on the introduction of the carboxy-group into the amine molecule:

$$RCH_2NH_2 + 2H_2O_2 \xrightarrow{Na_2WO_4} RCH{=}NOH \xrightarrow{2NaHSO_3} RCH(NH_2)SO_3Na \xrightarrow{NaCN} RCH(NH_2)CN \xrightarrow{H_3O(H^+)} RCH(NH_2)COOH .$$

On treatment with bisulphite, $RCH(NHOH)SO_3Na$ is probably formed as an intermediate and is then reduced to the amine by the excess bisulphite. Alanine, serine, and phenylalanine have been obtained in yields of 71, 68, and 75% respectively[185]. It is desirable to employ readily available amines in the synthesis of aminoacids by this procedure. The interaction of the sodium salt of a sulphonic acid with KCN for the introduction of the carboxy-group has also been used in the synthesis of α-methyl-DOPA.[186]

Isonitriles obtained in a preliminary step from amines have been carboxylated:

$$RCH_2NH_2 \rightarrow RCH_2NC \xrightarrow[NaH]{OC(OC_2H_5)_2} RCH(NC)COOC_2H_5 \xrightarrow{1)\ H_3O(H^+);\ 2)\ H_2OOH^-} \rightarrow RCH(NH_2)COOH .$$

$$RCH_2NH_2 \rightarrow RCH_2NHCHO \rightarrow RCH(NC)COOC_2H_5$$

Diethyl carbonate in dimethylformamide (DMF) in the presence of NaH was used as the carboxylating agent. The following percentage yields with respect to the isonitrile (in brackets) were obtained for different R: C_6H_5 (57); 4-$CH_3OC_6H_4$ (54); 4-$CH_3C_6H_4$ (51); 4-Cl—C_6H_4 (56); 3.4-$(CH_2O_2)C_6H_3$ (60); 2-furyl (55); H (32). Dimethyl carbonate and also ethyl chloroformate or CO_2 in the presence of butyl-lithium can be used as carboxylating agents. Conditions for the reaction with aliphatic amines, with the exception of methylamine, have not been found[187,188]. DL-Valine was obtained in 46% yield by treating a solution of isobutylamine in a mixture of dioxane and 35% HCl with 30% hydrogen peroxide, the reaction system being simultaneously bubbled with CO_2 at 30°C for 1.5 h. DL-Alanine was obtained similarly from ethylamine[189]. The direct carboxylation of amines, in particular methylamine, by formic acid, formates, or carbon dioxide is carried out under the influence of γ- or ultraviolet radiation. The yields are low[190].

4. From Nitroacetic Acid Esters

Nitroacetic acid esters O_2NCH_2COOR (R = CH_3 or C_2H_5), obtained from nitromethane, provide an almost

universal starting material for the synthesis of α-amino-acids. The method is based on the exceptional reactivity of the methylene group of the nitroacetic acid ester due to the presence of adjoining nitro- and ester groups. The nitroacetic acid ester contains a potential α-aminoacid grouping: different substituents are introduced into its molecule and the nitro-group is then reduced to the amino-group[191].

A general scheme for the synthesis of aminoacids from nitroacetic acid esters was published in 1969.[3] The most extensive studies in recent years dealt with the synthesis of tryptophan and phenylalanine. Attention was concentrated on reduction of β-substituted α-nitropropionates and α-nitroacrylates which are formed as intermediates.

The reduction of β-indolyl-α-nitropropionic acid esters does not present much difficulty and proceeds smoothly in both catalytic[192] and electrochemical[193] processes. The β-indolyl-α-nitropropionate, obtained by heating the gramine salt of the nitroacetic acid ester, yields DL-tryptophan after reduction of the nitro-group and hydrolysis[194]:

$$\mathrm{IndCH_2N(CH_3)_2 + O_2NCH_2COOC_2H_5 \rightarrow [gramine\ salt\ of\ NAE] \xrightarrow{110^\circ}}$$
$$\rightarrow \mathrm{IndCH_2CH(NO_2)COOC_2H_5 \xrightarrow{H_2;\,Raney\ Ni} IndCH_2CH(NH_2)COOC_2H_5 \rightarrow}$$
$$\xrightarrow{\mathrm{H_2O/C_2H_5OH(OH^-)}} \text{DL-tryptophan}$$

(Ind = β-indolyl; NAE = nitroacetic acid ester).

The reduction of aromatic derivatives of α-nitroacrylic acid is more difficult[192,195,196].

β-Indolyl-α-nitroacrylates have been obtained in two ways: by the condensation of indole with β-alkoxy-α-nitro-acrylates (without condensing agents)[195,197] and also by the condensation of indole-3-aldehyde with nitroacetic acid esters in the presence of acid catalysts[196,198,199]:

$$\left.\begin{array}{l}\mathrm{IndH + C_2H_5OCH{=}C(NO_2)COOCH_3}\\ \mathrm{IndCHO + O_2NCH_2COOC_2H_5}\end{array}\right\} \xrightarrow[\text{Ind = β-indolyl)}]{\text{HCl, SOCl}_2\text{, AlCl}_3} \mathrm{IndCH{=}CH(NO_2)COOR}\ .$$

The use of alkaline catalysts leads mainly to isoxazoline *N*-oxides[200]. The reduction of β-indolyl-α-nitroacrylates in the presence of Raney nickel in alcohol proceeds with considerable charring[196]. The best results were obtained using two successive hydrogenation stages: initially in the presence of palladium black and then in the presence of Raney nickel[195]. In the first stage β-indolyl-α-nitro-acrylate is partially converted (52%) into β-indolyl-α-nitropropionate ester, which is then readily hydrogen-ated to the tryptophan ester. Together with the catalytic procedure, a method was developed for the electrochem-ical reduction of β-indolyl-α-nitroacrylacrylate in aqueous alcoholic and aqueous dioxane mixtures at pH 1–3 in the presence of metals with a high hydrogen overvoltage. The yield of DL-tryptophan reaches 60%.[201,202] The characteristics of the electrochemical reduction were elucidated by polarography and electrolysis at a controlled potential. It was found that both electrochemical and catalytic reduction proceed in steps, but the saturated nitro-ester is not formed; the principal intermediate in the reduction reaction is the oxime[203,204]. The inadequate yield of the desired product can be accounted for by the instability of the oxime and also of the initial β-indolyl-α-nitroacrylate and other intermediates in the acid medium[193].

Electrochemical reduction of α-nitrocinnamic acid ester gives a 65% yield of DL-phenylalanine. Higher yields could not be achieved owing to the instability of the initial ester and the intermediates under the experimental conditions[193,205,206].

The catalytic reduction of phenyl nitroacrylates was carried out in alcoholic solutions[207], but the process may be complicated by the addition of the alcohol to the double bond and other side reactions[208–211]. On the other hand, β-isopropyl-ββ-dimethyl-, and β-ethyl-β-methyl-α-nitro-acrylates are hydrogenated in the presence of Raney nickel in methanol, yielding respectively DL-leucine, DL-valine, and DL-isoleucine[212,213]. Steric factors probably play a role in these reactions and the rate of hydrogenation exceeds the rate of addition of methanol[212].

Nitroacetic acid ester has been used to synthesise DL-lysine from butadiene:

$$\mathrm{H_2C{=}CH{-}CH{=}CH_2 \xrightarrow{N_2O_4,\,I_2} O_2NCH_2CH{=}CHCH_2I \xrightarrow{O_2NCH_2COOC_2H_5}}$$
$$\rightarrow \mathrm{[O_2NCH_2CH{=}CHCH_2CH(NO_2)COOC_2H_5} \xrightarrow{\text{1) H}_2\text{; Pd/C; 2) H}_2\text{O(H}^+\text{)}} \text{DL-lysine}\ .$$

The yields were about 20% and about 70% in the condensation and reduction stages respectively[161–164].

A number of aminoacids have been obtained by the *C*-alkylation of methyl nitroacetate by alkyl halides in aprotic dipolar solvents via the mechanism:

$$\mathrm{RX + O_2NCH_2COOCH_3 \xrightarrow{CH_3ONa} RCH(NO_2)COOCH_3 \xrightarrow{\text{1) H}_2\text{; Raney Ni; 2) H}_2\text{O(H}^+\text{)}}}$$
$$\rightarrow \mathrm{RCH(NH_2)COOH}\ .$$

The resulting nitro-esters are isolated in the form of crystalline ammonium salts, are hydrogenated for 1 h at 20°C and 3–3.5 atm, and the product is hydrolysed with 6 *N* HCl.[214,215]. The following products were obtained in this way (the yields are given with respect to nitro-acetic acid ester): DL-aspartic acid, 55% (90%[215]); DL-glutamic acid, 73.5% (83%[215]); DL-alanine, 63%; DL-valine, 13.5%; DL-phenylalanine, 40%; DL-αα-di-aminobutyric acid, 3.8%; DL-ornithine, 18.5%; DL-lysine, 12%.

Methods for the synthesis of γ-aminoacids, some of which have a sedative effect on the nervous system, have been developed on the basis of nitroacetic acid ester[216].

5. From Aliphatic, Aromatic, and Heterocyclic Compounds and Other Aminoacids

A new method for the preparation of α-aminoacids from carboxylic acids in a single stage consists of the amination of α-lithio-lithium salts of *O*-alkylhydroxylamines in hexametapol at −15°C:

$$\mathrm{RCH_2COOH \xrightarrow{LiN(n\text{-}C_3H_7)_2} RCHLiCOOLi \xrightarrow{NH_2OR'} R\ CH(NH_2)CCOH}\ .$$

The yields of phenylglycine and valine reached 55.5 and 33.9% for a 32.8% conversion of the initial acid. Best results are obtained with *O*-methylhydroxylamine[217].

DL-DOPA is obtained by the hydrolysis of 5-(3,4-iso-propylenedioxybenzyl)hydantoin, which is synthesised in five stages from 4-methylcatechol[218]. Lysine has been obtained from cyanobutyraldehyde by hydantoin synthesis with subsequent hydrogenation and hydrolysis[219,220]. A number of papers deal with the details of the hydrolysis of the hydantoins derived from various aminoacids. The hydrolysis is carried out as a rule under alkaline conditions in an autoclave with periodic release of the excess pressure[74,75,221–223]. A number of other improvements have been proposed to the cyanohydrin synthesis[224,225].

The hydroxylation of the aromatic ring is used for the synthesis of aminohydroxyacids. Thus L-DOPA is

obtained in about 50% overall yield from the methyl ester of *N*-acetyl-L-tyrosine[226]:

$$L\text{-}4\text{-}HOC_6H_4CH_2\overset{*}{C}H(NH_2)COOCH_3 \xrightarrow{(CH_3CO)_2O} \rightarrow L\text{-}4CH_3OCOC_6H_4CH_2\overset{*}{C}H(NHCOCH_3)COOCH_3 \xrightarrow{AlCl_3} \xrightarrow{AlCl_3} \rightarrow L\text{-}3,4\text{-}(CH_3CO)(OH)C_6H_3CH_2\overset{*}{C}H(NHCOCH_3)COOCH_3 \xrightarrow{1)\ H_2O_2,\ NaOH;\ 2)\ HBr} \rightarrow L\text{-}3,4\text{-}(OH)_2C_6H_3CH_2\overset{*}{C}H(NH_2)COOH.$$

Hydroxylation of the methyl ester of *N*-acyl-L-tyrosine by benzoyl peroxide gave L-DOPA in about 35% overall yield[227,226].

The hydroxy-group was introduced into the *N*-acyl-L-tyrosine molecule by reaction with atmospheric oxygen in the presence of Fe^{2+} and enediol compounds (ascorbic acid)[229]. Proline reacts with atmospheric oxygen in aqueous solutions on irradiation with ultraviolet or visible light in the presence of semiconducting metal oxides and sulphides. Proline is then converted into hydroxyproline in 1.5 h in 52% yield[230].

Methods have been proposed for the chlorination[231,232] of ω-benzoylaminocaproic acid, the ammoniolysis of the resulting chloro-derivatives[233], and subsequent hydrolysis[234,235], the overall process leading to DL-lysine. These reactions have been examined in detail in the present author's earlier review[191]. Diaminopimelic acid derivatives can serve as lysine precursors. Thus α-cyanopimelic acid diamide was converted into DL-lysine by the Hofmann rearrangement with subsequent hydrolysis[236].

A series of fairly complicated reactions permit the conversion of furfural into DL-glutamic acid[237,238]. Glutamic acid can serve as the starting material for the synthesis of other aminoacids. Thus L-proline and *N*-methyl-L-proline can be obtained from L-glutamic acid[239].

Optically active ornithine (D or L) can be obtained from optically active glutamic acid (D or L) in seven stages with an overall yield of 40%.[240] In its turn, each of the optically active forms of ornithine can serve as the starting material for the synthesis of L- and D-proline[241,242] and L-arginine can be obtained from L-ornithine in virtually one stage[243,244]. DL-Serine and its derivatives are used for the synthesis of DL-cystine[245-248]. L-Tyrosine can be converted into L-phenylalanine by the reduction of the *O*-tosylate[249,250].

6. From Simple Gases

In connection with the problem of the chemical evolution and the origin of life on earth, experiments were begun in 1953 on the non-biological synthesis of aminoacids under conditions simulating "earth's primary atmosphere". It was shown that aminoacids are formed comparatively readily from gaseous methane–water–ammonia mixtures in the presence or absence of hydrogen under the influence of various physical factors. These may be electrical discharges, irradiation, with visible and ultraviolet light as well as with hard ionising radiation, heating, and exposure to ultrasonic waves. Numerous experiments resulted in the formation of twelve of the natural aminoacids and various mechanisms for their formation from gaseous mixtures and certain other simple compounds, which had been synthesised beforehand under the same conditions, have been proposed[251-256]. In all experiments of this kind the yields of aminoacids are extremely low[251]. However, a method was recently patented where a mixture of methane, ethane, ammonia, and water in argon is subjected to the action of a shockwave and cooling by rapid expansion. A mixture of glycine, alanine, valine, and leucine is then obtained with 36% conversion with respect to ammonia[257].

7. From Glycine Derivatives

a. On the basis of isocyanoacetic acid esters. A familiar method for the alkylation of α-*N*-acylaminomalonic esters has been used to synthesise tryptophan[258,259], lysine[260], and glutamic acid[261]. Isocyanoacetic acid ester can be converted into higher homologues by alkylation in a similar manner. The isocyano-group is then converted into the formylamino-group and the aminoacid is obtained after hydrolysis. DL-Tryptophan was obtained in this way in 49% overall yield[262]:

$$IndCH_2N(CH_3)_3I + C{=}NCH_2COOCH_3 \xrightarrow{NaH} IndCH_2CH(N{=}C)COOCH_3 \rightarrow \xrightarrow{CH_3COOH,\ CH_3OH} IndCH_2CH(NHCHO)COOH \xrightarrow[(OH^-)]{H_2O/CH_3OH} \text{DL-tryptophan}.$$

(Ind = β-indolyl)

The reaction of isocyanoacetic acid ester with alkyl halides or tosylates cannot be stopped at the monoalkylation stage[263]. α-Amino-β-hydroxyacids can be obtained by the reaction of isocyanoacetates with aldehydes[264]:

$$C{=}NCH_2COOCH_3 + C_6H_5CHO \xrightarrow{(C_2H_5)_3N} C_6H_5CH(OH)CH(N{=}C)COOCH_3 \rightarrow \xrightarrow{1)\ CH_3OH(HCl);\ 2)\ H_2O(OH^-)} C_6H_5CH(OH)CH(NH_2)COOH.$$

The methyl ester of DL-DOPA was obtained by the same procedure in 83% yield from methyl isocyanoacetate and the dibenzyl ether of 3,4-dihydroxybenzaldehyde:

$$C{=}NCH_2COOCH_3 + 3,4\text{-}(C_6H_5CH_2O)_2C_6H_3CHO \xrightarrow{t\text{-}C_4H_9OK} \rightarrow 3,4\text{-}(C_6H_5CH_2O)_2C_6H_3\underset{\displaystyle O^-K^+}{\underset{|}{C}}HCH(N{=}C)COOCH_3 \xrightarrow{CH_3OH/H_2O(HCl)} \rightarrow 3,4\text{-}(C_6H_5CH_2O)_2C_6H_3CH{=}\underset{\displaystyle NH_2\cdot HCl}{\underset{|}{C}}{-}COOCH_3 \xrightarrow{H_2;\ Pd/C} 3,4\text{-}(OH)_2C_6H_3CH_2\underset{\displaystyle NH_2\cdot HCl}{\underset{|}{C}}HCOOCH_3.$$

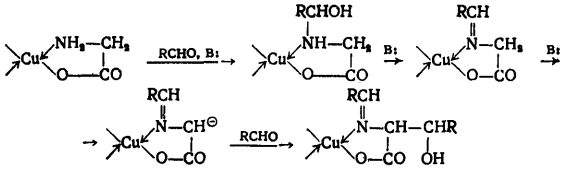
3,4-Methylenedioxy- and 3,4-dimethoxy-benzaldehydes can be used in the reaction. In this case the methylene or methyl groups are removed with BBr_3 after treatment of the isocyano-group and hydrogenation[265]. The report of the above investigation contains a reference to the possibility of obtaining a wide variety of aminoacids by this procedure. A partial asymmetric synthesis of α-methyl-DOPA, which is used as a hypotensive agent, involving the *C*-alkylation of α-isocyanopropionic acid esters by optically active alcohols, has been proposed[266].

The synthesis of silicon- and tin-containing aminoacids from ethyl *NN*-bis(trimethylsilyl)glycinate and the corresponding alkyl halides has been achieved; the reaction with carbonyl compounds yields α-amino-β-hydroxyacids[267].

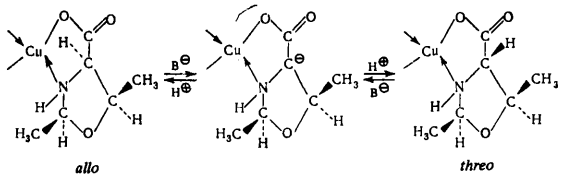
The sodio-derivative of this ester was used to synthesise 2-amino-6-nitrocaproic acid, which is used in peptide synthesis as a protected lysine derivative[268].

b. On the basis of glycine bound in a complex. Alkylation of glycine complexes by aldehydes and certain ketones permits the synthesis of a number of α-amino-β-hydroxyacids[269-277]. The akabori reaction, giving in a single stage threonine with an excess of the *threo*-form, is typical[52]. The study of the reaction mechanism showed that the intermediate reactive species is probably a copper complex of the Schiff base of the aminoacid and the aldehyde, which has a sufficiently acid C–H group for the formation of a carbanion in an alkaline medium and for its further reactions[278-280].

The reaction of copper glycinate with aldehydes proceeds as follows:



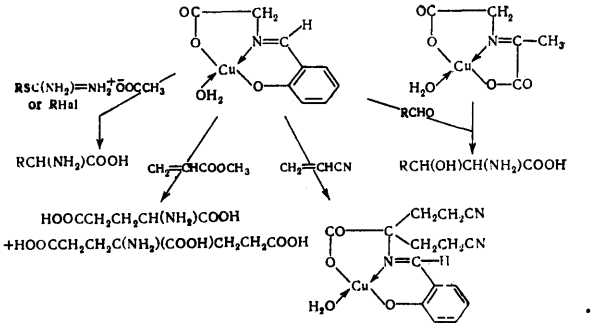
An X-ray diffraction study of crystalline copper threoninate ($C_{12}H_{20}O_6N_2Cu.2H_2O$) showed that the complex has a tetracyclic structure in which two five-membered rings are formed by the bonds between the aminoacids and copper and a further two oxazoline rings are formed by the intramolecular nucleophilic addition of the alkoxide ion to the C=N double bond[281,282]. The less hindered configuration of the substituents in the complex corresponds to the *threo*-form, which is the reason for the stereospecificity of the Akabori reaction and also for the conversion of the *allo*-form of the complex into the *threo*-form in an alkaline medium[57,58,278]:



allo *threo*

Thus, apart from being involved in the synthesis, the aldehydes plays the same role in the Akabori reaction that the pyridoxal molecule plays in alkylation processes catalysed by pyridoxal-dependent enzymes[283,284].

Further development of these studies led to the discovery of chemical systems which not only simulated certain aspects of enzymatic reactions but also gave rise to processes, which do not occur in the living organism. Such systems are the complexes of the Schiff bases of salicylaldehydes and aminoacids with transition metal ions. Salicylaldehyde plays the role of pyridoxal, preventing alkylation at the nitrogen atom[285] and increasing the reactivity of the C—H bond of the aminoacid, while the metal atom imparts in addition a rigidity to the system, which is ensured in nature by the enzyme protein. This permitted asymmetric synthesis with the aid of these systems[286]. The use of salicylaldehyde[283,284,287-289] and pyruvic acid[279,288,289,291] permitted the synthesis under mild conditions of threonine and other α-amino-β-hydroxyacids. In addition, the methylene group of glycine was alkylated by the reaction of alkyl halides[288] and acrylonitrile[285] with copper salicylidene- and 1-carboxy-ethylidene-glycinates and by the reaction of the latter with aldehydes. The alkylation of glycine bound in the complex can be represented by the following scheme:



The reaction with aldehydes has been most thoroughly investigated. Copper salicylideneglycinate was alkylated by aldehydes in water at about 25°C at pH 7.0—8.0. The following aminoacids were obtained by this procedure (the percentage yield and the ratio of the *threo*- and *erythro*-forms are indicated in brackets): threonine [89, (31—34)/(66—69)]; phenylserine [45, (79—84)/(21—26)]; hydroxyaspartic acid (51, 64/36), and serine (2.6, -).[283] The reaction of copper 1-carboxyethylideneglycinate with aldehydes was carried out in an atmosphere of nitrogen, in water or in methanol, at 25—30°C in a moderately alkaline medium. More than ten aliphatic, aromatic, and heterocyclic α-amino-β-hydroxyacids were obtained in this way, including serine, threonine, β-hydroxyleucine, and β-hydroxy-β-phenylalanine in yields of 28, 82, 75, and 67% respectively[179,280].

Copper salicylideneglycinate is alkylated by alkyl halides in dimethylformamide (DMF) at 65°C in the presence of KOH with formation of low yields of alanine, valine, leucine, isoleucine (traces), phenylalanine, and aspartic acid[288]. The alkylation of copper(II) or cobalt(II) salicylideneglycinate by thiuronium salts having the general formula $RSC(NH_2)=NH_2^+ CH_3COO^-$ in acetic acid in the presence of sodium acetate gives particularly good results. The yields of phenylalanine, aspartic acid, and glutamic acid obtained by this method are 50—60%.[292]

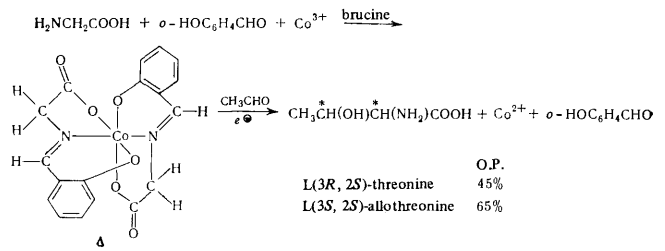
The interaction of copper salicylideneglycinate with methyl acrylate in water at 35°C and pH 11.4 in the course of 15 min results in the formation of 46% glutamic acid and 17% of 4-amino-4-carboxypimelic acid with a residue of 35% of unreacted glycine. When 1-carboxyethylideneglycinate is employed, similar results are obtained, but the contribution of side processes (deamination, decarboxylation) increases[284,289]. The above results show that, by employing glycine complexes, it is not only possible to simulate natural process but also to achieve processes which do not occur in nature, and this leads to new ways of synthesising aminoacids.

Inert octahedral cobalt(III) complexes such as sodium bis-(*N*-salicylideneglycinato)cobaltate, which have a fairly acid C—H group, can also be used for the *C*-alkylation of glycine by acrylonitrile, acetaldehyde, and methacrylate. The resulting inert complexes of the reaction products can be readily reduced electrochemically to labile cobalt(II) complexes, which dissociate into the aminoacid, salicylaldehyde, and Co^{2+}. The mixture is separated with the aid of ion-exchange resins. A significant advantage of the cobalt(III) complexes is the absence of side processes (bisalkylation, alkylation at the nitrogen atom) in the reaction with methyl acrylate. This results in the formation of glutamic acid in a single stage and in a high yield[293,294].

Cobalt(III) complexes are also interesting because they exhibit dissymmetry due to the rigid fixation of the ligands in the octahedron and also the asymmetry of the ligands themselves. The possibility, in principle, of employing dissymmetric mixed cobalt(III) complexes for the asymmetric synthesis of aminoacids was demonstrated in the synthesis of threonine (asymmetric yield 8%)[295] and alanine (asymmetric yield 14%)[296]. These syntheses are examined in detail in Morrison and Mosher's book[297]. The stereoselectivity of the reactions of cobalt(III) complexes with glycine Schiff bases permitted their employment for the asymmetric synthesis of aminoacids, i.e. essentially for the simulation of the stereospecificity of natural enzymes. For this purpose, potassium bis-(*N*-salicylideneaminoalkylcarboxylato)cobaltate was resolved into optical isomers, the absolute configurations of which were estab-

lished on the basis of circular dichroism spectra, ^1H NMR, and reactivity[298].

The reaction of Δ-isomers (−530) or Λ-isomers (+530) of potassium bis-(*N*-salicylideneglycinato)cobaltate with acetaldehyde (water, pH 11.2, acetaldehyde : complex = 100 : 1, temperature 12°C, time 6 h) is stereospecific with formation of L(*S*)- or D(*R*)-threonine respectively:

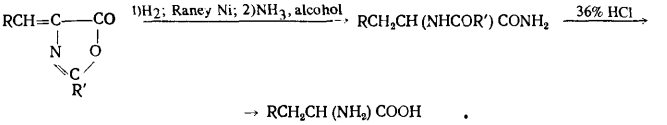


The overall yield is 86% and the ratio *threo* : *allo* = 1.25.[286]

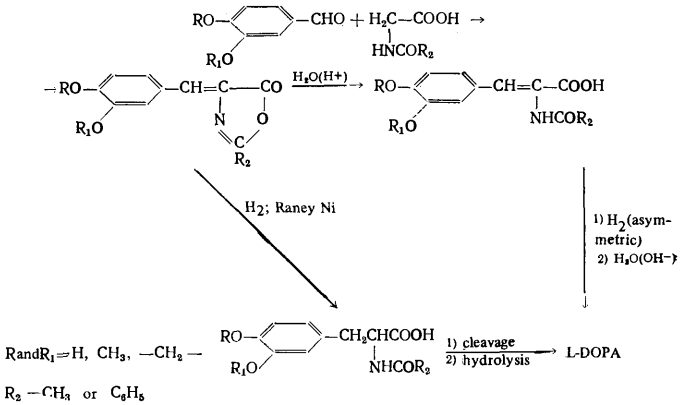
The replacement of one of the ligands in the complex with the absolute Δ-configuration of the glycine residue by the (*S*)-valine residue results in the formation of (*S*)-threonine with an asymmetric yield reaching 82%.[298] When account is taken of the synthetic possibilities of these complexes[293,294] and of a series of studies on their properties[298-300], the above approach to the problem of asymmetric synthesis of aminoacids can prove extremely fruitful.

c. On the basis of *N*-acylglycines.

N-Acylglycines are employed as compounds containing the α-aminoacid fragment in the synthesis of aminoacids by the azlactone method. In the classical version azlactones are obtained by the reaction of acylglycine with aromatic aldehydes in the presence of acetic anhydride. Hydrolysis or alcoholysis of the azlactone yields α-acylaminoacrylic acid or its ester, whose subsequent reduction and hydrolysis lead to the aminoacid[81]. Later it was shown that the reaction can also be carried out with aliphatic aldehydes and ketones[301]. It proved possible to achieve the catalytic reduction of azlactones in an alkaline medium, omitting the conversion stage into α-acylaminoacrylic acids. The resulting α-acylaminoacid amides are hydrolysed smoothly to the α-aminoacids:



The following aminoacids were obtained in this way (the percentage yield with respect to the azlactone is indicated in brackets): phenylalanine (84); tyrosine (78); 3,4-dimethoxyphenylalanine (64); 4-hydroxy-3-methoxyphenylalanine (46.5); valine (75); isoleucine (62); leucine (54); and certain other aminoacids[302]. The reduction of azlactones by hydrogen obtained as a result of the catalytic decomposition of HCOOH gave rise to the formation of *N*-acylaminoacids (derivatives of phenylalanine, tryptophan, and valine) in 85—93% yield[303]. The application of the method to the synthesis of cystine[304] and histidine[305] also gives good results. 4-Hydroxy-3-methoxy-,[306-309] 3,4-dihydroxy-,[310] 3,4-dimethoxy-,[311,312] and 3,4-methylenedioxy-benzaldehydes[313] have been used to synthesise L-DOPA by the azlactone method. The corresponding azlactones can be converted into L-DOPA in two ways. The first consists of the catalytic[306,310] or electrochemical[309] reduction of the azlactone with subsequent enzymatic separation[309] of the optical isomers of the β-aryl derivatives of *N*-acylalanines (DOPA precursors) via diastereoisomeric salts with acid[314] or alkaline[306-308,311-313,315] agents and also by selective crystallisation[316-318]. The hydrolysis of the corresponding L-isomers leads to L-DOPA.



The second procedure involves the hydrolysis of the azlactones with subsequent asymmetric catalytic hydrogenation of the resulting *N*-acylaminoacrylates in the presence of homogeneous dissymmetric phosphine—rhodium catalysts. This new method of asymmetric synthesis can probably be used for the industrial manufacture of optically active aminoacids from unsaturated precursors[120,319].

IV. ASYMMETRIC SYNTHESIS

1. Homogeneous Asymmetric Hydrogenation

The catalytic hydrogenation of unsaturated aminoacid precursors with the aid of dissymmetric catalysts has evident advantages over syntheses employing chiral agents to induce a new asymmetric centre—by the saving achieved as a result of the elimination of the expensive optically active starting material, the simplicity of the operations, and the minimal number of side reactions. Until recently, studies in this field concerned the modification of heterogeneous metallic catalysts with various chiral agents in order to make them stereospecific. The degree of asymmetric synthesis in hydrogenation using such catalysts is as a rule low or sometimes poorly reproducible results are obtained[297,320-323].

A new fruitful approach to this problem became possible as a result of two advances in the last decade: the discovery of homogeneous catalytic hydrogenation of olefins with the aid of rhodium(I) complexes with phosphine ligands[324] and the development of procedures for the synthesis of chiral phosphines[325,326]. The application of rhodium complexes with chiral phosphines as homogeneous catalysts for the hydrogenation of *N*-acylaminoacrylic acids permitted the asymmetric synthesis of α-aminoacids with a high degree of stereospecificity[120,319,327,328] and in high yields. The effect of the structure and the optical purity of the chiral phosphine and also of the hydrogenation conditions on the stereospecificity of the catalyst was investigated by Knowles et al.[120,327]. The results are in Table 2.

Table 2 shows that the employment of *o*-anisylmethylcyclohexylphosphine with 95% optical purity leads to a

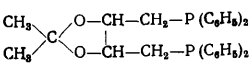
product with 85–90% optical purity, i.e. almost complete stereoselectivity is achieved. The optically pure enantiomer can be obtained by a single recrystallisation.

Table 2 (Knowles et al.[327]). Substrates: 3-(CH_3O)-4-(OH)C_6H_3CH=C($NHCOC_6H_5$)COOH (I) and 3-(CH_3O)-4-(CH_3OCO)C_6H_3CH=C($NHCOCH_3$)COOH (II).

Substrate	Phosphine R_1–P(R_2)(R_3)			Optical purity of product, %	
	R_2	R_3	R_3	OH, %	
I	*m*-$CH_3OC_6H_4$	CH_3	C_6H_5	80	1[b]
	o-$CH_3OC_6H_4$	C_6H_5	i-C_3H_7	80	1[b]
	CH_3	C_6H_5	i-C_3H_7	90	28[b]
	CH_3	C_6H_5	n-C_3H_7	90	28[b]
	C_6H_{11}	CH_3	C_6H_5	75	32[b]
	o-$CH_3OC_6H_4$	CH_3	C_6H_5	95	58[a]
	o-$CH_3OC_6H_4$	C_6H_{11}	CH_3	95	87[c]
	o-$CH_3OC_6H_4$	C_6H_{11}	CH_3	95	90[d]
II	*o*-$CH_3OC_6H_4$	CH_3	n-C_3H_7	95	20[b]
	o-$CH_3OC_6H_4$	CH_3	C_6H_5	95	55[a]
	o-$CH_3OC_6H_4$	C_6H_{11}	CH_3	90	77[e]
	o-$CH_3OC_6H_4$	C_6H_{11}	CH_3	95	85[c]
	o-$CH_3OC_6H_4$	C_6H_{11}	CH_3	95	87[d]

[a] Methanol, 5 atm, 50°C, with one equivalent of NaOH, substrate: catalyst = 3000 : 1;
[b] Methanol, 5 atm, 25°C; [c] 95% ethanol, H_2 at 500 mmHg;
[d] as for c with 2-propanol; [e] as for a with 0.05% of triethylamine instead of one equivalent of NaOH.

Acyl derivatives of α-aminoacids of the (*S*)-series (l-series) are obtained when (+)-phosphine–rhodium catalysts are used. The employment of catalysts with (-)-phosphine promotes the formation of aminoacids of the unnatural (*R*)-series (D-series)[120,319]. Kagan and Dang studied the hydrogenation of a series of *N*-acylaminoacrylic acids in the presence of a catalyst based on the bisphosphine derivative of natural (+)-tartaric acid[319,328].

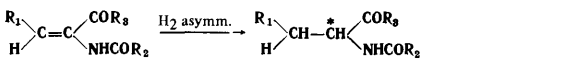

"Kagan's diphosphine".

The data for the asymmetric hydrogenation of *N*-acylaminoacrylic acid derivatives using homogeneous rhodium catalysts based on (+)-*o*-anisylmethylcyclohexylphosphine (A) and Kagan's (-)-diphosphine (B) are summarised in Table 3.

Table 3 shows that the hydrogenation of aromatic systems with chiral phosphine–rhodium catalysts leads to *N*-acylamino-derivatives of L-phenylalanine, L-3,4-dihydroxyphenylalanine, and L-tryptophan in a high optical yield. The above investigations led to the development of a method for the synthesis of L-DOPA from 4-hydroxy-3-methoxybenzaldehyde (vanillin) and its industrial manufacture on its basis has begun[120–122]. The results obtained with aliphatic aminoacid derivatives are more modest, but the limited number of systems investigated precludes definite conclusions at present. Under the conditions adopted, 4-benzylidene-2-methyloxazolone and 5-benzylidenehydantoin are not hydrogenated, although the catalyst retains its activity[319]. This is somewhat unexpected, since azlactones (see end of previous section) are capable of being reduced in the presence of heterogeneous catalysts to *N*-acylaminoacid amides[302].

Comparative characteristics of the catalysts show that both systems have high stereoselectivities, although catalyst B gives higher optical yields with *N*-acetyl derivatives, while in the presence of A the replacement of the acetyl group by the benzoyl group does not affect the stereoselectivity[120,319].

Table 3.



Groups			Catalyst	substrate / rhodium	Chemical yield, %	Optical purity, %	Configuration	Refs.
R_1	R_2	R_3						
C_6H_5	CH_3	OH	A	0.05[a]	—	85	*S*(*L*)	120
C_6H_5	CH_3	OH	B	30	80	72	*R*(*D*)	319, 328
C_6H_5	CH_3	OH	B	100	86	70	*R*(*D*)	319
C_6H_5	CH_3	OH	B	540	95	72	*R*(*D*)	319
C_6H_5	CH_3	OCH_3	B	150	90	55	*R*(*D*)	319
C_6H_5	CH_3	OH_3	B	75	72	71	*R*(*D*)	319
C_6H_5	C_6H_5	OH	A	0.05[a]	—	85	*S*(*L*)	120
C_6H_5	C_6H_5	OH	B	200	96	65	*R*(*D*)	319
3-(C_3O)-4-(CH_3OCO)C_6H_3	CH_3	OH	A	0.05[a]	—	88	*S*(*L*)	327
3-(CH_3O)-4-(OH)C_6H_3	C_6H_5	OH	A	0.05[a]	—	90	*S*(*L*)	327
3, 4-$CH_2O_2C_6H_3$	CH_3	OH	B	50	95	79	*R*(*D*)	319
p-Cl—C_6H_4	CH_3	OH	A	0.05[a]	—	77	*S*(*L*)	120
p-HO—C_6H_4	CH_3	OH	B	100	92	80	*R*(*D*)	319
p-HO—C_6H_4	CH_3	OH	B	80	95	62	*R*(*D*)	319
N—Ac—Ind	CH_3	OH	A	0.05[a]	—	80	*S*(*L*)	120
H	CH_3	OH	A	0.05[a]	—	60	*S*(*L*)	120
H	CH_3	OH	B	—	—	68	*R*(*D*)	328
i-C_3H_7	C_6H_5	OH	B	75	98	22	*R*(*D*)	319

[a] The amount of metal is expressed as a percentage.

Catalysts for asymmetric homogeneous hydrogenation can be obtained by mixing $[Rh(hexa\text{-}1,5\text{-}diene)Cl]_2$ or $RhCl_3.3H_2O$ with two molecules of a chiral ligand and brief preliminary hydrogenation[120]. The most convenient initial form of the catalyst consists of solid derivatives of the type $[Rh(diene)L_2]^+BF_4^-$, which are stable in air and which readily adsorb hydrogen to form the active catalysts. The latter apparently has an octahedral structure with two stable phosphine linkages. Hydrogen, the substrate, the solvent, and the reaction product are present in dynamic equilibrium in the remaining four coordination sites.

In a complex of this type there is a stereospecific (*cis*-addition) intramolecular transfer of hydrogen to the olefinic double bond with formation of a saturated compound. If the ratio phosphine : rhodium > 2, the complex loses its catalytic activity. The bonds between rhodium and a large number of phosphine molecules probably prevent simultaneous coordination with the olefin[319]. The structural correspondence between the substrate and the ligand is of first importance for high stereospecificity in hydrogenation. The hydrogenation stereoselectivity of the catalyst based on *o*-anisylmethylcyclohexylphosphine is promoted by the methoxy-group, which forms a hydrogen bond with the acylamino-group, thereby determining the relative positions of the substrate and the ligand in the reaction complex. In addition, the methoxy-group, which is a planar ligand, does not form a stable bond with the metal and does not affect its coordination with the other reacting molecules[120]. The high stereospecificity of the catalyst based on Kagan's diphosphine is due to the coordination rigidity of the diphosphine–rhodium chelate, which is increased as a result of the *trans*-configuration of the acetamide ring[319].

The rhodium(I)—neomenthyldiphenylphosphine system [based on natural (-)-menthol] has been used to hydrogenate *E*-β-methylcinnamic acid. This resulted in the formation of (+)-methylhydrocinnamic acid with an optical purity of 61% and in 80% chemical yield[329]. The employment of this catalyst for the hydrogenation of acylaminoacrylic acid would be interesting, since the enamide group in the substrate has been found to have a favourable effect on the steric course of the reaction[319].

2. Method of Asymmetric Induction†

The most extensive studies on the asymmetric synthesis of aminoacids by the reductive transamination of ketoacids with subsequent hydrogenolysis have been carried out by Hiskey and Northrop[330,331] and by Harada and coworkers[332-337]:

$$RCOCOOR' + R^*NH_2 \rightarrow RC(=NR^*)COOR' \xrightarrow{H_2;\ Pd/C} R\overset{*}{C}H(NHR^*)COOR' \rightarrow$$
$$\xrightarrow{1)\ H_2;\ Pd(OH)_2/C;\ 2)\ H_2O\ (H^+)} R\overset{*}{C}H(NH_2)COOH + R^*H + R'H\ .$$

[R* = ArĊH(NH₂) AlK; R' = H, Na, C_2H_5, or (-)-menthyl.]

The following aminoacids were obtained in this way (R and the percentage optical purity are indicated): CH_3, 40—80; C_2H_5, 32—42; i-C_3H_7, 28; $C_6H_5CH_2$, 5—14; C_6H_5, 24—30; $HOOCCH_2$, 45—58; $HOOCCH_2CH_2$, 6—56. The configuration of the newly formed asymmetric centre corresponds to the configuration of the chiral amine employed. The two groups of investigators used different methods for the treatment and isolation of the products and for this reason their results, while in general comparable, differ somewhat. The results of the investigations have been discussed in detail in reviews[297,320]. Attempts have been made in recent studies to elucidate the influence of temperature[338-340] and of the solvent[341,342] on the degree of asymmetric synthesis in these reactions.

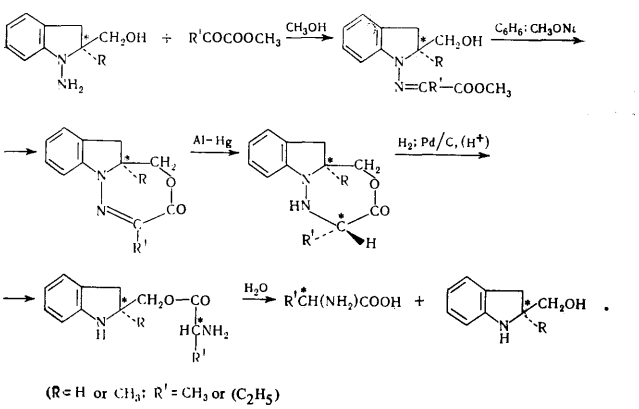
The same method was used to synthesise optically active dipeptides from the esters of the azomethine derivatives of *N*-(α-oxoacyl)-α-aminoacids:

$$CH_3C(=NCH_2C_6H_5)CONHCH(R)COO(i\text{-}C_4H_9) \xrightarrow{H_2;\ Pd/C}$$
$$\rightarrow CH_3\overset{*}{C}H(NH_2)CONH\overset{*}{C}H(R)COO(i\text{-}C_4H_9).$$

Here the aminoacid residue plays the role of the chiral agent and the L(S)-aminoacid induces a new asymmetric centre with L(S)-configuration when the group R is larger than CH_3. The groups R and the optical purities expressed as percentages were as follows: CH_3, 64; C_2H_5, 42; i-C_3H_7, 32; i-C_4H_9, 39; $C_6H_5CH_2$, 25; $CH_3COOC_4H_9$-i, 25; C_6H_5, 0.[343]

The catalytic hydrogenation of various prochiral substrates with C=O, C=C, or C=N bonds in the presence of optically active bases in various solvents leads to very low optical yields[344]. The reduction of the C=N double bond in the Schiff bases of ketoacids with the aid of $NaBH_4$ and subsequent hydrogenolysis give better results in terms of both chemical and asymmetric yield than catalytic reduction[345]. In almost all the known cases the optical purity of the aminoacids (without additional purification) is low. The inadequate stereospecificity of the non-enzymatic reductive transamination reaction in these examples is apparently due to the inadequate rigidity of the intermediates undergoing hydrogenation. Their conformation is such that the alternative approach of hydrogen to the prochiral centre is not fully excluded and this leads to partial formation of the aminoacid with the opposite configuration. Moreover, the irreversible loss of the chiral agent lowers the practical value of this method.

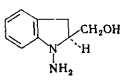
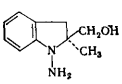
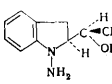
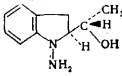
An asymmetric synthesis of α-aminoacids with high chemical yields and high optical purities was achieved by Corey and coworkers[346-348]. *N*-Amino-2-hydroxymethyl- and *N*-amino-2-(α-hydroxyethyl)-indolines were used as chiral aminating agents. The 2-hydroxymethylindoline formed in the reaction was reconverted by nitrosation and reduction into the initial *N*-amino-derivative with only slight losses. All the *N*-aminoindoline derivatives had the (*S*)(-)-configuration and induced the formation of the D(*R*)-configuration at the new asymmetric centre. The explanation is that the rigid conformation of the seven-membered ring in the intermediate hydrazonolactone ensures the approach of hydrogen, with formation of a new asymmetric centre, in the *cis*-position relative to the substituent (hydrogen or the methyl group) in the α-position with respect to the indoline nitrogen. The results are in Table 4.



(R = H or CH_3; R' = CH_3 or (C_2H_5))

When recrystallised hydrazinolactone is used, the optical purity of the resulting aminoacid is 99 ± 1% for alanine and 98 ± 2% for α-aminobutyric acid[347].

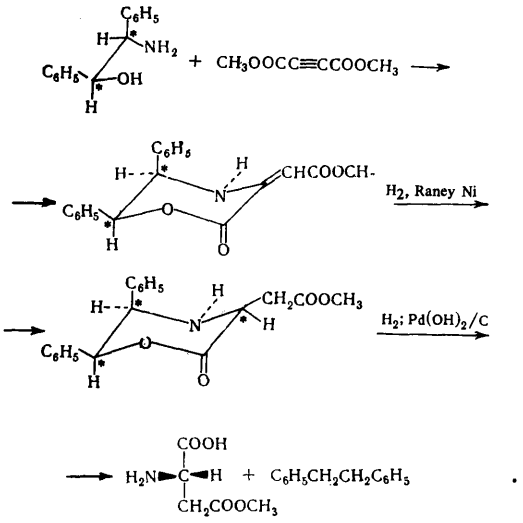
Table 4 (Corey et al.[347,348]).

D(*R*)-Aminoacid obtained	Chiral aminating (*S*)(-)-agent							
								
	yield, %		yield, %		yield, %		yield, %	
	total	optical	total	optical	total	optical	total	optical
Alanine	67	78—82	50	75	52	96	41	92
α-Aminobutyric acid	47	85—90	—	—	55	97	41	96
Valine	—	—	—	—	15	97	—	—
Leucine	—	—	—	—	54	99	—	—

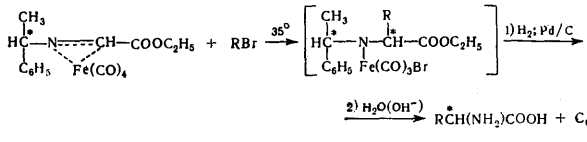
D-Alanine was obtained with an optical purity of 40% and a chemical yield of 10% by the transamination of ethyl pyruvate with chiral *N*-aminoanabasine, which can be regenerated[349,350].

† A new type of asymmetric induction—the synthesis of chiral α-aminoacids with the aid of dissymmetric cobalt(III) complexes—is examined in the section dealing with syntheses based on glycine bound in complexes.

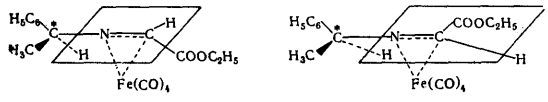
Almost complete stereoselectivity was achieved in the hydrogenation of the cyclic compound obtained by the condensation of *erythro*(+)-1,2-diphenylethanolamine and dimethyl acetylenedicarboxylate:



The stereospecificity of the hydrogenation of the exocyclic double bond is determined by the nature of the intermediate ring in which there is a difference between the degrees of steric hindrance of its two surfaces, namely the axial phenyl group prevents the approach of hydrogen from the axial side. In the hydrogenolysis of the reduced product, methyl L(S)-aspartate was obtained with an optical purity of 98% and in almost quantitative chemical yield[352,353]. High stereospecificity, owing to the rigid fixation of the reaction centre, is achieved in the alkylation by alkyl halides of the π-complexes of the α-methylbenzylimino-derivative of ethyl glyoxylate in the presence of iron nonacarbonyl:



The groups R used, the chemical yields, and the optical purities obtained (expressed as percentages) were as follows: $C_6H_5CH_2$, 53, 77; o-$CH_3OC_6H_4CH_2$, 28, 95; $C_2H_5OOCCH_2$, 24, 78. Alanine is not obtained when the complexes are alkylated with methyl iodide. The optical yield decreases with increase of temperature; the racemate of phenylalanine was obtained at 80°C with a chemical yield of 100%. A pair of diastereoisomeric complexes in proportions of 1:9 is obtained for each of the enantiomeric imines:

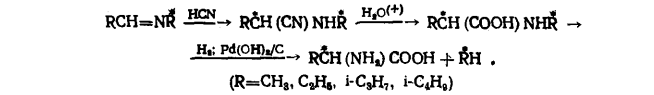


complexes obtained from the D-imine

When the diastereoisomer formed in excess is employed in the reaction, the L-amino-acid is obtained from the D-imine and conversely[354].

Chiral alkylarylamines have been used as aminating agents in yet another series of reactions but the optical purities of the resulting aminoacids are as a rule low.

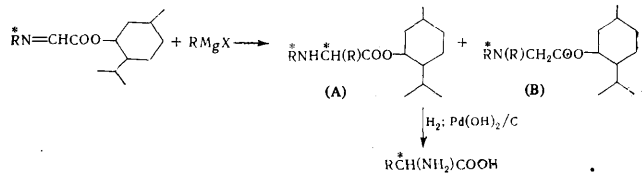
Thus optically active aminoacids have been obtained by the addition of hydrogen cyanide[355] or benzyl cyanide[356] to the azomethines obtained from aldehydes and chiral amines:



(R=CH_3, C_2H_5, i-C_3H_7, i-C_4H_9)

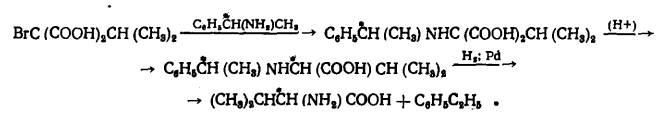
The chemical yields of the aminoacids are 9–58% [355] and 15–57% [356] and the optical purities are 22–58% [355] and 17–37%.[356] However, according to other data, a number of aminoacids with chemical yields of 40–60% and optical purities of 98–99% have been obtained by the addition of hydrogen cyanide to Schiff bases. The configuration of the resulting centre corresponds to that of the chiral amine[357].

The chiral imines of (-)-methyl glyoxylate combine with organomagnesium compounds by the following mechanism:

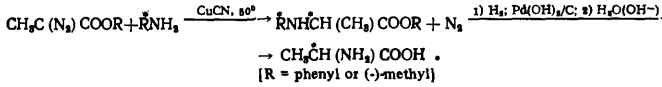


The overall chemical yield of A + B is 45–55%.[358,359] The mode of reaction depends on the structure of the group R in the organomagnesium compound. When R = CH_3, CH_2 = $CHCH_2$, or t-C_4H_9, A is the main addition product, which leads to an aminoacid. When R = C_2H_5, n-C_3H_7, s-C_4H_9, or $C_6H_5CH_2$, the main product is B, which yields *N*-alkylglycines. Optically active alanine was obtained in this way in a chemical yield of 41–45%. The configuration of the resulting aminoacid is determined by (-)-menthol and the optical purity depends on the configuration of the chiral amine: both (*S*)- and (*R*)-amines lead to L(*S*)-alanine with optical purities of 47.5 and 65%.[358] Organocadmium adds selectively to imines with formation of A exclusively. Alanine, norvaline, valine, and phenylalanine have been obtained with their aid in chemical yields of 55–70% and with optical purities of 38–46%.[359]

Valine has been obtained at 20°C in almost quantitative yield with an optical purity of 23% by the selective decarboxylation of (benzylmethylamino)isopropylmalonic acid and its configuration was the opposite of that of the amine employed[360]:



Optically active alanine was obtained by the insertion of the carbene formed in the decomposition of α-diazopropionic acid ester in the N–H bonds of a chiral amine:



[R = phenyl or (-)-menthyl]

The optical purity of the alanine was 12–26% and the configuration was the opposite of that of the inducing amine; the chirality of the ester group [(-)-menthyl] plays a secondary role[361].

Aspartic acid with an optical purity between 21 and 67% has been obtained from chloroacetonitrile and monochloroacetic acid anhydride by a series of reactions involving chiral amines:

$$\overset{*}{R}NH_2 + ClCH_2CN \rightarrow \overset{*}{R}NHCH_2CN \xrightarrow{(ClCH_2CO)_2O} \overset{*}{R}N(COCH_2Cl)CH_2CN \xrightarrow{B:}$$
$$\rightarrow \overset{*}{R}N{-}\overset{*}{C}HCN \xrightarrow{H_2O(H^+)} HOOC\overset{*}{C}HN(\overset{*}{R})CH_2COOH \xrightarrow{H_2;\ Pd(OH)_2/C}$$
(with $\overset{*}{R}N{-}\overset{*}{C}HCN$: $OC{-}CH_2$)
$$\rightarrow HOOCCH_2\overset{*}{C}H(NH_2)COOH .$$

The configuration of the resulting aminoacid is the opposite of that of the inducing amine. The optical purity depends on its structure: α-methylbenzylamine, α-ethylbenzylamine, and α-methylnaphthylamine give 41–49, 19–29, and 54–67% respectively[362]. The same dependence of the configuration of the resulting aminoacid on that of the inducing amine is observed in the synthesis of alanine from α-bromopropionamide. The optical yield of D(R)-alanine is between 11 and 36%.[363] The Baumgarten reaction[364] has been used for the asymmetric synthesis of aminoacids. Thus L(S)-phenylalanine, L(S)-alanine, L(S)-phenylglycine, and L(S)-leucine with optical purities of 62, 33, 27, and 75% respectively have been obtained by the rearrangement of (-)-menthyl N-chloroimidates. When (-)-2-methyl-1-butanol is used instead of (-)-menthol, better results are obtained[365].

The possibility of employing chiral alkylboranes[366] and aminoboranes[367] for the asymmetric synthesis of aminoacids has been demonstrated.

The following aminoacids have been obtained by the cyanohydrin synthesis using chiral amines [the aminoacids, their chemical yields (%) (in brackets), and optical purities (%) are listed]: alanine (42–47), 41–50; α-aminobutyric acid (27–32), 36–51; valine (17–26), 31–45; leucine (28–32), 22–39. The configuration of the resulting aminoacid is the same as that of the initial chiral amine. After additional purification, alanine can be obtained with an optical purity of 90%.[297,368] Aromatic S(L)-α-methylaminoacids (α-methyl-DOPA, tyrosine, and phenylalanine) have been synthesised from the corresponding methyl ketones by the cyanohydrin method. Virtually complete stereospecificity has been achieved with the aid of (4S, 5S)-(+)-5-amino-2,2-dimethyl-4-phenyl-1,3-dioxane as the chiral amine[369].

V. ENZYMATIC METHODS FOR THE SYNTHESIS OF AMINOACIDS

The employment of enzymes makes it possible to achieve under extremely mild conditions transformations which normally require cumbersome multistage synthesis. Moreover, enzymatic reactions are stereospecific and lead to the formation of only one enantiomer (usually the natural enantiomer). The culture liquids of various strains of micro-organisms and purified and immobilised enzymes are used for such reactions.

The widely employed selective enzymatic hydrolysis of acyl derivatives of L-aminoacids with the aid of acylases of various origins[370,371] is more correctly regarded as resolution of racemates and will not be considered here.

Enzymatic syntheses proper include, for example, the formation of L-tryptophan from indole, pyruvic acid and ammonia, which is carried out in a single stage in the presence of pyridoxal phosphate under the influence of the tryptophanase present in the culture liquid of *Escherichia coli*. For an initial concentration of 6.5%, 72% of tryptophan is obtained after 48 h (34°C and pH 8.8).[372] This synthesis was based on a study of the mechanism of the cleavage of tryptophan by the above enzyme. The reaction was reversed by increasing the concentration of the decomposition products. A complex of the enzyme with α-aminoacrylic acid served as an intermediate in this synthesis[373]. The exchange of the p-hydroxyphenyl group for the 3,4-dihydroxyphenyl group in the formation of L-DOPA by the interaction of L-tyrosine and catechol in the presence of crystalline β-tyrosinase and pyridoxal proceeds via the same complex. The replacement of catechol by other substrates leads to the possibility, in principle, of the formation of numerous aminoacids[374].

The synthesis of tryptophan from indole, pyruvic acid, and ammonia is catalysed by tryptophanase immobilised on Sepharose bound covalently to pyridoxal 5'-phosphate[375].

L-DOPA can be obtained by the enzymatic hydroxylation of L-tyrosine derivatives under the influence of enzymes from different strains of fungi[376–378]. The reaction occurs when L-tyrosine protected by acylation is incubated with the culture of the fungus in an appropriate nutrient medium. The protection of the amino-group prevents deamination and racemisation. The fermentation gives a mixture of 57% L-tyrosine and 25–30% of L-DOPA. Microorganisms can also convert D-tyrosine into D-DOPA. The authors of the method believe it to be one of the most economical[376]. Polyphenol oxidase with tyrosinase activity, bound covalently to DEAE-cellulose subjected to preliminary treatment with 6-amino-2,6-dichloro-s-thiazine, was used to synthesise L-DOPA by this method. A disadvantage is 75% loss of activity of the immobilised enzyme in 24 h.[379] A recently developed method for the continuous conversion of ammonium fumarate into L-aspartic acid has already been considered (see Section II, 6).

Data for the enzymatic synthesis of certain aminoacids are summarised in Table 5.

Table 5.

Enzymic transformation	Yield, %	References
L-Aspartic acid formed from fumaric acid and NH_3	90	90, 380
L-Alanine formed from L-aspartic acid	90	380
L-Tyrosine formed from phenol, pyruvic acid, and NH_3	90	380
L-DOPA formed from catechol, pyruvic acid, and NH_3	70	380
L-DOPA formed from L-tyrosine	65–70	377
L-Tryptophan formed from indole, pyruvic acid, and NH_3	72	372

The *meso*-form of diaminopimelic acid is known to be converted into L-lysine under the influence of decarboxylase in the presence of pyridoxal phosphate. It was obtained from synthetic diaminopimelic acid with the aid of partially purified microbial decarboxylase[381]. The racemic diaminopimelic acid remaining after the decarboxylation of the *meso*-form can be converted into the *meso*-form by epimerisation[382–384].

The esters of racemic acylaminoacids undergo selective hydrolysis under the influence of chymotrypsin or subtilisin, which results in a high yield of the L-acylaminoacid. The D-form remains as the non-hydrolysed ester. In particular, benzoyloxycarbonyl-L-phenylalanine was obtained by this procedure[385].

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Enantioselective Effects in Coordination Compounds

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The present Review represents the first attempt to unify and systematise the numerous data on the development of enantioselective effects in the formation and chemical reactions of coordination compounds, as well as in their catalytic and adsorption properties. Enantioselectivity (thermodynamic or kinetic), while being a consequence of the chiral structure of the inner coordination sphere of the complex, may develop even in processes involving only the ligands of the outer coordination sphere. The present state of the chemistry of coordination compounds not only permits but even requires that enantioselective effects should be considered separately from all types of stereospecific effects. A list of 307 references is included.

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I. INTRODUCTION

During recent decades the stereochemistry of coordination compounds has been a field of intense research by chemists of the most diverse schools and specialisation. On it converge the interests of biochemists attempting to understand the role of metal ions in the steric peculiarities of the action of metal enzymes, inorganic chemists investigating the electronic structure of coordination compounds and the nature of the metal–ligand bond, investigators of macromolecular compounds studying the part played by catalysts in stereoselective and stereospecific polymerisation, and finally organic chemists using asymmetric induction in complexes to effect asymmetric syntheses.

II. REFINEMENT OF STEREOCHEMICAL TERMINOLOGY

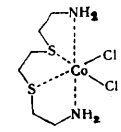
The variety of approaches to the stereochemistry of coordination compounds has led to ambiguity in the interpretation by different scientists of the same stereochemical terms. In many cases careless terminology makes an inadequate understanding of the stereochemical peculiarities of the processes investigated; moreover, it causes a substantial delay in the transition from a descriptive, qualitative study of these features to their accurate quantitative measurement.

The Reviewers consider that it is first necessary to delimit perfectly clearly the regions of application of the terms "selectivity" and "specificity": the former should be used for the characteristics of selection, of the choice of potential reactants present in the system; and the latter term to represent the specific direction of the reaction.

Processes should be termed *stereoselective* when a reactant species is able to select for reaction one of several stereoisomers of a second component. For example, we have a particular case of stereoselectivity—enantioselectivity—if the choice is made between two enantiomers. Such selection can be made, of course, only by a chiral reactant species. Thus we imply by *enantioselectivity* a difference between two molecules (or structures), which are optical enantiomers, in their interaction with a third chiral molecule (or structure).

The term *stereospecific* should be applied to processes leading to the preferential formation of one or more possible stereoisomers of the reaction product. For example, we have a particular case of stereospecificity—enantiospecificity—when a new asymmetric centre predominantly of one of two possible configurations appears in the reaction product. Asymmetry can be induced, of course, only when the initial compounds contain at least one chiral centre. Thus we shall understand by the *enantiospecificity* of a process the ability of chiral centres present in a system to dictate a certain configuration to newly formed chiral centres.

Among stereoselective processes, in the broad meaning of this term, we must include e.g. the selective reaction of boric acid (or acetone) only with those vicinal glycols whose hydroxy-groups are in the *cis*-position. An example of a stereospecific process is the exclusive formation of the symmetrical (±)-*cis*-complex of 3,6-dithiaoctane-1,8-diamine with cobalt(III)



although other stereoisomers of this complex are theoretically possible.

The stereochemical characteristics of reactions may be governed both by kinetic and by thermodynamic factors. Kinetic enantioselectivity, for example, is apparent in a difference in the rates of interaction of a chiral structure with enantiomers of a second reactant. Thermodynamic enantioselective effects are shown by differences in the stability or other properties of two labile diastereomeric adducts formed. Typical examples of kinetically and

thermodynamically enantioselective processes are respectively the difference in the rates of enzymic hydrolysis of the L- and D-isomers of amides of α-amino-acids and the difference in the adsorbability of these isomers on the surface of optically active quartz. The selective oxidation of D-isomers of amino-acids by D-amino-acid oxidase isolated from pigs' kidneys is an example of a kinetically enantioselective process leading to a decrease in the number of asymmetric centres in a system.

Enantiospecificity can by definition occur only in processes in which the number of chiral centres increases. For example, (+)-propylenediamine-*NNN'N'*-tetra-acetic acid interacts enantiospecifically with Co^{2+} ions to form the complex $(-)_{5461}$-[Co(+)-PDTA]$^{2-}$, in which the configuration of the asymmetric cobalt is unambiguous. Asymmetric syntheses are also the result of enantiospecific processes.

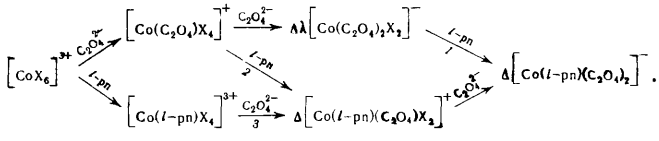
The delimitation of the concepts "selectivity" and "specificity" permits quantitative characterisation both of the selective ability of reactant species and of the directional nature of a process by use of the "degree of stereoselectivity α_{sel}" and the "degree of stereospecificity α_{sp}" respectively. The necessity of such discrimination is dictated by the fact that many processes exhibit both stereoselective and stereospecific effects, usually with different values of α_{sel} and α_{sp}.

Thus processes involving racemates and leading to an increase in the number of asymmetric centres in the system may be characterised by both enantioselectivity and enantiospecificity. In the reaction between racemic propylenediamine (*dl*-pn) and Co^{3+} ions in the presence of activated carbon, for example, Dwyer and his coworkers observed the formation of only four structures:

$$Co^{III} + dl\text{-pn} \begin{cases} \nearrow \Lambda(+)\,[Co(d\text{-pn})_3]^{3+} + \Delta(-)\,[Co(d\text{-pn})_3]^{3+} \\ \searrow \Delta(-)\,[Co(l\text{-pn})_3]^{3+} + \Lambda(+)\,[Co(l\text{-pn})_3]^{3+} \end{cases}$$
$$85\% \qquad\qquad 15\%$$

These data show that the degree of enantiospecificity of the process $\alpha_{sp} = (85 - 15)/(85 + 15) = 70\%$ is lower than the degree of enantioselectivity $\alpha_{sel} = 100\%$, since *d*-isomers of propylenediamine react only with those isomers of the complexes which already contain ligands of the same *d*-configuration, but form final tris-complexes of both Λ- and Δ-configurations.

It must be emphasised that knowledge of the reactants and the final reaction products alone may be insufficient for analysis of the steric aspects of the process. Thus the reaction of cobalt(III) with *l*-propylenediamine and oxalate ions leads to preferential formation of Δ-[$Co(C_2O_4)_2$*l*-pn]$^-$, which can be represented formally by the scheme



Only a knowledge of the reaction mechanism can indicate whether the final result is a consequence of enantioselective effects at stage *1* or of enantiospecific effects at stage *2* or *3*.

Previous reviewers of aspects of the stereochemistry of coordination compounds [1-7] have used the motley terminology of the original sources, and have not attempted to systematise the experimental results in conformity with the nature of stereochemical phenomena. The present Review is confined to a survey of enantioselective effects in coordination compounds. Enantiospecific aspects will be touched on only to the extent to which they appear in stereoselective processes.

III. ENANTIOSELECTIVITY IN COMPLEXES OF α-AMINO-ACIDS AND THEIR DERIVATIVES

Stereoselective and stereospecific effects in the equilibrium systems formed by kinetically labile complexes of copper, nickel, zinc, manganese, cobalt(II), aluminium, and iron with ions of alkali and alkaline-earth metals should be thermodynamic in nature. In non-equilibrium (reacting) systems of these complexes, however, the observed stereoselective and stereospecific effects would probably result from a combination of thermodynamic and kinetic contributions, as in the formation of kinetically inert complexes of cobalt(III), chromium(III), platinum-group metals, and several others.

1. Thermodynamic Effects

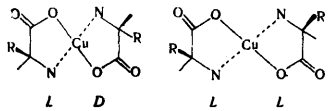
In contrast to tetrahedral and octahedral structures, the metal atom in square planar bis-complexes of copper with α-amino-acids (Aa) is not an independent centre of asymmetry. These complexes can therefore exhibit only enantioselective effects connected with the difference between the D- and L-isomers of the amino-acid in their interaction with an asymmetric structure such as the complex of the copper ion with one asymmetric amino-acid ligand. Enantioselectivity may thus occur at the stage of formation of the bis-complex. It should be apparent in a difference in thermodynamic stability between the optically active structure [$Cu(L\text{-}Aa)_2$] and the *meso*-structure [Cu(D-Aa)(L-Aa)] or in a difference in some properties of their solutions. Since the complexes are not stable diastereomers in solution, even a difference in their electronic spectra† must be ascribed to enantioselectivity, for a change in position of the energy levels of the *d*-orbitals of the copper ion indicates a difference in interaction between ligands within these two structures. Spectral differences may in principle be connected also with displacement of the *cis-trans* isomeric equilibrium, but bis-complexes of copper with bidentate α-amino-acids are assumed to have a *trans*-structure in dilute solutions [9-11].

It must be emphasised that the difference in properties between the crystalline complexes [$Cu(L\text{-}Aa)_2$] and [Cu(D-Aa)(L-Aa)]—including their solubilities—cannot be identified with the stereoselectivity of their formation. The properties of the solid phase are determined by the totality of other interactions, which, although characterised by exceptionally high stereoselectivity, are only indirectly related to the processes involved in formation of the complexes.

A conformational examination of complexes of α-amino-acids led Corey and Bailar [12] to the conclusion that five-membered chelate rings formed by the ligand with the central metal ion have an almost planar structure. There is then hardly any interaction between two chelate rings

†The molar extinction of a racemate would in general differ from that of the optically active enantiomers in the region in which the latter exhibit circular dichroism [8]. In most cases, however, this difference is vanishingly small.

in a complex. Substituents R attached to α-carbon atoms of ligands in square planar bis-complexes are separated by considerable distances



L D *L L*

and are also unable to produce stereoselective effects. Later calculations of the conformation of five-membered amino-acid chelate rings have shown[13] considerable flexibility, absence of any one preferred puckered conformation, and insignificant interactions between two chelate rings. In fact, most of the experimental results obtained until recently supported this theoretical conclusion that stereoselectivity was absent in amino-acid complexes of copper.

The slight difference (2–3%) in molar extinction observed originally[14] between solutions of copper complexes of optically active and of racemic alanine (Ala) and phenylalanine (Phe) was disproved by the later investigations of Gillard and his coworkers, who showed[15,16] that the spectral characteristics of the D-alanine and L-alanine complexes were unaffected when their solutions were mixed in equal proportions, and that the pH dependence of the spectra of the L-alanine and DL-alanine complexes was the same, which suggests that the homogeneous and mixed complexes—[Cu(L-Ala)$_2$] and [Cu(D-Ala)(L-Ala)]—have the same stability (degree of formation).

The absence of enantioselective effects leads to a purely random distribution of ligands, in which the equilibrium concentrations of the bis-complex structures [M(D-Aa)$_2$], [M(D-Aa)(L-Aa)], and [M(L-Aa)$_2$] are in the proportions[17] 1 : 2 : 1, and those of the tris-complex structures [M(D-Aa)$_3$] [M(D-Aa)$_2$(L-Aa)], [M(D-Aa)(L-Aa)$_2$], and [M(L-Aa)$_3$] are[18] 1 : 3 : 3 : 1. In both cases the potentiometric titration curves of L- and DL-amino-acids in the presence of metal ions M coincide exactly.

Table 1. Formation constants for mono- and bis-complexes (lgβ_1 and lgβ) of metals with alanine (pK_1 = 2.54 ± 0.04 and pK_2 = 9.93 ± 0.06) and with phenylalanine (pK_1 = 2.41 ± 0.04 and pK_2 = 9.35 ± 0.06) in 0.37 M $NaNO_3$ at 20 ± 0.1 °C.

Ion	Configuration of ligand	Alanine		Phenylalanine	
		lg β_1	lg β	lg β_1	lg β
Cu^{2+}	*L*	8.16	14.98	7.93	15.10
	D	8.14	15.00	8.00	15.08
	DL	8.20	15.04	8.03	15.14
Ni^{2+}	*L*	5.23	9.91	5.23	9.72
	D	5.22	9.87	5.24	9.70
	DL	5.21	9.96	5.19	9.66
Cd^{2+}	*L*	4.09	7.40	3.90	6.73
	D	4.00	7.40	3.87	6.72
	DL	3.98	7.40	3.84	6.75
Pb^{2+}	*L*	4.20	9.34	4.02	8.86
	D	4.16	9.40	3.99	8.88
	DL	4.08	9.42	4.03	8.79
Zn^{2+}	*L*	4.63	~9	4.43	~8.5
	D	4.62	~9	4.43	~8.5
	DL	4.65	~9	4.41	~8.5

Simeon and Weber tried to detect enantioselectivity in the formation of the bis-complexes of alanine and phenylalanine with several metals[19], making a careful potentiometric titration of these systems with the use of D-, L-, and DL-amino-acids. The formation constant of the bis-complex (lgβ in Table 1) was independent of the steric configuration of the ligands, within the limits of experimental error (±0.05 for copper and nickel, and ±0.10 for the remaining ions). This applies not only to the square planar complexes of copper but also to the more complicated structures formed by metal ions of coordination number exceeding 4.

Potentiometric titration did not reveal enantioselectivity in complexes of copper with alanine, valine (Val)[16,20], proline (Pro)[16], or leucine (Leu), nor in bis-complexes of nickel with alanine, valine, and leucine[20]. Study of the optical rotatory dispersion of bis-complexes of copper with several L-amino-acids and their mixed complexes with optically inactive ligands led to the conclusion[21] that steric interactions between the two ligands in the [Cu(L-Aa)$_2$] system are so small that the Cotton effect is almost unaffected. While reaching this conclusion, the authors do not comment on their earlier report[22,23] of some difference in the pH dependence of the electronic spectra of complexes with optically active and with racemic alanine, valine, and especially proline, indicating that the homogeneous structures are less stable than the *meso*-complex [Cu(D-Aa)(L-Aa)].

The long standing view[1-4] that enantioselectivity is absent from copper complexes with bidentate amino-acids was not inconsistent with the difference (within the limits of experimental error) between the stability constants of mixed copper complexes of L-proline with L- and D-valine (lgβ = 16.89 ± 0.09 and 17.00 ± 0.20 respectively) calculated from the optical rotatory dispersion of the system[24]. Nor was this view disproved by some difference[25,26] in the electron spin resonance spectra of vitrified aqueous–methanolic solutions of copper complexes of L- and DL-alanine, -valine, -proline, and -serine (Ser), since there was no certainty that microcrystals of these complexes differing markedly in the e.s.r. properties were not formed when the solutions were cooled.

The first measurements of the stability of copper complexes of the terfunctional α-amino-acid–asparagine (Asp-NH_2)—potentiometric titration showed that the homogeneous structures—[Cu(D-As-NH_2)$_2$] and [Cu(L-Asp-NH_2)$_2$]—were more stable than the mixed complex [Cu(D-Asp-NH_2)(L-Asp-NH_2)], and that the quantities of the former in the equilibrium solution exceeded the concentration of the mixed complex fourfold[27]. However, more careful potentiometric measurements of the stability constants have shown that enantioselectivity is absent from the bis-complexes of copper with such terfunctional amino-acids as asparagine[28-30], aspartic acid (Asp), glutamine (Glu-NH_2), glutamic acid (Glu)[29,30], 2,3-diaminopropionic acid, and histidine (His)[20,31], as well as from mixed complexes[32] of histidine with threonine (Thr).

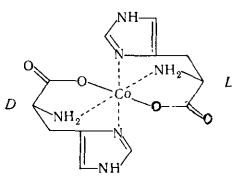
The presence of thermodynamic enantioselectivity in octahedral bis-complexes of cobalt(II) with terdentate histidine was first demonstrated in 1963 by McDonald and Phillips[33]. These workers observed, in the proton magnetic resonance spectra of solutions of the complex with DL-histidine, signals that were absent from solutions of the optically active complex, and they attributed the signals of the *meso*-complex [Co(D-His)(L-His)]. Study of the dependence of their intensity on the concentration ratio of D- and L-isomers of the ligand led to the calculated constant $K = 11.5$ for the equilibrium

$$[Co(L\text{-}Aa)_2] + [Co(D\text{-}Aa)_2] \rightleftharpoons 2[Co(L\text{-}Aa)(D\text{-}Aa)]$$

(in the absence of enantioselectivity $K = 4$[17]). Thus the mixed complex is formed preferentially in this system, its stability exceeding that of the homogeneous complex by 0.32 kcal mole^{-1}.[34] These results have been confirmed

by potentiometric titration[20,31,34]. Selectivity is still greater in complexes of histidine with nickel(II): the difference $\delta\Delta G^\circ$ in the Gibbs free energies of the individual structures reaches 0.49 kcal mole^{-1}.[34] The contents of the mixed structure in the complexes of DL-histidine with bivalent cobalt, nickel, zinc, cadmium, and copper are respectively 62%, 72%, 63%, 53%, and 50%,[31] corresponding to degrees of enantioselectivity of 24%, 44%, 26%, 6%, and 0. The high enantioselectivity observed with the nickel complexes is apparent also in their spectral properties: the absorption bands of the complex with L-histidine at 356 and 556 nm are rather wider and below the bands of the racemic complex, which moreover are somewhat displaced to longer wavelengths[31].

Enantioselectivity in octahedral histidine complexes is attributed[30,31,34] to the tendency of the bulky imidazole and similarly charged carboxylate donors to occupy *trans*-positions, which is possible only if the two histidine molecules have opposite configurations:



The degree of enantioselectivity then depends on the regularity of the octahedron and on the diameter of the central metal ion[30,31]. It is interesting that the rates of formation of [MHis$_2$] complexes in which M = Ni, CoII, Zn are independent of the configuration of the ligands. The poorer stability of the structures [M(D-His)$_2$] and [M(L-His)$_2$] than of [M(D-His)(L-His)] is evident in higher rate constants of the reverse reaction (dissociation) for the homogeneous structures[35,36]. It is noteworthy that, in contrast to the situation existing in solution, the crystalline complexes of nickel and zinc with DL-histidine are constructed from the homogeneous structures [M(D-His)$_2$] + [M(L-His)$_2$].

No stereoselectivity has been found in octahedral bis-complexes of terdentate 2,3-diaminopropionic acid with nickel[31], aspartic and glutamic acids with nickel and cobalt[29,30], and cysteine (CySH) with nickel and zinc[30,37]. On the other hand, Ritsma[30] has observed considerable intensification of enantioselective effects in histidine complexes on the introduction of alkyl substituents into the α-amino-group (Table 2). Benzyl- and dimethyl-histidine exhibit appreciable enantioselectivity even on coordination with copper, but the resulting complexes undoubtedly differ in structure from the square complexes of α-amino-acid type. Furthermore, Ritsma[30] finds that the optically active protonated complexes of copper with histidine are rather more stable, whereas at pH > 6 the *meso*-structure is apparently slightly more stable[32].

Barnes and Pettit studied the thermal effects accompanying the formation of copper complexes of alanine, valine, proline[38], and aspartic acid, copper and nickel complexes of glutamic acid and histidine, and also the zinc complex of histidine[38,39]. Enantioselective effects were observed only with histidine: differences between calculated enthalpies of formation of the individual *meso*-complex and the optically active complexes $\delta\Delta H^\circ$ were +0.67 ± 0.17, +0.57 ± 0.05, and −0.67 ± 0.17 kcal mole^{-1} with nickel, zinc, and copper respectively. Thus the enhanced stability of the symmetrical *meso*-complexes of nickel and zinc is mainly an enthalpy effect, as is suggested by the closeness of the values of $\delta\Delta H^\circ$ and $\delta\Delta G^\circ$

Table 2. Difference in Gibbs free energies $\delta\Delta G^\circ$ (in kcal mole^{-1}) of mixed and homogeneous structures—[M(D-Aa)(L-Aa)] and [M(L-Aa)$_2$]—from results of potentiometric titration with μ = 0.1 M at 25°C. Negative values indicate that the mixed structure is the less stable[30].

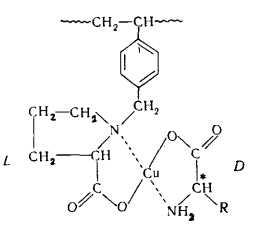
Amino-acid	Co^{II}	Ni^{II}	Cu^{II}	Zn^{II}
Histidine	+0.32	+0.49	0.0	+0.28
N-Methylhistidine	+0.69	+1.03	0.0	+0.49
N-Benzylhistidine	+0.28	+0.74	−0.25	<0.0
NN-Dimethylhistidine	+1.06	+1.62	+0.56	+1.20
N-*o*-Hydroxybenzylalanine	−0.71	−0.83	0.0	<0.0
Cysteine		0.0		~0.0
Penicillamine		−0.55		>0.0

(Table 2). With copper, on the other hand, complexes with ligands of the same configuration should be preferred. (This unexpected result was ascribed to the tendency of copper to form tetragonal *cis*-structures in which histidine is coordinated through the imidazole ring and the amino-group.) However, the considerable enthalpy effect is probably balanced by entropy factors.

Complexes of cobalt(II) with L- and with DL-histidine differ not only in thermodynamic stability but also in the rate constants of their reversible oxidation[40] by molecular oxygen to the structure [CoHis$_2$]$_2$O$_2$.

The presence of enantioselectivity in complexes of bifunctional amino-acids was first shown unambiguously by Davankov and Rogozhin[41,42], by using a new method—ligand-exchange chromatography[43]—for studying kinetically labile mixed complexes. If one ligand (stationary) is bound covalently to an insoluble polymeric support, chromatography of a mixture of mobile ligands on such a sorbent in the presence of complexing metal ions permits determination of the relative thermodynamic stabilities of all the mixed complexes whose formation involves the stationary ligand. The stability of these mixed complexes increases in the same sequence as the affinity of the mobile ligands for the sorbent. Racemic amino-acids were subjected to chromatography, in the presence of copper, nickel, or zinc ions, on sorbents having chiral amino-acid groups. These ions become centres for the formation of mixed sorption complexes of the stationary chiral ligands of the sorbent and the mobile ligands, i.e. molecules of the separable racemate. Thermodynamic enantioselective effects in the formation of these sorption complexes are responsible for the separation of the isomers of the racemate, which is transported by the mobile phase in a column of such sorbent.

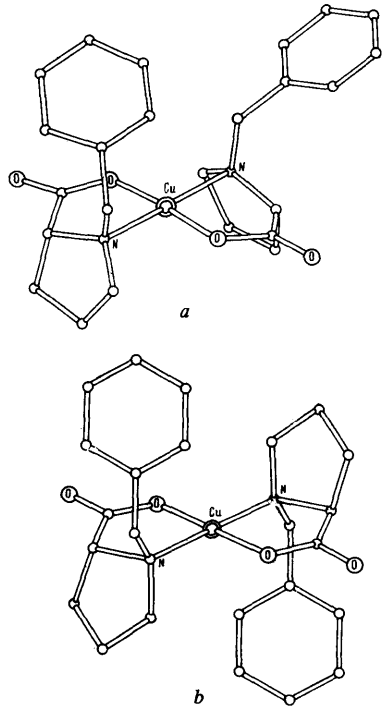
In the presence of copper ions, for example, a sorbent obtained by reaction between L-proline (or L-hydroxyproline) and a chloromethylated macrocellular styrene copolymer forms considerably more stable mixed complexes with D-than with L-amino-acids[44]:



If the mobile ligands are D- and L-proline, the difference in their free energies of sorption reaches $\delta\Delta G^\circ$ = 0.45 kcal

mole^{-1} (determined under static conditions)[45,46]. The simplicity and great sensitivity of ligand-exchange chromatography enabled thermodynamic enantioselectivity to be detected in many labile complexes of bi- and ter-dentate amino-acids, hydroxy-acids, amino-alcohols, and other compounds[47,48].

The presence of enantioselectivity in solutions of complexes of several bifunctional amino-acids with copper was then demonstrated also by classical methods. Davankov et al. first studied complexes of *N*-benzylproline as a model of the unit in the dissymetric sorbent used. Potentiometric titration indicated[49,50] that an equilibrium is established with *N*-benzyl-DL-proline in aqueous solution, in which the concentration of the *meso*-complex [Cu(*N*-$C_6H_5CH_2$-D-Pro)(*N*-$C_6H_5CH_2$-L-Pro)] exceeds that of each of the two homogeneous complexes by factors of 14 ± 4. This corresponds to a degree of enantioselectivity of complex formation α_{sel} = 75%, or $\delta\Delta G^\circ$ = 1.15 kcal mole^{-1}. The poorer stability of the homogeneous structure [Cu(*N*-$C_6H_5CH_2$-L-Pro)$_2$] is conclusively supported by spectrophotometric investigations and by polarimetric titration, the latter of which can also be used[50] to calculate α_{sel}. X-Ray examination of the complexes[51-54] suggests that the benzyl radicals tend to occupy apical positions in the coordination sphere of copper, which is possible (see diagram) for both ligands only if they differ in configuration[54].



Structures of the complexes: *a*) [(*N*-$C_6H_5CH_2$-L-Pro)$_2$Cu]; *b*) [(*N*-$C_6H_5CH_2$-D-Pro)(*N*-$C_6H_5CH_2$-L-Pro)Cu].

The enantioselectivity of formation of copper complexes of amino-acids is a consequence of unequal interaction between the two ligands in the structures [Cu(D-Aa)(L-Aa)] and [Cu(L-Aa)$_2$]. Such interaction can occur by direct contact between individual fragments of the ligands (as in the *N*-benzylproline complexes), through solvent molecules coordinated in axial positions, or finally through the solvent sheath (outer coordination sphere). Interligand interactions may lead to distortion of the chelate unit of the complex, which is clearly apparent in a difference between the electronic spectra of [Cu(L-Aa)$_2$] and [Cu(D-Aa)(L-Aa)], or distortion of the conformation of the ligands and purchasing of the five-membered chelate rings. If such distortions occur in the optically active complex [Cu(L-Aa)$_2$], they can easily be detected by comparing its optical rotatory dispersion or circular dichroism spectra with those of the mixed complex with glycine [Cu(L-Aa)Gly]. The intensity ratio of these spectra is exactly 0.5 (without displacement of the maxima) only in the absence of distortion in the [Cu(L-Aa)$_2$] structure. This method has been used to investigate complexes of alanine, valine, proline, and hydroxyproline (Hypro) containing various combinations of methyl and benzyl substituents in the amino-group[55]. Maximum interligand interactions (and hence stereoselective effects) are observed in complexes of amino-acids containing two substituents in the amino-group, e.g. in complexes of *N*-benzylproline, *N*-benzyl-*N*-methylalanine, and hydroxy-*N*-methylproline.

Transmission of interligand interactions through axially coordinated water molecules must be adduced e.g. to explain why the complex [Cu(*N*-$C_6H_5CH_2$-L-Pro)(L-Pro)] is less stable than [Cu(*N*-$C_6H_5CH_2$-L-Pro)(D-Pro)]. The value $\delta\Delta G^\circ$ = 0.9 ± 0.2 kcal mole^{-1} calculated for this system from the circular dichroism spectra[56,57] agrees satisfactorily with ligand-exchange sorption data[45].

Solvation of the complexes also has a very considerable influence on interligand interactions, until the sign of the enantioselective effect is reversed on passing from one solvent to another[58]. The first example of the successful study of the influence exerted on enantioselective effects by the structure of the outer coordination sphere may well be an investigation[59] of the e.s.r. spectra of the [Cu(*N*-$C_6H_5CH_2$Pro)$_2$] complexes in methanol and in a chloroform–toluene mixture.

The work of Davankov, Rogozhin, and Kurganov has shown that enantioselectivity is extremely widespread in the copper complexes of α-amino-acids, but only after thorough investigation by potentiometric and polarimetric titration, spectrophotometry, circular dichroism, etc. can the presence or absence of enantioselectivity in a particular system be stated with certainty. The most sensitive method, however, is ligand-exchange chromatography.

Bernauer et al.[60] used this method to show that the chiral complex of iron(III) with 2′-hydroxyethyl-D-propylenediaminetriacetic acid L-[Fe(D-HEPDTA)]$^-$ forms mixed complexes more readily with the D-isomers of acetyl and benzoyl derivatives of leucine, alanine, phenylalanine, and methionine (Met) than with their enantiomers ($\delta\Delta G^\circ$ falls in this sequence from 0.10 to 0.02 kcal mole^{-1}). In the reaction of the (–)- and (+)-isomers of α-methylbenzylamine with the copper, nickel, and zinc complexes of D(–)-propylenediaminetetraacetic acid $\delta\Delta G^\circ$ reaches 0.3 kcal mole^{-1} [61] (investigation of the same system by partition between water and heptane gives $\delta\Delta G^\circ \simeq 0.14$ kcal mole^{-1}). Thus enantioselectivity is revealed even with unidentate ligands, which probably replace one of the acetate groups in the complexes of the above multidentate ligands.

Angelici and his coworkers have made a series of studies on the enantioselectivity of complex formation by α-amino-acids whose amino-group contains substituents

tending to coordinate with a metal, e.g. the carboxymethyl (Cm) and pyrid-2-ylmethyl (Pc) groups. Potentiometric titration showed[62] that *N*-carboxymethyl-L-valine forms somewhat more stable mixed copper complexes with L-leucine, L-phenylalanine, L-alanine, L-serine, D-valine, and L-leucine ethyl ester than with their enantiomers. *N*-Carboxymethyl derivatives of L-isoleucine (Ileu), L-serine, *N*-benzyl-L-alanine, and *N*-benzyl-L-leucine also form mixed copper complexes preferentially[63] with the L-isomers of valine, leucine, and threonine. *N*-Carboxymethyl-L-aspartic and *N*-carboxymethyl-L-glutamic acids, on the other hand, show greater affinity for the D-isomers of amino-acids. The authors attempted to explain the observed effects by the *cis*-structure of the bisamino-acid complex of copper, in which the *N*-carboxymethyl group occupies an axial position[63]. However, X-ray examination has shown[64] that the carboxymethyl group in the complex $[Cu(N\text{-Cm-L-Val})(H_2O)_2]$ is situated in the main plane of coordination. It is equally difficult to explain the fact that *N*-pyrid-2′-ylmethyl-L-aspartic acid and its *N*-6′-methylpyrid-2′-ylmethyl analogue form more stable mixed copper (and nickel) complexes with the L-enantiomers of alanine, phenylalanine, tryptophan (Try), threonine, leucine, and valine[65]. The situation is somewhat clearer with the bis-complexes of nickel and cobalt(II) with the *N*-*o*-hydroxybenzylalanine, where the homogeneous structures are more stable (Table 2). All three donor atoms of this ligand are clearly located in the same plane [sic], but nevertheless Ritsma[30] is rightly cautious in interpreting interligand interactions in its complexes.

Enantioselective effects obviously result from the action of many factors, whose contributions are at present still difficult to assess. Only detailed and comprehensive investigation will enable enantioselectivity to be explained even in the simplest systems, e.g. the fact that with *N*-benzylvaline the homogeneous complex $[Cu(N\text{-}C_6H_5CH_2\text{-L-Val})_2]$ is the most stable[58], where as with *N*-benzyl-D-proline, in contrast, the *meso*-structure $[Cu(N\text{-}C_6H_5CH_2\text{-D-Pro}).(N\text{-}C_6H_5CH_2\text{-L-Pro})]$ is the more stable.

2. Kinetic Effects

In an interesting case of kinetic enantioselectivity reported by Hix and Jones[66] catalysis of the alkaline hydrolysis of a histidine ester by histidinatonickel(II) is preceded by formation of the mixed complex $[NiHisHisOCH_3]^+$. The overall rate of hydrolysis is 40% lower when histidine and its ester have the same configuration than when the ligands have opposite configurations. The bidentate ligand $HisOCH_3$ can add to the complex $[NiHis]^+$ in six different ways, but only in one case—with the ligands having opposite configurations—can the preferred *trans*-structure be formed with the ester group in a position favourable for coordination. Since thermodynamic enantioselectivity is not observed in a mixed complex, the differences in rates of hydrolysis result from coordination of the ester carbonyl. It is significant that enantioselectivity is absent if complexes of histidine with copper are used for catalysis[67,68]: the coordination number 4 of copper ions leaves no vacant positions for the coordination of ester groups.

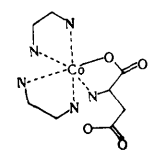
Blackburn and Jones[69-71] extended study of catalysis of the hydrolysis of amino-acid esters by complexes of nickel with amino-acids to another seventeen different systems, but only in one system $[NiTryHisOCH_3]^+$ was appreciable enantioselectivity found. Nevertheless, Angelici[62] observed that the complex $[Cu(N\text{-Cm-L-Val})]$ catalyses hydrolysis of the methyl esters of D-leucine and D-phenylalanine rather more strongly than that of the L-isomers. Similar though smaller effects were observed in catalysis by the copper complex of *N*-carboxymethyl-D-phenylglycine.

A difference (2–4-fold) has been observed in the rates of hydrolysis of the methyl esters of D- and L-phenylalanine in the presence of a copper complex of poly-L-lysine. The catalytic effect becomes stronger with increase in the molecular weight of the polymer. It is supposed[72,73] that at pH 7 hydrolysis is catalysed in a mixed complex, which is more easily formed with D-phenylalanine. Finally, there are indications[74] that the ethyl ester of L-phenylalanine is hydrolysed more rapidly in the presence of *trans*-$[CoCl_2(l\text{-pn})_2]Cl$ than in the presence of its enantiomer *trans*-$[CoCl_2(d\text{-pn})_2]Cl$. The mechanism of this process is quite complicated, and the stage at which stereoselective effects develop is difficult to assess.

In 1929 Shibata and Tsuchida[75] discovered that the laevorotatory complex $[CoClNH_3en_2]^{2+}$ accelerates selectively the oxidation of L-3′,4′-dihydroxyphenylalanine (dopa). Although a subsequent check[76] on this report has not shown the presence of enantioselectivity, but has merely established a general catalytic effect by the complex independent of its configuration, the enantiomers of dopa are in fact oxidised at different rates in the presence of a mixed copper complex of protoporphyrin with L-histidine or with its cyclic dimer[77] and also in the presence of a copper complex of poly-L-lysine[78-80].

A special group of kinetically enantioselective processes are involved in the formation of inert complexes of cobalt(III) from compounds of which one is a racemate, while the other is optically active. Enantiospecificity is usually also observed in these processes. Unfortunately, most authors omit both a detailed analysis of the stereochemical features of these reactions and also the important experimental data (e.g. conversion and yield of product) required for much analysis.

The fact that the Λ-isomers of the complexes are the first to react when L-glutamic acid interacts with racemic $\Delta\Lambda$-$[CoCO_3en_2]ClO_4$[81] and with racemic $\Delta\Lambda$-$[Co(H_2O)_2en_2].(ClO_4)_3$[82] must be regarded as a case of kinetic enantioselectivity. The preferentially formed Λ-$[Co(L\text{-Glu})en_2].ClO_4$, furthermore, is sparingly soluble, and separates in optically pure form. Analogous enantioselectivity is observed when *d*-tartaric acid is used[81,82] instead of L-glutamic acid, but is absent when bidentate amino-acids[81,83] and lactic acid[81] are employed. Gillard and his coworkers[81,82,84] attributed this to three-point interaction of L-glutamic acid with the complex by formation of a hydrogen bond between the γ-carboxyl and an amino-group of ethylenediamine, which is possible only when the complex itself has the Λ-configuration:



However, X-ray examination has shown[83] that such a hydrogen bond is not formed, at least in the crystalline state.

Even the fact of kinetic enantioselectivity in the systems studied by Gillard has since been subjected to criticism[85,86]. The proportions of Λ- and Δ-complexes in the final equilibrium mixtures from the reactions of $\Delta\Lambda$-$[CoCO_3en_2]^+$ with L-glutamic and L-aspartic acids in the presence of

activated carbon were found to be 70 : 30 for $[Co(L\text{-}Glu)en_2]^+$ and 60 : 40 for $[Co(L\text{-}Asp)en_2]^+$. The observed effects are regarded [85] as thermodynamic in character. From a check on these results and study of the alkaline epimerisation of L-glutamic acid in the final complex it has been concluded [86] that no selective or specific effects occur in this system at all.

The absence of kinetic enantioselectivity in the interaction of racemic *cis*-bisethylenediaminecobalt(III) with optically active alanine [81-83], leucine, and phenylalanine [83] is fully consistent with the absence of enantiospecificity observed earlier [87] in the formation of a chiral configuration of cobalt on the reaction of symmetrical *trans*-$[CoCl_2en_2]Cl$ with the L-isomers of these amino-acids.

Among the 24 possible structures each containing 2 amino-acid residues which may result from the reaction of a hexanitrocobaltate(III) with DL-alanine, only the 4 complexes

$(+)_{589}[Co(L\text{-}Ala)_2(NO_2)_2]^-$ $(+)_{589}[Co(D\text{-}Ala)_2(NO_2)_2]^-$
$(-)_{589}[Co(L\text{-}Ala)_2(NO_2)_2]^-$ $(-)_{589}[Co(D\text{-}Ala)_2(NO_2)_2]^-$

are formed stereospecifically [88]. In the main coordination plane they contain two carboxylate anions and two nitro-groups in *cis*-positions [89]. Enantioselectivity is apparent in this system in the identical configuration of the two amino-acid residues in each structure. The enantiospecificity of complex formation is less marked: the two L-alanine molecules produce only slight predominance of the $(-)_{589}$-complex over the $(+)_{589}$-structure.

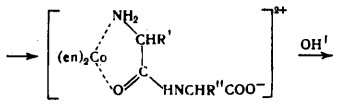
A very complicated mixture of complexes $[CoAla_{3-n}(L\text{-}Asp)_n]^{n-}$ (n = 0–3) is formed by the reaction of $[Co(CO_3)_3]^{3-}$ with L-aspartic acid and DL-alanine in the presence of activated carbon [90]. Here selective and specific effects should be examined separately for each group of structures. The mer-Λ-structures of the complexes $[CoAla(L\text{-}Asp)_2]^{2-}$ contain mainly L-alanine, but the fac-Δ-structures contain D-alanine. The analysis for a system containing L-proline and D- or L-aspartic acid is just as complicated [91].

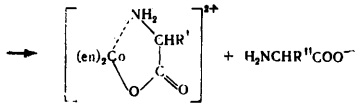
Contrary to expectation, enantioselectivity has not been found in the kinetically controlled reaction of L-proline with racemic β-$[CoOH(H_2O)trien]^{2+}$ or with its dichloro-analogue [92-94]: in both cases roughly equal quantities of Δ- and Λ-isomers of β_2-$[Co(L\text{-}Pro)trien]^{2+}$ are formed. X-Ray examination has shown [93,95] that steric interactions between ligands are in considerable measure eliminated by distortion of the angles of the coordination octahedron.

Nor have departures from a random distribution of complexes been observed in the reaction of *trans*-*NN'*-ethylenebisacetylacetoniminatodiaquocobalt(II) with DL-alanine, DL-valine, and DL-α-methylbenzylamine respectively [96]. In the final complexes two unidentate amino-acid ligands coordinated through the amino-groups occupy *trans*-positions in the coordination octahedron, and are unable to influence each other.

Nor is kinetic enantioselectivity observed in the reaction of the dipeptide L-leucylglycine with racemic $[CoOH(H_2O)en_2]^{2+}$. [97] If, on the other hand, an L-amino acid is a *C*-terminal group, as e.g. in glycyl-L-phenylalanine and glycyl-L-tyrosine, such a dipeptide reacts with the Δ-isomer of the complex twice as rapidly as with the Λ-enantiomer:

$$[Co(en)_2(H_2O)(OH)]^{2+} + H_2NCHR'CO{-}HNCHR''COO^- \longrightarrow$$





However, the dipeptide L-leucyl-L-tyrosine, which contains two L-amino-acids, reacts almost exclusively with the Λ-complex [97]. (It may be mentioned here that thermodynamic enantioselectivity has not been observed in the copper complex of glycylphenylalanine [98].)

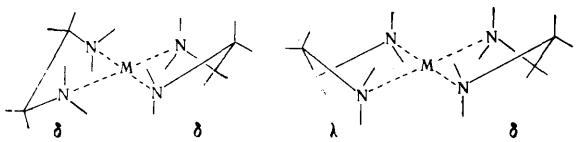
IV. COMPLEXES OF DIAMINES AND THEIR DERIVATIVES

Enantioselective effects were discovered considerably earlier in diamine complexes than in amino-acid complexes. In 1920 Smirnoff [99] detected only the two complexes Δ-$[Pt(l\text{-}pn)_3]^{3+}$ and Λ-$[Pt(d\text{-}pn)_3]^{3+}$ in the products of the reaction of platinum(IV) salts with *dl*-propylenediamine: i.e. the reaction occurred with complete enantioselectivity and enantiospecificity. Analogous situations were found in the formation of complexes of cobalt(III) with propylenediamine [100] and of cobalt(III) and rhodium(III) with cyclopentane-*trans*-1,2-diamine (cpn) [101]. The instability of complexes containing ligands differing in configuration is confirmed by their ease of disproportionation into homogeneous structures. For example, only Λ-$[Co(d\text{-}cpn)_3]^{3+}$ and Δ-$[Co(l\text{-}cpn)_3]^{3+}$ are formed by the action of *l*-cyclopentanediamine on Λ-$[CoCl_2(d\text{-}cpn)_2]^+$. [101,102] High selectivity is already observed at the stage of formation of the bis-complexes. Thus the oxidation of cobalt(II) in the presence of *dl*-cyclopentanediamine leads to the formation of *trans*- or *cis*-$[CoCl_2(d\text{-}cpn)_2]^+$ and $[CoCl_2(l\text{-}cpn)_2]^+$, but not that of $[CoCl_2(d\text{-}cpn)(l\text{-}cpn)]^+$. [101,103] The results of these investigations led Jaeger [104] to the conclusion that complexes of mixed structure are not in general stable, while the optical configuration of the metal atom is determined unambiguously by the configuration of the ligand.

However, the formation of diamine complexes does not always follow this rule strictly. Thus Werner [105] was able to obtain all eight theoretically possible isomers of $[Co(NO_2)_2enpn]^+$. Both possible isomers Δ- and Λ-$[Co(l\text{-}cpn)en_2]Cl_3$ are also formed by the action of *l*-cyclopentanediamine on ΔΛ-*cis*-$[CoCl_2en_2]Cl$, although only two of the four possible structures—Δ-$[Co(l\text{-}cpn)en_2]^{3+}$ and Λ-$[Co(d\text{-}cpn)en_2]^{3+}$—are formed enantioselectively by racemic *dl*-cyclopentanediamine [101,106]. Thus kinetic enantioselectivity, which undoubtedly occurs in the formation of octahedral tris-complexes with diamines, may remain unnoticed, as occurs in the first case, where the reaction conditions constrain *l*-cyclopentanediamine to react not only with Δ-$[CoCl_2en_2]^+$ but also with its Λ-enantiomer. Reaction of *d*-tartaric acid with both enantiomers of $[CoCO_3en_2]^+$ can be achieved in just the same way [107,108], although the Δ-isomer is the first to react [108], forming Δ-$[Co(d\text{-}tart)en_2]^+$. Both isomers of *dl*-tartaric acid can be made to react with Δ-$[CoCO_3(l\text{-}pn)_2]^+$, [109] whereas, when excess of tartaric acid is used, the complex reacts selectively with *d*-tartaric acid to form stable Δ-$[Co(d\text{-}tart)(l\text{-}pn)_2]^+$. [110] Its less stable diastereomer Δ-$[Co(l\text{-}tart)(l\text{-}pn)_2]^+$, being in contact with excess of the *dl*-acid, exchanges its acid ligand selectively for *d*-tartrate, so that the uncomplexed tartaric acid is considerably enriched with the *l*-enantiomer [110,111]. Similarly Δ-$[CoCO_3(l\text{-}pn)_2]^+$ prefers to exchange its carbonate ligand for the (−)-enantiomer of α-chloro- or α-bromo-propionic acid and for the (−)-lactate ion [110], which can be used for the partial resolution of racemates of these acids. On the

other hand, optically active lactic acid resolves the racemate of $[CoCO_3en_2]^+$, undergoing ligand exchange only with one isomer [112]. Nevertheless, appreciable enantioselectivity was not observed [106] in the exchange of Δ-$[CoCO_3(l\text{-pn})_2]^+$ with DL-alanine.

Corey and Bailar in their classic paper [12] made a conformational analysis of the complexes of diamines in order to elucidate the causes of the enantioselective and enantiospecific effects. Since the angle in a complex is only 86–88°, the theory of these workers indicates that the five-membered chelate ring should be puckered considerably more strongly than the cyclopentane ring, and there should be a clear difference between equatorial and axial positions for substituents. Interaction between the two chelate rings occurs through the hydrogen atoms of the chelated amino-groups. In square planar structures this interaction is about 1 kcal mole^{-1} smaller with the same conformation of the two rings, e.g. $\delta\delta$, than in a *meso*-structure, e.g. $\delta\lambda$



The difference in energy in tetrahedral structures is rather smaller. In octahedral tris-complexes interaction between the three rings is minimal when they have the same configuration: $\delta\delta\delta$- and $\lambda\lambda\lambda$-conformations of the rings are preferred respectively for the Λ- and Δ-configurations of chiral tris-complexes. The energy of the isomeric complexes increases by 1.8 kcal mole^{-1} in the sequence

$$\Lambda[\delta\delta\delta] < \Lambda[\delta\delta\lambda] < \Lambda[\delta\lambda\lambda] < \Lambda[\lambda\lambda\lambda] .$$

Interaction between chelate rings and a tendency for substituents to occupy an equatorial position may lead to the appearance of enantioselective effects in complexes of substituted 1,2-diamines. In tetrahedral and in octahedral *cis*-biscomplexes, as well as in octahedral tris-structures, moreover, enantiospecific formation of the configuration of the metal atom itself must be expected.

Satisfactory agreement with theory has since been found [95,113] in experimental verification of the views developed by Corey and Bailar. Dwyer, Sargeson, et al. made a detailed study of complex formation by cobalt(III) [114–119] and platinum(IV) [120,121] with propylenediamine. In contrast to earlier investigations, they discovered the existence of complexes containing ligands differing in configuration [117, 118,121] and even the formation of diastereomeric pairs of tris-*l*-propylenediamine [117,114,120,121]. On the hypothesis that thermodynamic equilibrium is established among all structures in the reaction mixture with cobalt(III) complexes in the presence of activated carbon, the authors calculated the differences in their free energies, which reached 1.6 kcal mole^{-1}, close to the values calculated by Corey and Bailar (Table 3).

Closely similar values have been obtained [122] by cobalt-59 nuclear magnetic resonance spectroscopy, which enables the composition of a mixture of trispropylenediaminecobalt(III) complexes to be analysed. The same method shows that, in the presence of activated carbon, equilibrium is displaced towards statistically more probable though energetically less favourable structures. However, it remains unproven whether carbon enables true equilibrium to be established. Diastereomers may well possess different sorbabilities of carbon, but hence also different rates of conversion. In any case it is clear that in this system kinetic enantioselective and enantiospecific effects differ from thermodynamic effects.

A more detailed study has begun of the composition of complexes of cobalt(III) and chromium(III) with cyclopentane-*trans*-1,2-diamine [123] and of cobalt(III) with cyclohexane-*trans*-1,2-diamine (chn) [95].

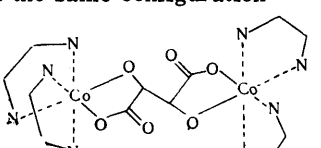
Table 3. Differences in Gibbs free energies $\delta\Delta G^\circ$ (kcal mole^{-1}) of diastereomers of complexes of cobalt(III) with propylenediamine.

Complex	Diastereomers		$\delta\Delta G^\circ$	Ref.
$[Co(l\text{-pn})(C_2O_4)_2]^-$	Λl	Δl	0.27	116
$[Co(l\text{-pn})_2(C_2O_4)]^+$	Λll	Δll	0.20	116
$[Co(en)_2(pn)]^{3+}$	Λl	Δl	0.45	117
$[Co(en)(pn)_2]^{3+}$	Λll	Δll	1.2	117
$[Co(pn)_3]^{3+}$	Λlll	Δlll	1.6	117
	Λddl	Λddd	0	118
	Δddl	Λddl	0.52	118
	Λlll	Λdll	0.53	118

The conformational ideas of Corey and Bailar have since been re-examined by Gollogly and Hawkins [124,125], who conclude that the chelate ring of a 1,2-diamine can assume many energetically similar conformations and that the $\Lambda(\delta\delta\delta)$ structure for $[M\,en_3]$ is more favourable than $\Lambda(\lambda\lambda\lambda)$ by at most 0.85 kcal mole^{-1}, while there is hardly any difference in energy between the $(\lambda\delta)$- and $(\delta\delta)$-structures for the *trans*-biscomplex. This last conclusion is consistent with the absence of thermodynamic enantioselectivity in complexes of propylenediamine, cyclohexane-*trans*-1,2-diamine, butane-2,3-diamine, and stilbenediamine with copper and nickel [126,127]. This unexpected result was obtained by calorimetric, potentiometric, and spectrophotometric methods.

Good examples of kinetic enantioselectivity are the reactions of $\Lambda(+)_{5461}$-$[CoEDTA]^-$ [128] and $\Lambda(-)_{5461}$-$[Co(+)\text{-PDTA}]^-$ [129] with racemic *dl*-propylenediamine, resulting in the formation of $\Lambda(+)$-$[Co(d\text{-pn})_3]^{3+}$, while the optically pure *l*-diamine remains in solution, since it does not undergo ligand exchange. When racemic $[CoEDTA]^-$ is treated with optically active *l*-propylenediamine, on the other hand, only the Δ-complex undergoes exchange [128].

A molecule of *d*-tartaric acid, on reacting in acid medium with racemic $\Delta\Lambda$-$[CoCO_3en_2]^+$, at once replaces carbonate ions in two complexes, always selecting a pair of complexes of the same configuration [108,130], e.g.



Enantioselectivity was unexpectedly high in electron transfer from $[Cr\,phen]^{2+}$ to $[Co\,phen_3]^{3+}$, where "phen" denotes 1,10-phenanthroline. When Λ-$[Co\,phen_3]^{3+}$ was used as oxidant, the racemic chromium complex yielded Δ-$[Cr\,phen_3]^{3+}$ of optical purity 92%. [131] A possible explanation is that only Δ-$[Cr\,phen_3]^{2+}$ undergoes oxidation, while the Λ-enantiomer is rapidly racemised. Very slight (1–2%) enantioselective effects have been observed [132] on the exposure of $[CrC_2O_4phen_2]^+$, $[Cr(C_2O_4)_2phen]^-$, and $[Cr\,bipy_3]^{3+}$ to the circularly polarised beam of an argon laser. The rates of isomerisation of enantiomers are

obviously different under these conditions. Ordinary light has a similar effect on the complex $[Cr\,phen_3]^{3+}$ if antimony *d*-tartrate is present in solution[133].

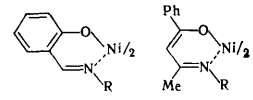
The Pfeiffer effect, first discovered in complexes of zinc with phenanthroline and with bipyridyl[135], is closely connected with enantioselective phenomena[134]. Three principal aspects—asymmetric induction, asymmetric transformation, and asymmetric synthesis—are distinguished at the present time[136], among which the first process has no connection with stereoselectivity. Asymmetric transformation involves a displacement, under the influence of an optically active compound, of the equilibrium between two labile enantiomers[137]. With the racemate of *cis*-$[CoCl_2en_2]^+$ in (−)-butane-2,3-diol, for example, the proportions of (+)- and (−)-isomers become 4 : 1.[138] The *trans*-$[CoCl_2en_2]^+$ complex can exist as three conformers (δδ, δλ, λλ), one of which is a *meso*-structure, while the other two are enantiomers distinguished by opposite puckering of the chelate rings. One of these chiral forms is stabilised in the optically active solvent, and the complex exhibits the Cotton effect[136]. A similar explanation applies to the appearance of Cotton effects with *cis*-$[CrCl_2en_2]^+$ and *cis*-$[CoCl_2trien]^+$ in (−)-butane-2,3-diol[136], with trisphenanthroline complexes of nickel, zinc, and cadmium in the presence of *l*-lactic acid[139,140] and of mercury in that of dibenzoyl-*d*-tartaric acid[139], and with $[Ni\,bipy_3]^{2+}$ in the presence of *l*-lactic acid[140]: the asymmetrising action of the optically active component is attributed to the difference in energy of its interaction (solvation or association) with the enantiomers of the complex. In the case of the diastereomeric ion-pairs of $[Ni\,phen_3]^{3+}$ with *d*-α-bromocamphorsulphonic acid this difference is $\Delta\delta G^\circ = 0.07$ kcal mole^{-1}.[141] Such considerable enantioselective effects with complexes are explained by the inclusion of the optically active component in the outer coordination sphere. In individual cases a chiral solvent may probably play a direct part in ligand exchange, as in the dissolution of *cis*-$[CoCl_2en_2]^+$ in *l*-propane-1,2-diol, which replaces chloride ions predominantly in the Λ-complex[142].

In the case of the Pfeiffer effect asymmetric synthesis implies the conversion of a non-chiral compound into an optically active structure. For example, the complex *trans*-$[CoOHCl\,en_2]^+$, which dissolves in (−)-butane-2,3-diol when heated to 70 °C, exhibits absorption and circular dichroism spectra identical with those of the optically active *cis*-$[CoOHCl\,en_2]^+$ in aqueous–methanolic solution. The degree of enantiospecificity of this isomerisation is evidently quite high[136].

A difference in the interaction of two enantiomeric complexes with an optically active solvent may also be evident in a difference in solubility[138]. The presence of an optically active con ponent in solution may change significantly the diffusion constants of the enantiomers[143–145]. Enantioselectivity in the association processes underlying such phenomena was demonstrated on the systems formed by *d*-tartaric acid with the enantiomers of $[Co\,en_3]^{3+}$[146] and by the enantiomeric tartaric acids with Λ-$[Co(d\text{-}pn)_3]^{3+}$.[147]

V. COMPLEXES OF SCHIFF BASES

Less detailed study has been made of enantioselective phenomena in complexes of Schiff bases. Fundamental investigations were made by Holm and his coworkers, who showed[148–151] that an equilibrium is established between tetrahedral and square planar forms of bis-complexes of Schiff bases with nickel(II) in non-coordinating solvents. The position of equilibrium depends mainly on the size and type of radical R attached to the nitrogen atom. Since the square planar form is diamagnetic, while the tetrahedral form is paramagnetic, signals from the two forms are easily distinguishable in the nuclear magnetic resonance spectrum. In the latter case the signals from *meso*-structures and optically active molecules, formed when a racemic Schiff base is used, can also be distinguished. Three pairs of diastereomers

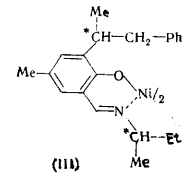


(I) (II)

are then formed, but complexes with optically active ligands give only one series of signals owing to rapid inversion[151,152] of the tetrahedral configuration $\Delta \rightleftharpoons \Lambda$.

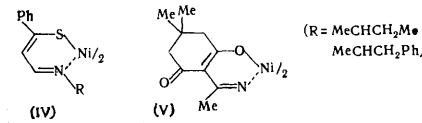
$$\Delta(ll),\ \Delta(dd),\ \Delta(ld) \equiv \Lambda(dd),\ \Lambda(ll),\ \Lambda(dl).$$

With *NN'*-disubstituted disalicylideniminatonickel(II) complexes (I: R = $CH_3CH_2CH(CH_3)$ or $C_6H_5CH_2CH(CH_3)$) the total concentration of *meso*(*dl*)-complexes (in square planar and tetrahedral forms) is roughly double the total concentration of each of the optically active structures[149,151]. With the *meso*-structure, however, the equilibrium is shifted further towards the tetrahedral form than with the optically active structures[148–152]. This difference is especially marked with nickel and zinc complexes of types (I) and (II) having a bulky substituent attached to nitrogen (R = $C_6H_5CH(CH_3)$): in this case the tetrahedral *meso*-complexes are more stable than the tetrahedral optically active structure by 0.08 kcal mole^{-1}.[152]



(III)

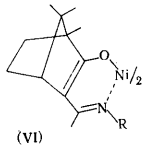
Six pairs of diastereoisomers may be formed by tetrahedral complexes of the Schiff base (III), which contains two asymmetric atoms[153]. Signals characteristic of each pair have been observed in the nuclear magnetic resonance spectrum, and the free energy of interconversion of planar square into tetrahedron has been determined from the temperature dependence of the signals. As in the preceding cases, the *meso*-structures of the complexes show a greater preference for the tetrahedral form than do the optically active complexes, the difference in the free energies of transition amounting to 0.3–0.4 kcal mole^{-1}. The considerable difference in the equilibrium positions is apparent in enhanced extinction and enhanced magnetic susceptibility of a solution of the complexes obtained from the racemic ligand in comparison with a solution of the optically active complex[153].



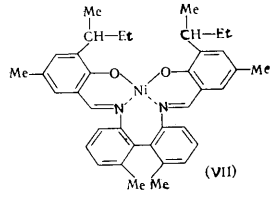
(IV) (V) (R = MeCHCH$_2$Me, MeCHCH$_2$Ph)

This difference is still larger in nickel complexes of γ-imino-thiols (IV).[154,155] When R = $C_6H_5CH_2CH(CH_3)$, the magnetic moments determined for complexes of the racemic and optically active ligands are respectively 2.40 and 2.08 β, whence the magnetic moment of the pure *meso*-form was calculated as 2.68 ± 0.12 β. The difference in

the free energies of interconversion of planar square into tetrahedron for *meso*-structure and optically active complex is 0.7 kcal mole^{-1}, so that the equilibrium proportions of the corresponding tetrahedral form are respectively 77% and 54%.[155] Considerably smaller effects are observed in *N*-substituted 2-acetiminodimedonato-complexes (V), where square planar forms predominate with both *meso*-structures and optically active bis-complexes[156]. The opposite situation is found in nickel complexes of *N*-alkylated aminomethylenecamphors (VI), where the equilibrium for the optically active complexes—but not for the *meso*-structures—is displaced further towards the tetrahedral form[157,158]. Thus, in a large number of bis-complexes of Schiff bases with nickel ions, enantioselectivity is apparent in a difference in stability ratios of square planar and tetrahedral forms between *meso*-complexes and the two optically active complexes.



(VI)



(VII)

An interesting case of the enantioselective solvation of complexes of quadridentate Schiff bases (VII) has been described by Ernst et al. In such complexes the Δ or Λ configuration at the metal atom is determined unambiguously by the configuration of the atropoisomeric ligand, and equilibrium between planar and tetrahedral structures is established without racemisation of the complex[159]. In non-chiral solvents the n.m.r. spectrum contains signals from three pairs of diastereomers, but signals from all the enantiomers—Δ(*ll*) and Λ(*dd*), Δ(*dd*) and Λ(*ll*)—can also be distinguished in chiral solvents. If, however, the solvent used is not 100% optically pure, the splitting of the signals observed initially from these diastereomeric pairs gradually disappears (with pinene of optical purity 90% in about 1 h). This unusual pattern was explained[160] by selective solvation of the Δ(or Λ)-isomers of the complex by *d*(or *l*)-pinene, with the formation now of the enantiomeric, n.m.r.-equivalent pairs Δ*d* and Λ*l*. Initially both Δ- and Λ-isomers are more strongly solvated by the solvent enantiomer present in excess, but the spectrum contains signals of the two pairs of enantiomers. With the establishment of equilibrium Δ- and Λ-enantiomers undergo enantioselective solvation, and the splitting of their signals disappears.

Complexes of Schiff bases obtained from pyridoxal and α-amino-acids have aroused considerable research interest in connection with their important role in biological transaminations. Complexes of zinc and aluminium with alanine derivatives[161] and of aluminium with derivatives of serine[162,163], alanine, leucine, threonine, α-aminobutyric acid, and norvaline[163] have been studied by n.m.r. spectroscopy. Octahedral complexes containing two planar terdentate ligands exist as three diastereomeric pairs. The homogeneous diastereomers of the optically active L-serine derivative differ by about 0.9 kcal mole^{-1} in energy; the *meso*-complex occupies an intermediate position with respect to stability[162]. Appreciable enantioselectivity has not been observed in complexes of the Schiff base of alanine: the quantities of the *meso*-structure and of optically active complexes in the equilibrium solution are roughly the same[161].

Nevertheless, Holm[152] reported the presence of enantioselectivity in the zinc and nickel complexes of the Schiff bases obtained from esters of alanine and phenylalanine with salicylaldehyde. Different properties have also been found[164] in copper complexes of *N*-salicylidene derivatives of aspartic acid. The greater stability of the homogeneous structure than of the *meso*-structure was shown by polarimetric titration for the copper complexes of Schiff bases of salicylaldehyde and α-methylbenzylamine[165].

When a chiral ketone (*S*-2-hydroxy-6,6′-dimethyl-2′-nitro-5-nitrosodiphenyl) is used to catalyse the racemisation of D- and L-alanine in the presence of copper ions, some difference (3–5%) is observed in the rates of racemisation of the enantiomers. Racemisation probably takes place in a complex of the resulting Schiff base[166].

VI. COMPLEXES WITH OTHER LIGANDS

The first communication on enantioselectivity in complexes probably appeared as early as 1900, when copper complexes of *dl*-tartaric acid were found[167] to be more stable than those of the optically active acid. It has been observed also that the solution obtained by mixing equal quantities of complexes of *l*- and *d*-tartaric acids absorbs light 19% more strongly than does either of the initial solutions[168–171]. In acid medium only monotartratocopper was detected, its formation constant being the same for *l*- and *dl*-tartaric acids[172,173]. More detailed investigations of this system showed that differences arise in alkaline solution, where polynuclear complexes are formed[171], whose composition is different with *l*- and with *dl*-tartaric acids. Electron spin resonance data[174] and X-ray diffraction[175] also indicate that the complexes are dinuclear.

The vanadyl ion also forms more stable complexes with *dl*-tartaric acid than with the optically active acid[171,176]. Both e.s.r. data[176] and X-ray examination[177] show that the complex is dinuclear and that steric interactions are smaller if the ligands differ in configuration[177]. The absorption spectra of complexes of VO^{2+} with *dl*- and *l*-tartaric acids also differ sharply[176], the former being red–brown in colour, and the latter violet. A difference is apparent also in resistance to oxidation[178], although the oxidation products are the same with the two complexes. A detailed survey has been made of the stereochemistry of dinuclear complexes of tartaric acid[179]. Stereoselectivity of formation of tartaric-acid complexes has been observed also with nickel[180] and antimony(III),[181] structures containing two ligands of the same configuration being the more stable here.

In the case of eight-coordinated zirconium(IV) and hafnium(IV) complexes, *dl*-hydroxy-acids (mandelic, lactic) ensure better formation of hydrogen bonds than do optically active ligands, whose complexes are less stable[182].

Different equilibrium positions and different activation energies of the transition between planar square and tetrahedron have been found for bis-complexes of nickel and cobalt(II) with racemic and optically active phosphines[183]. Considerable enantioselectivity develops in bis-complexes of nickel with penicillamine (ββ-dimethylcysteine), where the optically active structures are more stable than the *meso*-structure by 0.55 kcal mole^{-1}. These diamagnetic complexes probably have a square planar structure with a paired *cis*-arrangement of β-thiol and α-amine donors[30,37].

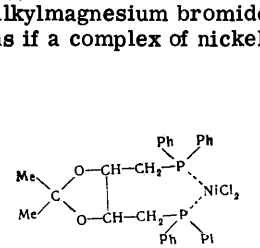
Selective photochemical decomposition by circularly polarised light of cobalt(III) and chromium(III) trioxalates[184–187] and of chromium(III) trisacetylacetonate[188]

leads merely to a slight enrichment of the mixture with one of the enantiomers. Measurement of the relative viscosity of solutions of optically active and racemic [$CrAcac_3$] in the presence of di-isopentyl *d*-tartrate has been used to study enantioselective effects of solvation of the complex[189]. Considerable Pfeiffer effects have been observed in complexes of tin(IV) and titanium(IV) with acetylacetone and dibenzoylmethane[190], as well as on aluminium tris-acetylacetonate, cobalt(III) and chromium(III) trioxalates, and zinc bisbenzoylacetonate[134].

The occurrence of kinetic enantioselective effects in labile complexes enables stereoselective polymerisation to be accomplished by means of coordination catalysts, which ensure selection, and addition to the growing polymer chain, of monomers of only one steric configuration. As a result, optically active polymer chains are formed from a racemic monomer mixture. For example, the complex of diethylzinc with methanol effects stereoselective polymerisation of racemic methyloxiran, which is proved by the possibility of separating the final polymer into two fractions of opposite optical activity[191-193]. Enantioselectivity with respect to monomers is due to the presence in the complex of a chiral terminal unit of the growing chain. The configuration of the whole chain is obviously determined by the chance configuration of the first monomer unit which entered the coordination sphere of the complex. If, however, the initial catalytic complex contains a chiral ligand, it already exerts control at the stage of reaction with the first monomer molecule. The whole of the polymer formed is then optically active, while the unchanged monomer is enriched with the second enantiomer. Such stereoselective polymerisation of *dl*-methyloxiran is catalysed by complexes of diethylzinc with optically alcohols (e.g. borneol)[194-198], amines[199], glutamic ester[200], amino-acids[201], complexes of iron(III) chloride with bornyl ethyl ether[202] and of triethylaluminium with the *N*-carboxy-anhydride of L-alanine[203], and also by magnesium *d*-tartrate[204,205].

Analogous processes of stereoselective and stereo-elective polymerisation by means of coordination catalysts have been reported for racemic alk-1-enes[206-210], α-amino-acid *N*-carboxyanhydrides[211,212], and also mixtures of methyloxiran and such anhydrides[213,214]. The possibility exists for using this process for the partial resolution of racemic compounds[215], e.g. methylthi-iran, where the effects of kinetic enantioselectivity are especially considerable.

The ability of an asymmetric complex catalyst to effect the selection of substrate enantiomers explains such reactions as the enantioselective oxidation of catechol in the presence of (+)-[$CoClNH_3en_2$]Br_2[76,213] and the reduction of racemic methylmethoxynaphth-1-ylphenylsilane by means of lithium tetrahydroaluminate in the presence of (+)-quinidine to optically active methylnaphth-1-ylphenyl-silane[217]. Similarly, the reaction of halogenated alkenes with a racemic s-alkylmagnesium bromide yields optically active hydrocarbons if a complex of nickel with an optically active diphosphine



is used as catalyst[218].

VII. USE OF ENANTIOSELECTIVE EFFECTS IN COMPLEXES FOR THE RESOLUTION OF RACEMATES

All methods for the resolution of racemates (in contrast to the separation of diastereomers) are inevitably based in some way on enantioselective processes. Resolution of a racemate entails either selective chemical modification of one of the enantiomers or its transfer to a separate phase. Kinetic enantioselective effects correspond to the first condition. The use of thermodynamic enantioselectivity in labile complexes for the practical separation of enantiomers is possible only in two-phase systems.

The first attempts to use enantioselective effects in complex formation for the resolution of racemates were undertaken by Bailar[106] as early as 1939. Only considerably later was partial resolution of tartaric acid accomplished by reaction with [$CoCO_3(l\text{-pn})_2$]$^+$.[110,111] The optical purity of *l*-tartaric acid, which showed less tendency to replace the carbonate ligand in the complex, reached 80%. A similar effect was observed with lactic and α-chloropropionic acids, where 30% resolution was achieved[110]. Considerable enrichment of the solution with *l*-propylenediamine occurs in the reaction of the *dl*-diamine with Λ(+)-[CoEDTA]$^-$.[128] Complete resolution of the diamine is possible when Λ(−)-[CoPDTA]$^-$ is used[129]. Similarly, *dl*-cyclohexanediamine can be successfully resolved by means of [$CoCO_3(l\text{-pn})_3$]$^+$,[219] and the resolution of (±)-[CoEDTA]$^-$ effected by means of *l*-propylenediamine[129].

The propylenediamine which distils from a solution containing the copper or nickel complex of *d*-tartaric acid and excess of the *dl*-diamine exhibits weak negative rotation[220] (optical purity 2–3%). On the other hand, distilling the diamine over [Cu_2(L-Glu)$_2H_2O$] gives 4% enrichment with *d*-propylenediamine. If excess of DL-alanine is added to a solution containing the copper complex of *d*-tartaric acid or L-glutamic acid, [$CuAla_2$] precipitates out enriched 3.8% with D-alanine or 3.3% with L-alanine[220]. Harada has reported[221-223] the resolution of DL-aspartic acid on its addition to a solution of the copper complex of L-glutamic acid, L-proline, or L-alanine. In all cases the complex [Cu(D-Asp)$_2$] is precipitated, in the last case in 40% yield of optical purity 95%. Detailed study of this process showed[224] that the presence of L-alanine in solution considerably accelerates crystallisation of the copper complex of D-aspartic acid in comparison with that of the L-aspartic-acid complex only in the pH range 2.7–5.3, while the proportions of copper and aspartic acid in the precipitate vary in the range 1 : 1.2–1.3. After deposition of the D-aspartic-acid complex, its enantiomer begins to crystallise with equally high optical purity. Similarly, D-lysine tungstophosphate crystallises preferentially[225] on the addition of dodecatungstophosphoric acid to a solution containing DL-lysine hydrochloride and $\Delta(-)_{5461}$-[CoEDTA] (or the complex cobalt(III) cyclohexanediamine-tetra-acetate). The true nature of the enantioselective processes leading to acceleration of the crystallisation of one enantiomer of a racemate from a solution containing an optically active component or a solid[226] is still not clear.

The enrichment with D-alanine (by 13.8%) of the complex [$CoAla_3$], formed when [Co(L-Asp)$_2$]$^-$ is treated with excess of DL-alanine at pH 9.5–10 in the presence of activated carbon, is probably due to kinetically controlled enantioselective exchange of ligands. The additional presence of powdered cellulose raises the optical purity

of D-alanine in the precipitated complex to 30–35%.[227] A still greater effect is produced by chitosan and its derivatives[228]. Accompanying this process by the action of DL-alanine and L-aspartic acid on $\Delta\Lambda$-$[Co(CO_3)_3]^{3-}$ showed[229] that ligand exchange involved the intermediate formation of (–)-$[CoCO_3(L\text{-}Asp)_2]^{3-}$, after which (–)-$[Co(D\text{-}Ala)_2L\text{-}Ala]$ was precipitated.

The possibility of using stereoelective polymerisation tion[215] or enantioselective hydrogenation[217] to resolve racemates has been mentioned in preceding Sections. Gillard[230] indicates that micro-organisms may be used to resolve $[CoGly_3]$.

A very large number of publications have appeared on the separation of enantiomers of stable complexes by chromatographic methods using dissymmetric stationary phases. The peculiarities of the chromatographic method in practice enable even very slight enantioselective effects of ligand exchange in the outer coordination sphere of these complexes to be exploited. Thus the different degrees of association of the enantiomers of $[M\,en_3]^{3+}$ (M = Co^{II}, Cr^{III}, Rh^{III}) with *d*-tartaric acid[231] or with aluminium(III) *d*-tartrate[232,233] permit complete separation of these enantiomers by thin-layer chromatography or electrophoresis. Trisacetylacetonates of these metals are partly resolved during extraction with di-isopentyl-*d*-tartrate[234] or with a solution of (+)-$[Co\,en_3]^{3+}$.[235]

Selective sorption on optically active quartz was proposed[236,237] for the separation of enantiomers of $[CoClNH_3en_2]^{2+}$ and $[CoClNH_3DMG]^{+}$ (where DMG = dimethylglyoximato). This method proved acceptable also for separating enantiomers of $[CoCO_3(NH_3)_2en]^{+}$,[238] $[CoDMG_3]$,[239] disalicylidenetriethylenetetraminecobalt(III),[240] and several others[241]. Chromatography on columns of optically active quartz has effected the resolution of several cobalt and chromium complexes[241–244] (some of these results have not been confirmed[245,246]), $[CoEDTA]^{-}$,[247] bisbenzoylacetonatoberyllium(II),[248] tetrahedral nickel complexes of formazans[249,250], oxalate[244] and acetylacetonate[251] complexes of cobalt(III) and chromium(III), and the complex of platinum(II) with *N*-ethyl-*N*-methylglycine[252]) which contains an asymmetric nitrogen atom). The enantiomers of trishexafluoroacetylacetonatochromium(III) have been separated by gas chromatography[253,254]. Sodium perchlorate crystals have been reported[255,256] as possessing a similar ability to resolve racemates of complex compounds.

The largest effects in the separation of enantiomers are usually observed in chromatography on carbohydrates (Table 4). The hydroxy-groups of these sorbents obviously play an active part in forming the outer coordination sphere of the complexes. In some cases the efficiency of the chromatographic process can be considerably enhanced (up to complete separation of the enantiomers) if an optically active eluant, e.g. sodium *d*-tartrate solution, is used[284,285].

Significantly more modest successes have been achieved in the separation of enantiomeric complexes by means of synthetic dissymmetric ion-exchange resins containing optically active groups—quinine[286], tartrate or antimonyltartrate anions, and also Λ-$[Co\,en_3]^{3+}$ anions[287].

Rogozhin and Davankov's proposed[288–292] ligand-exchange chromatography[43] of racemates—a new principle for the separation of enantiomers capable of complex formation—is based on enantioselective effects of inner-sphere ligand exchange. Chromatography is conducted on a sorbent having chiral complexing groups, in the presence of metal ions (copper, nickel, zinc, etc.) giving kinetically labile complexes. Thermodynamic enantioselective effects develop in the formation of a mixed sorption complex incorporating in the chiral stationary ligand, the metal ion, and the mobile ligand (the racemate molecule). These workers synthesised a wide range of dissymmetric sorbents based on a cross-linked macro-network polystyrene framework with bidentate[293–295] and terdentate[296–300] stationary ligands like α-amino-carboxylic and α-amino-phosphonic[301] acids. Racemates of many compounds capable of complex formation—amino-acids, amino-alcohols, diamines, heterocycles, etc.—have been resolved on these sorbents[44,47,48]. The high enantioselectivity of complex formation in these systems ($\delta\Delta G^{\circ}$ may exceed 1 kcal $mole^{-1}$ [50,56–58]) ensures exceptionally high selectivity of sorption of enantiomers, which can be exploited for their separation not only on an analytical but also on a preparative scale. Better separations are observed when the total denticity of stationary and separable ligands coincides with the coordination number of the metal atom[44]. The efficiency of separation is influenced by the degree of saturation of the sorbent with metal ions[45,46], temperature, eluant concentration, and several other factors[302].

Table 4. Resolution of racemates of coordination compounds by chromatography on carbohydrates.

Sorbent	Resolvable complex	Ref.
D-Lactose	Cr^{III} trisacetylacetonate	189,257,260
	Co^{III} trisacetylacetonate	257-262
	Rh^{III} trisacetylacetonate	259-261
	Ru^{III} trisacetylacetonate	259
	Y^{III}, Gd^{III} trisacetylacetonates	263
	Co^{III} trisbenzoylacetonate	259
	Cr^{III} trisbenzoylacetonate	264
	Ni^{II}, Cu^{II} bis-β-keto-imines	265
	bisacetylacetonatopropylenediaminevanadyl	266
	tris-5-methylhexane-2,4-dionatocobalt(III)	267
Starch	trisethylenediamine-cobalt(III), -chromium(III)	268,269
	trisglycinatocobalt(III)	268-271
	Co^{III} trisdithiocarbamate	268,269
	Co^{III} trisdithiocarbaminate	269
	Co^{III}, Cr^{III} trioxalates	269
	bisglycylglycinatocobalt(III)	271
	bisethylenediaminecobalt(III)	272
	tris-L-α-aminoisobutyratocobalt(III)	273
	hexamethyl-1,4,8,11-tetra-azacyclotetradeca-1,7-dienatonickel(II)	274
Cellulose	Co^{III} trioxalate	272,275
	tris-α-amino-carboxylatocobalt(III)	275
	trisalkylene-1,2-diaminecobalt(III)	276,277
	tribenzo[*b*, *f*, *j*]-1,5,9-triazacyclododecenato-nickel(II)	278
Carboxymethylcellulose	hexakis-2-aminoethylthiolatotricobalt(III)	279
	Co^{III} bisiminodiacetate	280
	Co^{III} trimethylenediaminetetra-acetate	280
	dichlorobisphenanthrolinerhodium(III)	281
Diethylaminoethylcellulose	Co^{III} ethylenediaminetetra-acetate	282
Phosphorylated cellulose	trisethylenediaminecobalt(III)	282
	Co^{III} bisiminodiacetate	282
	bisdiethylenetriaminecobalt(III)	282
SE-Sephadex	bisdiethylenetriaminecobalt(III)	283

Similarly, a sorbent based on a styrene—divinylbenzene copolymer with *N*-carboxymethyl-L-valine—a stationary terdentate ligand—has been synthesised by Angelici et al.[303,304]. In the presence of copper ions racemates of isoleucine—and rather less effectively those of valine and alanine—are partly resolved on this sorbent.

Bernauer [60,61,305,306] proposed a somewhat modified method of ligand-exchange chromatography: a stationary chiral complex of iron(III) with 2'-hydroxyethyl-D-propylenediaminetriacetic acid L-[Fe(D-HEPTA)]$^-$ was bound by an ionic bond—not a covalent bond—to a polymeric carrier (Dowex 1 × 2 anion-exchange resin). Only acid racemates, which preserve the overall negative charge of the complex when one of its acetate ligand groups is replaced, can be resolved on such a solvent. This condition is satisfied by acetyl and benzoyl derivatives of leucine, alanine, phenylalanine, and methionine, which were in fact partly resolved by ligand chromatography. In all cases the more stable mixed complexes formed derivatives of D-amino-acids, the ratio of sorbed D- and L-ligands falling in the above sequence of amino-acids from 1.08 to 1.03 ($\delta\Delta G^\circ$ = 0.10–0.02 kcal mole^{-1}). Bernauer [61] has used a chiral stationary complex of copper, nickel, or zinc with D(−)-propylenediaminetetra-acetic acid of total charge 2- to strengthen the bonding of the complex to the anion-exchange resin carrier. On such a sorbent 60% separation of α-methylbenzylamine isomers is observed ($\delta\Delta G^\circ$ = 0.3 kcal mole^{-1}).

It is interesting that Bruschtein [307], in an earlier study of the interaction of polymers of *N*-acryloyl and *N*-methylacryloyl derivatives of L-amino-acids (glutamic and aspartic acids, glycine, asparagine) with copper complexes of propylenediamine and of tyrosinamide, detected no enantioselective effects.

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Thus a fairly large number of processes, in which thermodynamic or kinetic enantioselective effects develop in one form or another, are already known in the chemistry of coordination compounds. These effects are observed both in the coordination of chiral ligands and in processes involving only the outer coordination sphere of the complex. The literature on enantiospecific effects is equally vast, but could not be considered within the scope of the present Review.

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Quantitative Effect of the Pentafluorophenyl Ring on the Reactivity of Substituents

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The quantitative effect of the pentafluorophenyl ring on the reactivity of substituents (hydrogen, alkyl, aryl, carboxyl, amino, hydroxyl, and halogens) is surveyed. The efficiency with which fluorine atoms at different positions in the benzene ring influence a reaction centre is discussed. An analysis of the σ-constants of the pentafluorophenyl group is also given. A list of 106 references is included.

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I. INTRODUCTION

The chemistry of polyfluorinated aromatic compounds has developed rapidly during recent years[1-7]. One of the main lines of research in this field has been the study of reactions that involve nuclear substituents while leaving nuclear fluorine atoms unchanged.

The introduction of fluorine atoms instead of hydrogen atoms into an aromatic ring has a significant effect on the properties of substituents attached to the ring, which sometimes leads to reactions uncharacteristic of the corresponding hydrocarbon derivatives. No generalisations have been published on the quantitative effect of a polyfluorinated aromatic ring, in particular pentafluorophenyl, on the reactivity of atoms and groups, so that it is of interest to discuss the published information. Since the great majority both of synthetic papers and especially of papers on quantitative aspects of the effect of a polyfluorinated aromatic ring are concerned with pentafluoro-derivatives of benzene, the present Review will deal with the effect of the pentafluorophenyl ring on the reactivity of substituents attached to it. In several cases the effect of the pentafluorophenyl group is compared with those of other groups, e.g. mono-, di-, and poly-fluorophenyl, pentachlorophenyl, nitrophenyl, and trifluoromethyl†.

Since the effect of a pentafluorophenyl ring on a substituent varies with the nature of the latter (or its reactive centre)[9], a detailed study of this effect on key groups—such as alkyl, carbonyl, amino, nitro, etc.—may give information on the specific properties of polyfluorinated aromatic compounds. Here, therefore, we shall first discuss the effect for each specific group, and at the end of the Review attempt to generalise the data on the effect of the pentafluorophenyl ring.

† The effect of the trifluoromethyl group on the reactivity of functional groups has been reviewed[8].

II. HYDROGEN ATOMS

The electron-accepting properties of the fluorine atoms in fluorinated benzenes confer an acidic character on the carbon—hydrogen bonds, which is apparent e.g. in increased rates of isotopic exchange compared with benzene[10-12].

Table 1. Relative rates of exchange of deuterium and tritium at various positions in fluorobenzene and benzylidyne trifluoride with lithium cyclohexylamide in cyclohexylamine at 25°C.[11]

Compound	Rate relative to benzene	
	D	T
o-Deutero(tritio)fluorobenzene	6.3×10^5	3.4×10^5
m-Deutero(tritio)fluorobenzene	107	86
p-Deutero(tritio)fluorobenzene	11.2	9.1
m-Deutero(tritio)benzylidyne trifluoride	580	390

The data in Table 1 suggest that the acidity of the carbon—hydrogen bond will increase strongly as fluorine atoms accumulate in the benzene ring. The kinetic parameters of the base-catalysed exchange of tritium in polyfluorobenzenes (Table 2) show that *ortho*-fluorine atoms make the most significant contribution to the kinetic acidity of polyfluorobenzenes, and are followed by *meta*-fluorine atoms and finally the *para*-fluorine atom (by factors respectively of 260 000, 247, and only 23). The enhanced reactivity of pentafluorobenzene in comparison with *m*-difluorobenzene and 1,2,3,4-tetrafluorobenzene is due primarily to the difference in activation energy[13].

Results on the thermodynamic acidity of polyfluorobenzenes have been obtained by Streitwieser et al.[14] in a study of equilibria of the type

$$ArH + R^-Cs^+ \overset{K}{\rightleftarrows} Ar^-Cs^+ + RH$$

in cyclohexylamine, where ArH is a polyfluorobenzene, and RH an indicator hydrocarbon (Table 3).

Table 2. Rate constants and activation parameters of the exchange of tritium in polyfluorobenzenes in methanolic sodium methoxide at 40°C.[13]

Compound	Rate constant $10^4 k_2$, $M^{-1}\,s^{-1}$	Activation	
		energy ΔH^*, kcal mole^{-1}	entropy ΔS^*, e.u.
C_6HF_5	1360	18	—5.6
1,2,4,5-$C_6H_2F_4$	58	—	
1,2,3,5-$C_6H_2F_4$	5.6	—	
1,3-$C_6H_4F_2$	0.0061	27.9	1.9
1,2,3,4-$C_6H_2F_4$	0.0053	27.3	—0.3

It is interesting to compare results obtained on the kinetic and thermodynamic acidities of polyfluorobenzenes. Streitwieser et al.[14] evaluated the partial reaction rate factors for the exchange of deuterium in methanolic sodium methoxide (Table 2) or tritium in cyclohexylamine (CHA) (Table 1), as well as the equilibrium factors (Table 3) for fluorobenzenes, these being the difference between the thermodynamic acidities of benzene and of the fluorobenzene (Table 4). Good agreement between factors calculated from kinetic and from thermodynamic data is evident from Table 4.

Table 3. Thermodynamic acidity of polyfluorobenzenes and benzene in cyclohexylamine relative to 9-phenylfluorene (pK_a = 18.49).[14]

Compound	pK_a (at 34°C)	Indicator hydrocarbon (pK_a)
C_6HF_5	25.85	9-t-butylfluorene (24.23)
1,2,3,4-$C_6H_2F_4$	31.52	di-*p*-biphenylylmethane (30.83) triphenylmethane (31.45)
1,2-$C_6H_4F_2$	34.98	tri-*p*-tolylmethane (34.98)
C_6H_6	43	

The difference in thermodynamic acidity between benzene and pentafluorobenzene is easily calculated by means of these factors. Replacement of five hydrogen atoms in the benzene molecule by fluorine increases the equilibrium acidity (pK_a) of the carbon—hydrogen bond by 15.8—17.1. Approximately the same result was obtained from polarographic data for symmetrical organomercury compounds: values of pK_a for benzene, pentafluorobenzene, and pentachlorobenzene were respectively 37, 23, and 30.5.[15,16]

The considerably more acidic character of the carbon—hydrogen bond in pentafluorobenzene than in pentachlorobenzene is obviously due primarily to the strong inductive effect of fluorine atoms, which is the predominant factor in stabilising aryl anions whose lone electron pair is located in a σ-orbital. The acidic character of this bond in pentafluorobenzene is shown in its ability to react even with alkyl-containing Grignard reagents[17], which usually react only with compounds having $pK_a \leq 21$.[18]

The introduction of fluorine into an aromatic ring lowers the reactivity of the latter towards electrophilic reagents. Thus the rate of nitration of fluorobenzene in sulphuric acid at 25°C is lower than that of benzene by a factor of 8.5.[19] The electrophilic reactivity diminishes considerably with increase in the degree of fluorination of the aromatic ring (Table 5).[20-22]

Table 4. Partial rate and equilibrium factors for fluorobenzenes.

Position of fluorine	Partial rate factors		Equilibrium factors (Ref.14)
	MeONa—MeOH[a]	LiCHA—CHA (Refs.11,14)	
ortho-	5.25	5.43	5.7
meta-	2.07	1.95	2.3
para-	1.13	1.03	1.1

Quantum-chemical calculation of the electron density (allowing for π-and σ-charges) on the carbon atoms in the isomeric tetrafluorobenzenes and in pentafluorobenzene predicts the sequence

$$1,2,4,5\text{-}C_6H_2F_4 < 1,2,3,4\text{-}C_6H_2F_4 < C_6HF_5 < 1,2,3,5\text{-}C_6H_2F_4$$

of increasing reactivity towards electrophilic reagents[23].

Table 5. Rate constants of the sulphonation of polyfluorobenzenes in oleum (100.12% H_2SO_4) at 25°C.[22]

Compound	k, s^{-1}	Compound	k, s^{-1}
1,4-$C_6F_2H_4$	16.1	C_6F_5H	0.000512*
1,2,3,4-$C_6F_4H_2$	0.0079		

* Concentration of oleum 101.17%.

This sequence diverges somewhat from results for the sulphonation (Table 5) and nitration of polyfluorobenzenes[24]. The experimental reactivity sequence for electrophilic substitution in polyfluorobenzenes is

$$1,2,4,5\text{-}C_6H_2F_4 < C_6HF_5 < 1,2,3,4\text{-}C_6H_2F_4 \sim 1,2,3,5\text{-}C_6H_2F_4.$$

Thus deactivation of the aromatic ring towards electrophilic reagents depends on the positions and the number of fluorine atoms present. This is supported also by a study of the protiodesilylation and protiodestannylation of fluoroaryltrimethyl-silanes and -stannanes respectively (Table 6).[25] Additivity of the effects of the fluorine atoms is not observed in these processes (partly owing to steric acceleration of the reactions).

Polychlorobenzenes show a similar pattern: pentachlorobenzene is nitrated more rapidly than 1,2,4,5-tetrachlorobenzene by factors of ~4,[19] whereas the nitration of

Table 6. Relative rate of the protiodestannylation of fluoroaryltrimethylstannanes $ArSn(CH_3)_3$.[25]

Ar	k_{rel}	Ar	k_{rel}
Ph	1.0	*m*-FC_6H_4	0.22
p-FC_6H_4	0.93	C_6F_5	0.43
o-FC_6H_4	0.41		

chlorobenzene takes place correspondingly more slowly than that of benzene[19]. The variety of effects of the halogens in a polyhalogenated system obviously cannot be explained by the principle of additivity. Furthermore, pentafluorobenzene is inert towards nitric acid in 90% sulphuric acid, whereas pentachlorobenzene is nitrated under these conditions[19].

III. ALKYL AND ARYL GROUPS

The kinetic acidity of an α-C—H bond in toluene is enhanced by fluorine atoms in *ortho*- and *meta*-positions, but is diminished by a *para*-fluorine atom (Table 7).[26]

Table 7. Relative rates of exchange of substituted α-deuterotoluenes and α-tritiotoluenes $RC_6H_4CH_2D(T)$ with lithium cyclohexylamide in cyclohexylamine at 50°C.[26]

R	relative rate		
	ortho	*meta*	*para*
H	1	1	1
F	12	22	0.73
CF_3	—	60	180

The rate of deuterium exchange for α-deutero-2,5-difluorotoluene in cyclohexylamine at 25°C exceeds the corresponding rate for α-deuterotoluene by a factor of 350.[11] The strong acidifying effect of a *meta*-fluorine atom is obviously due to its inductive, electron-accepting effect, whereas a mesomeric, electron-donating effect is also exerted by *ortho*- and *para*-fluorine atoms. The superposition of these effects explains why a *p*-fluorine atom becomes a weak donor and destabilises the benzyl anion, whereas *o*-fluorine exerts a weaker acceptor effect than does *m*-fluorine[27]. The electron-donor character of a *p*-fluorine atom has been observed also in a study of the effect of substituents on the rate of alkaline cleavage of *para*- and *meta*-substituted benzyltrimethylstannanes[28].

The effect of *ortho*- and *para*-fluorine atoms on the acidity of an α-C—H bond in fluorotoluenes is similar to the effect of fluorine atoms on an α-carbanion centre in aliphatic systems, the "Hine effect".[29-33] If the carbanion is planar, *p*—*p* interaction between the lone electron pair of the fluorine atom and the lone pair of the negatively charged carbon atom leads to its destabilisation[29-33]. If, on the other hand, the carbanion is pyramidal, it is stabilised by the electron-accepting inductive effect of the α-fluorine atom[33,34]. Thus, in contrast to the *p*-fluorobenzyl anion, which is probably planar, the carbanion generated from 2-*p*-fluorophenyl-2-hydrohexafluoropropane is more stable than its analogue unsubstituted in the ring; in the absence of steric hindrance, this indicates the pyramidal geometry of such carbanions[35].

Thus it follows from the above data that the stability of fluoroarylated carbanions is determined primarily by the relation between the oppositely directed inductive and mesomeric effects of the fluorine atoms. Not only the type of hybridisation of the carbon atom with the lone electron pair but also steric factors preventing coplanarity of the benzene ring and the neighbouring carbanion centre are important for stabilisation of the carbanion. Thus the thermodynamic acidity of 2—6-pentafluorotoluene considerably exceeds that of toluene ($\Delta pK_a = 10$).[36] This can probably be explained by the existence of the pentafluorobenzyl anion in a conformation such that the adjacent carbanion centre, probably of sp^2 type, does not lie in the plane of the benzene ring (values of pK_a for $C_6H_5CH_3$, $C_6F_5CH_3$, *p*-$NO_2C_6H_4CH_3$, and *p*-$CF_3C_6H_4CH_3$ are respectively 35,[15] 25,[36] 26,[37] and 28 [36]). The stability of the pentafluorobenzyl anion is close to that of the *p*-nitrobenzyl anion, and exceeds that of the *p*-trifluoromethylbenzyl anion.

Table 8. Thermodynamic acidity of substituted methanes.

Methine acid	System	pK_a	Ref.
Ph_3CH	CHA-CsCHA*	31.5	38
	DMSO**	28	39
$(C_6F_5)_2CH—CH(C_6F_5)_2$	CHA	22.6	40
$(p\text{-}CH_3OC_6F_4)_3CH$	CHA	19.2	40
$(p\text{-}CH_3C_6F_4)_3CH$	CHA	17.8	40
$(C_6F_5)_3CH$	CHA	15.8	40
$(p\text{-}NO_2C_6H_4)_3CH$	DMSO	12.2	39
$(CF_3)_2CH$	CH_3ONa-CH_3OH	11	41
	***	7	16
Ph_2CH_2	CHA	33.1	38
	DMSO	28.6	42
$(C_6F_5)_2CH_2$	CHA	21.2	40
$(p\text{-}NO_2C_6H_4)_2CH_2$	C_2H_5OH-DMSO	15.85	43
$(CF_3)_2CH_2$	***	22	16

* CHA = cyclohexylamin(d)e.
** DMSO = dimethyl sulphoxide.
*** From polarography of mercury derivatives.

Table 8 compares the stabilities of polyfluorinated di- and tri-arylmethyl anions with those of their non-fluorinated analogues. Successive replacement of phenyl by pentafluorophenyl in a series of di- and tri-arylmethanes leads to an increase in the thermodynamic acidity (pK_a) of the α-C—H bond by 5—6. Roughly the same increase is produced by replacing phenyl by *p*-nitrophenyl. Trifluoromethyl has a greater acidifying effect than has phenyl, as can be seen from the values of pK_a for tris-trifluoromethylmethane and trispentafluorophenylmethane.

The triphenylmethyl anion, in which the α-carbon atom possesses hybridisation approximating to the sp^2 type[44], is a convenient model for revealing the inductive effects of substituents, since the benzene rings assume a propeller conformation (mean angle of deflection of ring 31.7°,[44] close to the 35° calculated theoretically[45]), which diminishes substantially their resonance interaction with the carbanion centre. This factor is most important for polyfluorinated triphenylmethyl anions‡, and is reflected

‡ It may be supposed that the mean angle of deflection of the pentafluorophenyl rings in the trispentafluorophenylmethyl anion will also be at least 31.7°.

in their enhanced thermodynamic stability in comparison with non-fluorinated analogues. However, transmission of the effect of a substituent by a conjugation mechanism is not completely excluded in polyfluorinated triarylmethyl anions: thus the introduction of an electron-donating substituent (methyl, methoxy) at a *para*-position in trispentafluorophenylmethane weakens the thermodynamic acidity of the corresponding methine acid. The contribution of each pentafluorophenyl group ($\Delta pK_a \simeq 5.2$) to the thermodynamic stability of the trispentafluorophenylmethyl anion, which is due predominantly to the inductive effect of the fluorine atoms, can be confirmed by calculation based on a different model, the 9-pentafluorophenylfluorenyl anion. Here the carbon atom with a lone pair of electrons is in the sp^2-hybrid state, but the pentafluorophenyl group should occur mainly in a conformation§ preventing resonance interaction of the fluorine atoms with the carbanion centre owing to steric repulsion of the hydrogen atoms at positions 1 and 8 in fluorene and the *ortho*-fluorine atoms of the pentafluorophenyl group. The differences ΔpK_a between the thermodynamic acidities of phenyl- and pentafluorophenyl-fluorenes have been calculated by means of the correlation[48] $pK_a = -4.557\sigma^* + 21.85$, representing the dependence of the thermodynamic acidity of 9-substituted fluorenes on the Taft induction constant σ^* of the 9-substituent. Substitution of the constant $\sigma^* \simeq 1.9$ for the pentafluorophenyl group[49] with the use of $pK_a = 18.6$ for 9-phenylfluorene[48] yields the difference $\Delta pK_a = 5.4$, which coincides with the contribution of the pentafluorophenyl group to the thermodynamic acidity of trispentafluorophenylmethane.

The possibility of varying the ratio of resonance and inductive effects of the pentafluorophenyl group has been shown for mesomeric carbanions of the type $[C_6F_5C^-RR']Na^+$, where R = R′ = $COOC_2H_5$, CN, COC_6H_5, etc.[50–53] It is significant that the carbon atom with the lone pair in these carbanions is usually in an sp^2-hybrid state, which favours resonance interaction of the fluorine atoms when the pentafluorophenyl group is coplanar with the carbanion centre. Depending on the relative parts played by the electron-accepting groups R and R′ in delocalisation of the negative charge and also on their spatial requirements, however, the conformation of the pentafluorophenyl group may change substantially, and hence also the relative contributions of resonance and inductive effects of this group. The influence of the fluorine atoms of the pentafluorophenyl group on the stability of mesomeric carbanions can be traced in the differences in acidity $\Delta pK_a = 0.5$, 0.4, 0.1, and 0 for the series of *para*-substituted methine acids—$XC_6F_4CH(COOC_2H_5)_2$, $XC_6F_4CH(CN)COOC_2H_5$, $XC_6F_4CH(CN)C_6F_5$, and $XC_6F_4CH(CN)C_6H_5$—where X = H, F respectively. Whereas the *para*-fluorine atom acts as an acceptor in derivatives of polyfluorinated phenylmalonic acids, in polyfluorinated diarylacetonitriles replacing a *para*-hydrogen by fluorine either does not affect or diminishes pK_a, so that the *para*-fluorine atom is now a donor rather than an acceptor[53].

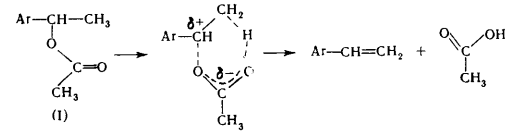
The thermodynamic acidities of various polyfluorinated carbonyl compounds and their non-fluorinated analogues show (Table 9) that the effect of the pentafluorophenyl group on the stability of mesomeric carbanions depends on the type of carbanion. Thus steric interaction between the two pentafluorophenyl groups in the carbanion from bispentafluorophenylmethyl phenyl ketone $(C_6F_5)_2CHCOC_6H_5$ deflects them from coplanarity, and the mesomeric carbanion is largely destabilised by the inductive effects of these groups. Whereas introduction of a phenyl group into deoxybenzoin $C_6H_5CH_2COC_6H_5$ leads to weakened thermodynamic acidity in diphenylmethyl phenyl ketone[54], bispentafluorophenylmethyl phenyl ketone is more acidic than is pentafluorodeoxybenzoin ($\Delta pK_a = 3.8$).

Table 9. Thermodynamic acidity of polyfluorinated carbonyl compounds and their non-fluorinated analogues with respect to 2,4-dinitrodiphenylamine in 1,2-dimethoxyethane.

Compound	pK_a	ΔpK_a per C_6F_5	Ref.
$PhCH(COOEt)_2$	14.2	1.4	50
$C_6F_5CH(COOEt)_2$	12.8		
p-$NO_2C_6H_4CH(COOEt)_2$	12.6	—	50
$PhCH_2COPh$	16.1	0.8	54
$C_6F_5CH_2COPh$	15.3		51
$C_6F_5CH_2COC_6F_5$	11.7		51
$Ph_2CHCOPh$	16.6	2.5	54
$(C_6F_5)_2CHCOPh$	11.5		52

The relation $\Delta pK_a = -0.077\delta_p + 14.508$ has been established[53] for polyfluoroarylated mesomeric carbanions $[C_6F_5C^-RR']Na^+$, where ΔpK_a is the difference between the thermodynamic acidities of non-fluorinated and fluorinated methine acids—C_6H_5CHRR' and C_6F_5CHRR'—and δ_p is the chemical shift (from trichlorofluoromethane as internal standard) of the *para*-fluorine atom in the pentafluorophenyl group of the fluorinated carbanion (in 1,2-dimethoxyethane as solvent). Since the chemical shift δ_p in pentafluorobenzene derivatives represents primarily the resonance effect of the substituent[23,55], the fractional destabilising effect of *ortho*- and *para*-fluorine atoms, expressed as the chemical shift δ_p in the fluorinated mesomeric carbanions, correlates with the difference in relative stability between non-fluorinated and fluorinated carbanions ΔpK_a. It follows from this correlation that, the greater the degree of conjugation of the pentafluorophenyl group with the carbanion centre (the greater the chemical shift δ_p), the smaller the difference in stability between the mesomeric carbanions of benzyl type containing phenyl or pentafluorophenyl groups.

Data have been obtained also on the effect of the pentafluorophenyl group on the positively charged benzyl carbon atom. In a kinetic study of the pyrolysis of α-methylfluorobenzyl acetates



(I)

(in the transition state the positive charge is concentrated mainly on the benzyl carbon atom) Taylor[56] found that the effects of fluorine atoms in the benzene ring were not additive. The acetate (I) with Ar = C_6F_5 is less reactive than that with Ar = C_6H_5 by a factor of 4.6, whereas a calculation based on additivity would indicate a factor of 7.75. The fact that the five fluorine atoms together are less strongly electron-accepting than if they had acted

§ The phenyl group in the 9-phenylfluorenyl anion is not coplanar with the carbanion centre, the angle of deflection being 30–39°.[46,47]

separately further confirms the peculiarity of the polyhalogenated system noted above in discussing the reactivity of incompletely fluorinated aromatic compounds.

Interesting results have been obtained by Taylor[57] in a study of the protiodetritiation of mon- and penta-fluorobiphenyls containing tritium in the *ortho*-, *meta*-, and *para*-positions of the non-fluorinated benzene ring (Table 10). In this typical electrophilic aromatic substitution the pentafluorophenyl group is primarily *para—ortho* orienting, although in comparison with the electronic effect of the phenyl group, of course, it quite strongly deactivates the aromatic ring towards electrophilic agents. Comparison of the observed partial rate factor of 0.0158 for the *para*-position in pentafluorobiphenyl with the calculated additive value of 0.044 also indicates a relative weakening of the electron-accepting power of the fluorinated phenyl group as fluorine atoms accumulate.

Table 10. Partial rate factors of the protiodetritiation of fluorinated biphenyls ArC_6H_4T.[57]

Ar	Position of tritium		
	ortho	*meta*	*para*
Ph	45	0.81	48
p-FC_6H_4—	—	—	26.3
o-FC_6H_4—	5.13	—	6.42
m-FC_6H_4—	4.25	—	4.65
C_6F_5—	0.0095	0.0053	0.0158

It is interesting to compare the above kinetic results on electrophilic reactions with data on the effect of the pentafluorophenyl group on the thermodynamic stability of carbonium ions of the triarylmethyl type. Successive replacement of phenyl by pentafluorophenyl in a triarylmethanol results in a decrease in stability (pK_{R^+}) of the corresponding polyfluorinated triarylmethyl cation by 3.2—4.0 (Table 11)[58-60]. About the same decrease in stability of the triphenylmethyl cation occurs on introduction of a *p*-nitro-group.

Table 11. Values of pK_{R^+} of substituted triarylmethanols.

Carbinol	pK_{R+}	Ref.	Carbinol	pK_{R+}	Ref.
Ph_3COH	— 6.63	61	$(4\text{-}NO_2C_6H_4)_3COH$	—16.27	61
$C_6F_5(Ph)_2COH$	—10.5	59	$(p\text{-}FC_6H_4)_3COH$	— 6.05	58
$(C_6F_5)_2PhCOH$	—13.7	59	$(m\text{-}FC_6H_4)_3COH$	—10.72	60
$(C_6F_5)_3COH$	—17.5	58	$(m,\ m\text{-}F_2C_6H_3)_3COH$	—14.2	60
	—17.7	60			
$(4\text{-}NO_2C_6H_4)Ph_2COH$	— 9.15	61	$(o,\ o\text{-}F_2C_6H_3)_3COH$	—11.12	60

The calculated additive value of pK_{R^+} for trispentafluorophenylmethanol, allowing for the values in Table 11, is −18.1, which agrees quite well with the experimental value. A possible explanation of the additivity of the effects of fluorine atoms in this equilibrium process, in contrast to the kinetics of the pyrolysis of aryl acetates and the kinetics of protiodetritiation, is that the requirement of the reaction centre for resonance stabilisation cannot be satisfied in polyfluorinated triarylmethyl cations of propeller structure¶. Nevertheless, in the transition state of the protiodetritiation of pentafluorobiphenyl, for example, the pentafluorophenyl group may approach coplanarity with the non-fluorinated benzene ring, which will increase the electron density at the *ortho*- and *para*-positions[57].

Table 12. Values of pK_{R^+} for trisperfluoroarylmethanols and triarylmethanols.

$(p\text{-}XC_6F_4)_3COH$ X	pK_{R+}^{60}	ΔpK_{R+} $[pK_{R+}(X) - pK_{R+}(H)]$	$(p\text{-}XC_6H_4)_3COH$ X	pK_{R+}^{61}	ΔpK_{R+} $[pK_{R+}(X) - pK_{R+}(H)]$
MeO	—11.3	5.8	MeO	+0.82	7.45
Me	—14.3	2.8	Me	—3.56	3.07
H	—17.1	0.0	H	—6.63	0.0
F	—17.7	—0.6	F	—6.05	0.58
CF_3	—25.8	—8.7	—	—	—

These considerations are supported by a comparison of the effects of *para*-fluorine atoms on the thermodynamic stability of trismono(and per)fluoroarylmethyl cations (Table 12). Whereas the introduction of *para*-fluorine atoms into the triphenylmethyl cation increases the stability of the carbonium ion $(p\text{-}FC_6H_4)_3C^+$ ($\Delta pK_{R^+} = 0.58$), the corresponding replacement of hydrogen by fluorine in the cation $(p\text{-}HC_6F_4)_3C^+$ leads to a diminution of stability in the cation $(C_6F_5)_3C^+$ (−0.6). Since values of ΔpK_{R^+} for all the substituents studied are lower with the polyfluorinated carbinols than with their non-fluorinated analogues, while the contribution of the three 2, 3, 5, 6-tetrafluorophenyl groups to destabilisation of the cations remains about the same ($\Delta pK_{R^+} = 10.5—12.1$), good correlation is not observed between the pK_{R^+} for the polyfluorinated carbinols $(p\text{-}XC_6F_4)_3COH$ and the σ^+-constants of the substituents[60]. Filler et al. also suggested[60] the correlation

$$pK_a = 0.534\,pK_{R+} + 25.35$$

linking the pK_{R^+} of polyfluorotriarylmethanols and the pK_a of the corresponding triarylmethanes.

IV. CARBOXYL GROUP

The dissociation constants of fluorinated benzoic acids show (Table 13) that the effect of a fluorine atom on acidity depends on its position. Thus the acidity diminishes on passing from *ortho*- to *para*-derivatives. The electron-accepting influence of chlorine atoms is so much stronger than that of fluorine atoms that pentachlorobenzoic acid approaches 2, 4, 6-trinitrobenzoic acid in strength, whereas pentafluorobenzoic acid is only about as strong as 2, 5-dinitrobenzoic acid. Additive calculation of pK_a for several polyfluorinated benzoic acids gives good agreement with experimental values. It must be noted that additivity of the effects of substituents in the benzene ring is not peculiar to fluorine atoms, but is exhibited by other substituents—both acceptor (chloro, bromo, nitro) and donor (methyl, hydroxy)[65].

¶ The calculated[45] angle of deflection of the benzene rings in the triphenylmethyl cation is 44°. The corresponding angle in the trispentafluorophenylmethyl cation may be assumed to be at least as large.

In connection with the additivity of the effects of fluorine atoms on the acidity of benzoic acids, Table 14 shows that the influence of a *para*-substituent R on acidity is about the same in the tetrafluorobenzene as in the benzene ring ($\Delta pK'_a \simeq \Delta pK''_a$), the contribution of the four fluorine atoms being almost identical for all the *para*-derivatives studied ($\Delta pK'''_a = 2.25-2.39$). The form of the correlation dependence of pK_a on the σ_p-constants of the substituent is therefore the same for *para*-substituted benzoic acids as for their fluorinated analogues[63].

Table 13. Acidities of substituted benzoic acids ArCOOH.

Ar	pK_a expt.	Ref.	pK_a calc.	Ar	pK_a expt.	Ref.	pK_a calc.
Ph	4.20[a]	65	—	2, 3, 5, 6-F_4C_6H	1.50[a]	9	1.68
	5.78[b]	60	—		1.87[a]	63	
o-FC_6H_4	3.27[a]	62	—		1.84[c]	63	
m-FC_6H_4	3.87[a]	62	—	C_6F_5	1.48[a]	9	1.62
p-FC_6H_4	4.14[a]	62	—		1.75[a]	63	
	5.50[b]	60	—		1.67[c]	63	
2,6-$F_2C_6H_3$	2.31[a]	9	2.34		3.38[a,d]	64	
	3.92[b]	60	—	o-$NO_2C_6H_4$	2.17[a]	62	—
3,5-$F_2C_6H_3$	4.80[b]	60	—	2,4-$(NO_2)_2C_6H_3$	1.425[a]	65	—
2,3,4,5-F_4C_6H	2.71[a]	9	2.55	2,5-$(NO_2)_2C_6H_3$	1.62[a]	65	—
				2,4, 6-$(NO_2)_3C_6H_2$	0.65[a]	65	—
				2,6-$Cl_2C_6H_3$	1.594[a]	65	—
				C_6Cl_5	—		0.51[e]

[a] Determined in water at 25°C.

[b] Determined in 50% aqueous ethanol.

[c] Determined from shifts of infrared absorption band ν_{OH} (in carbon tetrachloride).

[d] Too high.[9]

[e] Calculated from data in Ref. 65.

Table 14. Acidities of *para*-substituted benzoic and 2,3,5,6-tetrafluorobenzoic acids.

p-RC_6H_4COOH R	pK'_a	Ref.	$\Delta pK'_a = pK'_{a(H)} - pK'_{a(R)}$	p-RC_6F_4COOH R	pK''_a [63,a]	$\Delta pK''_a = pK''_{a(H)} - pK''_{a(R)}$	$\Delta pK'''_a = pK'_a - pK''_a$
OH	4.53[a]	65	−0.33	OH	2.27	−0.4	2.26
Me	4.37[a]	65	−0.17	Me	2.00	−0.13	2.37
H	4.20[a]	65	0.0	H	1.87	0.0	2.33
	5.67[b]	8	0.0				
F	4.14[a]	62	0.06	F	1.75	0.12	2.39
Cl	3.98[a]	62	0.22	Cl	1.69	0.18	2.29
Br	3.97[a]	62	0.23	Br	1.66	0.21	2.31
CF_3	4.95[b]	8	0.72	CF_3	2.7[b60]	—	2.25
					1.44	0.33	—

[a] In water at 25°C.

[b] In 50% aqueous ethanol.

The influence of the pentafluorophenyl group on the acidity of the carboxy-group, accomplished through a system of double bonds, can be followed in *p*- and *m*-pentafluorophenylbenzoic acids (Table 15). The effects of a *para*-substituent R are about the same in benzoic and tetrafluorobenzoic acids ($\Delta pK'_a \simeq \Delta pK''_a$), except when R = C_6F_5. Whereas the effect of a *p*-pentafluorophenyl group on acidity is quite large on the fluorinated acid ($\Delta pK_a = 0.42$), the effect is very small on benzoic acid (+0.06). Such anomalous behaviour of *p*- and *m*-pentafluorophenylbenzoic acids may be attributed to the specific influence of the medium (75% methanol + 25% water), in which unexpected results have been obtained for other polyfluorinated substituents, e.g. perfluoroisopropyl[66].

Table 15. Acidities of *para*- and *meta*-substituted benzoic and tetrafluorobenzoic acids.

RC_6H_4COOH R	pK'_a	Ref	$\Delta pK'_a = pK'_{a(H)} - pK'_{a(R)}$	RC_6F_4COOH R	pK''_a	Ref.	$\Delta pK''_a = pK''_{a(H)} - pK''_{a(R)}$
H	6.05[a]	66	0.0	H	1.84[c]	63	0.0
	5.65[b]	67	0.0		—		—
m-Ph	5.57[b]	67	+0.08	—	—		—
p-Ph	5.66[b]	67	−0.01	p-Ph	1.88[d]		−0.04
m-C_6F_5	6.11[a]	66	−0.06	—	—		—
p-C_6F_5	5.99[a]	66	+0.06	p-C_6F_5	1.42[c]	63	+0.42
p-CF_3	5.30[a]	66	+0.75	p-CF_3	1.17[c]	63	+0.67
m-CF_3	5.31[a]	66	+0.74		—		—

[a] Determined in 75% methanol + 25% water at 39.8°C.

[b] Determined in 50% 2-butoxyethanol at 25°C.

[c] Determined from shifts of infrared absorption band ν_{OH} (in carbon tetrachloride).

[d] Calculated from data of Ref. 63 with $\delta_p = -0.01$ for the phenyl group[67].

Table 16. Acidities of some fluorinated arylacetic and α-amino-β-arylpropionic acids.

RCH_2COOH R	pK_a expt.	Ref.	$RCH_2CH(NH_3^+)COO^-$ R	pK_a expt.	Ref.
Ph	4.31[a]	62	Ph	2.16[c]	69
o-FC_6H_4	4.07[a]	9	o-FC_6H_4	2.12[c]	69
m-FC_6H_4	4.13[a]	68	m-FC_6H_4	2.10[c]	69
p-FC_6H_4	4.22[a]	68	p-FC_6H_4	2.13[c]	69
2,3,5,6-F_4C_6H	3.47[a]	9	—	—	
C_6F_5	3.48[a]	9	C_6F_5	1.88[a]	9
	3.43[b]			1.93[b]	
COOEt	3.35[a]	62			

[a] In water at 25°C.

[b] Calculated by an additive scheme.

[c] In 0.1 *N* NaCl at 24°C.

Sheppard[66] suggested the alternative explanation that the decrease in acidity of *p*- and *m*-pentafluorophenylbenzoic acids is due to $p-\pi$ donation of unshared electrons of the *ortho*-fluorine atoms to the π-system of the adjacent non-fluorinated ring. However, the existence of such an effect of fluorine atoms in the biphenyl system is doubtful, for *o*-fluorotritiobenzene and 2-fluoro-4′-tritiobiphenyl undergo protiodetritiation at almost the same rate, although the latter reaction would have been the more rapid in the presence of $p-\pi$ donation[57].

The acidity of carboxylic acids falls, of course, when the substituent and the carboxyl are separated by one or especially several methylene groups. The substituent, in particular a pentafluorophenyl group, will then have only an inductive effect on the reaction centre. Table 16

shows that the effects of fluorine atoms at different positions in the benzene ring, exerted through methylene bridges on the acidity of carboxylic acids, fit well into an additive scheme of calculation of pK_a for the pentafluorophenyl group, whose total electron-accepting power is comparable with that of the ethoxycarbonyl group.

V. AMINO-GROUP

The pK_a values of the fluorinated conjugate acids of anilines show (Table 17) that the acidity of the conjugate acid of pentafluoroaniline can be calculated additively from the pK_a values for the conjugate acids of monofluoroanilines. The predominant contribution to the acidity is made by the *ortho*-fluorine atoms, while the *meta*-fluorine atoms have rather less effect. In polyfluoroanilines greater acceptor effects are exerted by a *p*-bromine atom and by 2,4-chlorine atoms than by fluorine atoms at these positions. The total electron-accepting effect of the five fluorine atoms on the acidity of the conjugate acids of anilines can be compared with that of an *o*-nitro-group; trifluoromethyl has a considerably smaller effect.

Table 17. Acidities of substituted conjugate acids of anilines $ArNH_3^+$ (in aqueous sulphuric acid at 25°C).

Ar	pK_a expt.	Ref.	Ar	pK_a expt.	Ref.
Ph	4.58	62	4-Br—2,3,5,6-F_4C_6	−0.93	70
o-FC_6H_4	3.20	62	2,4-Cl_2—3,5,6-F_3C_6	−1.28	70
m-FC_6H_4	3.59	62	*p*-$NO_2C_6H_4$	1.02	62
p-FC_6H_4	4.65	62	*o*-$NO_2C_6H_4$	−0.29	62
C_6F_5 *	−0.28	9	2,5-$(CF_3)_2C_6H_3$	+0.38	70
	−0.36	70	*p*-$CF_3C_6H_4$	2.6	62
				2.93	8
			m-$CF_3C_6H_4$	3.5	62

* Calculated additive value of $pK_a = -0.18$.

Table 18. Acidities of conjugate acids of *NN*-dimethylanilines $RC_6H_4NH(CH_3)_2^+$ (in 45% aqueous dioxan at 25°C).

R	pK_a	Ref.	R	pK_a	Ref.
H	4.14	66	*p*-CF_3	1.56	71
m-C_6F_5	2.64	66	*m*-$CF(CF_3)_2$	1.79	71
p-C_6F_5	2.33	66	*p*-$CF(CF_3)_2$	1.33	71
m-CF_3	2.06	71			

The conductance through a system of conjugated bonds of the effect of the pentafluorophenyl group on the ionisation of the conjugate acids of amines has been estimated only for *m*- and *p*-pentafluorophenyl-*NN*-dimethylanilines, since it is difficult to estimate the basicity of the anilines because of their sparing solubility in aqueous systems[66]. Table 18 shows that the electron-accepting effect of both *m*- and *p*-pentafluorophenyl groups on the ionisation of the conjugate acids of *NN*-dimethylaniline is considerably smaller than that for perfluorinated alkyl groups, which parallels the effects observed in the ionisation of substituted benzoic acids (Table 15). The greater electron-accepting effect of the *para*- than of the *meta*-group can be attributed to non-coplanarity of the benzene rings and a consequent diminution in the effect of conjugation of the pentafluorophenyl group[57].

Table 19. Acidities of conjugate acids of some amines (in water at 25°C).

$RCH_2NH_3^+$ R	pK_a	Ref.	$RCH_2CH(NH_3^+)COO^-$ R	pK_a	Ref.
Ph	9.3	62	Ph	9.12	69
C_6F_5	7.7	72		9.09	8
COOEt	7.7	72	*o*-FC_6H_4	9.01	69
COOMe	7.66	62	*m*-FC_6H_4	8.98	69
CHF_2	7.5	72	*p*-FC_6H_4	9.05	69
CF_3	5.7	72	C_6F_5	8.47	9
	5.87	73		8.55 *	

* Calculated by an additive scheme[9].

The inductive effect of the pentafluorophenyl group on the ionisation of conjugate acids of amines can conveniently be traced in systems in which the group is separated from the reaction centre by a methylene bridge (Table 19). Such systems are characterised by additivity of the effects of fluorine atoms at different positions in the ring, as noted above for carboxylic acids of the type $Ar[CH_2]_nCOOH$ (Table 16). The pentafluorophenyl group is comparable in its inductive effect with such groups as alkoxycarbonyl and difluoromethyl, but weaker than trifluoromethyl.

VI. HYDROXY-GROUP

Fluorinated phenols and aromatic alcohols may be expected to be more acid than their non-fluorinated analogues, in view of the electron-accepting inductive effect of the pentafluorophenyl group. Table 20 gives data on the effect of aromatically bound fluorine atoms on the acidity of phenols, with for comparison the effects of a nitro-group and chlorine atoms. Additivity of the effects of fluorine atoms at different positions in the benzene ring is evident for phenols, as for benzoic acids and anilines, the main contribution to the acidity of pentafluorophenol being made by the *ortho*-fluorine atoms, and a rather smaller contribution by the *meta*-atoms, while a *para*-fluorine atom has almost no effect on the acidity of phenol.

Table 20. Acidities of substituted phenols ArOH (in water at 25°C).

Ar	pK_a	Ref.	Ar	pK_a	Ref.
Ph	9.98	62	C_6Cl_5	5.26	75
o-FC_6H_4	8.81	62		4.82	76
	8.71	74			
m-FC_6H_4	9.28	62	*p*-$NO_2C_6H_4$	7.15	62,76
	9.21	74	2,4-$(NO_2)_2C_6H_3$	4.07	77
p-FC_6H_4	9.95	52			
	9.91	63			
C_6F_5	5.53	75			
	5.76 *	9			
	6.21 *				

* Calculated by additivity from data in Refs. 62 and 74.

The electron-accepting power of the pentachlorophenyl group is considerably stronger than that of the pentafluorophenyl group, because fluorine atoms at *ortho*- and *para*-positions are more efficient than are chlorine atoms

in supplying electron density by a mechanism of conjugation to the reaction centre. The effect of the pentafluorophenyl group on the acidity of the hydroxyl exceeds that of *p*-nitrophenyl and approaches that of 2,4-dinitrophenyl.

Table 21. Acidities of some fluorinated alcohols.

RCH_2OH R	pK_a	Ref.	$RR'R''COH$ R	R'	R''	pK_a	Ref.
Ph	15.4*	78	Ph	CF_3	CF_3	8.80	81
	15.44*	78	C_6F_5	CF_3	CF_3	7.90	81
	14.86*	49	C_6F_5	C_6F_5	CF_3	9.20	81
m-FC_6H_4	14.47*	49	C_6F_5	C_6F_5	C_6F_5	~11	81
p-FC_6H_4	14.95*	49	CF_3	CF_3	CF_3	5.4	80
C_6F_5	13.30*	49	C_6F_5	CF_3	$C(CF_3)(C_6F_5)OH$	8.85	81
CF_3	12.37	79	CF_3	CF_3	$C(CF_3)_2OH$	5.95	82
	12.8	80					

* Calculated value.

As a consequence of the electron-accepting inductive effect of fluorine atoms, fluorinated aromatic alcohols are more acidic than their non-fluorinated analogues (Table 21). The trifluoromethyl group has a stronger acidifying action on alcohols than has the pentafluorophenyl group. It is noteworthy that the latter group makes different contributions to the acidities of primary and of tertiary alcohols: whereas the difference between the pK_a values of benzyl and pentafluorobenzyl alcohols is 1.5, the corresponding difference between the tertiary alcohols $C_6H_5C(CF_3)_2OH$ and $C_6F_5C(CF_3)_2OH$ is only 0.9. If one trifluoromethyl group in perfluoro-t-butyl alcohol is replaced by pentafluorophenyl, the acidity (pK_a) of the alcohol falls by 2.5. When two trifluoromethyl groups are replaced, the acidity of the alcohol falls by only 1.9 (per pentafluorophenyl group). Further substitution produces almost no change in the contribution of a pentafluorophenyl group to the acidity of the alcohols, since the difference in pK_a between trispentafluorophenylmethanol and perfluoro-t-butyl alcohol is ~5.6, which gives ~1.9 per pentafluorophenyl group.

VII. HALOGENS

Whereas the introduction of fluorine atoms into an aromatic ring lowers its reactivity towards electrophilic reagents (Section II), the reactivity of the polyfluorinated aromatic ring towards nucleophilic reagents is sharply increased[4,7]. Results for the reaction of mono-, di-, and poly-fluorobenzenes with methanolic sodium methoxide show (Table 22) that the rate of nucleophilic substitution increases significantly with the accumulation of fluorine atoms. The position of these atoms relative to the reaction centre is extremely important: thus the rate of nucleophilic substitution is least in 1,2,4,5-tetrafluorobenzene among its isomers, owing to $I-\pi$ repulsion of the *para*-fluorine atom in the transition state (an intermediate structure of the Wheland type is the least stable)[88,89]. As with aromatic electrophilic substitution (Section II) the effects of the fluorine atoms in polyfluorobenzenes on nucleophilic substitution are not additive: the calculated rates are higher than the experimental values. Thus the accumulation of fluorine atoms in the benzene molecule leads to a relative slowing down of nucleophilic aromatic substitutions on the one hand, and to a relative increase in the rate of electrophilic aromatic substitutions on the other. Quantum-mechanical calculation of the electron density (allowing for π- and σ-charges) on the carbon atoms bearing fluorine in polyfluorobenzenes predicts the reactivity sequence

$$C_6H_2F_4 > 1,2,3,4\text{-}C_6H_2F_4 > 1,2,4,5\text{-}C_6H_2F_4;\ C_6HF_5 > C_6F_6$$

towards nucleophilic reagents[23]. This corresponds satisfactorily to experimental results allowing for the statistical factor for hexafluorobenzene.

Table 22. Rates of nucleophilic substitution of fluorine in certain fluorinated benzenes on reaction with methanolic sodium methoxide at 50°C.

Compound	Rate constant k_2, $M^{-1}\,s^{-1}$		Ref.
	expt.	calc. additively[a]	
C_6H_5F	$2.16\cdot10^{-13}$	—	83
m-$C_6H_4F_2$	$7.25\cdot10^{-10}$[b]	$1.0\cdot10^{-9}$	—
p-$C_6H_4F_2$	$7.95\cdot10^{-13}$[b]	—	—
1,2,4,5-$C_6H_2F_4$	$< 10^{-8}$	$1.29\cdot10^{-7}$	13
1,2,3,4-$C_6H_2F_4$	$1.8\cdot10^{-6}$	—	13
1,2,3,5-$C_6H_2F_4$	$4.9\cdot10^{-6}$	—	13
C_6HF_5	$0.866\cdot10^{-4}$		85
	$1.0\cdot10^{-4}$	$5.76\cdot10^{-4}$	86
	$0.795\cdot10^{-4}$		87
C_6F_6	$3.01\cdot10^{-4}$	$2.12\cdot10^{-3}$	85
	$3.16\cdot10^{-4}$		87

[a] Contributions of fluorine atoms to reaction velocity calculated from rate constants for mono-, di-, and tetrafluorobenzenes: $F_o = 35$; $F_m = 467$; and $F_p = 3.68$.

[b] Rates calculated by means of suggested[84] Hammett correlation equations.

Table 23. Comparative kinetic data for nucleophilic substitutions of certain halogenated benzenes with sodium methoxide.

Compound	Solvent	Relative rate at		Activation energy, kcal mole^{-1}	lg *A*	Ref.
		50°C	60°C			
C_6HF_5	MeOH	—	1	22.6	11.2	87
		—	1	22.9	11.4	86
		1	—	20.2	9.6	85
	dioxan–MeOH (5:1 by vol.)	1	—	19.0	10.5	85
C_6F_6*	MeOH	—	0.65	21.4	11.0	87
		—	0.90	22.4	11.0	86
		0.58	—	20.4	10.2	85
	dioxan–MeOH (5:1 by vol.)	0.87	—	19.7	11.6	85
C_6Cl_5F	MeOH	—	26	18.9	10.2	87
		39	—	18.9	10.3	85,89
C_6Cl_6*	MeOH	—	$3.5\cdot10^{-3}$	22.0	10.1	87
p-$FC_6H_4NO_2$	MeOH	—	28	20.1	11.0	90
o-$FC_6H_4NO_2$	MeOH	—	19	19.9	10.7	91

* Relative rate allowing for statistical factor.

Table 23 gives the relative rates and kinetic parameters of the reactions of halogenated benzenes with sodium methoxide. The relative lability of a fluorine atom in hexafluorobenzene is closely similar to that of the *para*-fluorine atom in pentafluorobenzene, owing to the approximately equal difference in stabilities of both ground and

transition states for these compounds[89]. The lower mobility of a fluorine atom in hexafluorobenzene than in pentachlorofluorobenzene shows that the five fluorine atoms are less strongly accepting than are the five chlorine atoms, since $I-\pi$ repulsion is greater for a fluorine atom than for a chlorine atom[89]. Effective participation of *p*-electrons of lone pairs on fluorine atoms in destabilising the carbanion type of transition state obviously reverses the sequence of the halogens observed in the stability of polyhalogenated aryl anions (Section II). Table 23 shows that the total electron-accepting effect of five fluorine atoms and five chlorine atoms is close to that of a nitro-group *ortho* or *para* to a halogen.

Table 24. Rates of nucleophilic substitution of *para*-fluorine atom in compounds *p*-RC_6H_4F (k_2') and C_6F_5R (k_2'') with methanolic sodium methoxide at 50°C.

R	Reaction rate constants k_2' and k_2'' ($M^{-1}\,s^{-1}$) and their ratios					
	k_2'*	$\frac{k_2'(R)}{k_2'(H)}$	k_2''	Ref.	$\frac{k_2''(R)}{k_2''(H)}$	$\frac{k_2''}{k_2'}\cdot 10^5$
NO_2	$2.4\cdot10^{-3}$	$1.11\cdot10^9$	$3.09\cdot10^2$	86	$3.09\cdot10^6$	1.28
CN	$3.02\cdot10^{-5}$	$1.4\cdot10^7$	$3.95\cdot10^1$	85	$3.95\cdot10^5$	13.1
CF_3	$4.36\cdot10^{-7}$	$2.02\cdot10^5$	3.70	85	$3.70\cdot10^4$	84.7
Cl	$1.23\cdot10^{-10}$	$5.7\cdot10^1$	$1.74\cdot10^{-3}$	86	$1.74\cdot10^1$	141
F	$7.95\cdot10^{-12}$	3.69	$3.16\cdot10^{-4}$	87	3.16	397
H	$2.16\cdot10^{-12}$	1	$1.0\cdot10^{-4}$	86	1	463

* Rates calculated by proposed[84] Hammett correlation equation.

Since additivity is lacking in the effect of fluorine atoms on the rate of nucleophilic substitution, it is of interest to examine comparative data on the effect of a substituent on the rate of substitution of a *para*-fluorine atom in fluorinated and in non-fluorinated benzene derivatives. Table 24 shows that the transmissibility of the effect of the substituent R from the *para*-position to the reaction centre is different for compounds of types *p*-RC_6H_4F and C_6F_5R, since the ratios $k_2'(R)/k_2'(H)$ and $k_2''(R)/k_2''(H)$ are unequal. On the other hand, the contribution of the four fluorine atoms at positions 2, 3, 5, and 6 vary for different substituents R, which is responsible for differences in the ratio k_2''/k_2'. It follows from this analysis of the rates of nucleophilic substitution of the *para*-fluorine atom in compounds *p*-RC_6H_4F and C_6F_5R that the electron-accepting effects of substituents such as nitro, cyano, and trifluoromethyl are weaker in polyfluorinated compounds than in their non-fluorinated analogues, whereas the effects of weakly accepting substituents (chloro and especially fluoro) are quite close with the two types of compounds. Therefore no correlation is observed between the rates ($\lg k$) of the reactions of sodium methoxide with substituted pentafluorobenzenes and the σ_p-constants of the substituents[86]. A satisfactory correlation is obtained if σ_p^--constants are used for strongly accepting substituents, and σ_p-constants for weakly accepting substituents[84,92,93].

Table 25 shows that the relative rates of nucleophilic substitution of the *para*-fluorine in pentafluorobenzene derivatives C_6F_5R are considerably dependent on the reagent and the solvent[92-98]. The rates with charged nucleophiles (methoxide and phenoxide ions) exceed the rates with uncharged nucleophiles (piperidine). The influence of the solvent helps to explain the differing reactivities of polyfluorinated benzenes. Table 26 shows that methanol has a slight effect on the rate of reaction of the substituted pentafluorobenzenes with piperidine, especially when R = C_6F_5.[93] The probable reason is solvation by methanol of the substrates in initial and transition states, that of the fluorine atoms tending to lower the accepting power of the pentafluorophenyl group (Table 29). Weakening of the acceptor character of this group in 75% methanol has been noted earlier in connection with the acidity of benzoic acids (Table 15).

Table 25. Relative rates of nucleophilic substitution of *para*-fluorine atom in substituted pentafluorobenzenes C_6F_5R as function of reagent and solvent.

R	Relative rates (C_6HF_5 = 1)						
	MeONa — MeOH, 50°	Ref.	MeONa–dioxan–MeOH, 50°C (Ref.85)	piperidine–MeOH, 50°C (Ref.93)	piperidine–dioxan, 50°C (Ref.93)	piperidine–*n*-hexane, 50°C (Ref.93)	C_6F_5ONa–$CH_3CON(CH_3)_2$, 106°C (Ref.95)
H	1		1	1	1	1	1
Me	0.438	86	0.0737	—	—	—	—
F[a]	0.58	85	0.87	0.326	0.235	0.373	0.91
	0.66	87					
Cl	17.4	86	—	5.02	3.5	8.5	32
Br	19.9	85	16.1	—	—	—	39
C_6F_5	—		—	$4.18\cdot10^2$	$5.49\cdot10^2$	$3.63\cdot10^3$	$7.3\cdot10^2$
COOMe	—		—	$8.85\cdot10^3$	—	$6.16\cdot10^3$	$2.9\cdot10^3$[b]
CF_3	$4.28\cdot10^4$	85	—	$1.375\cdot10^4$	$4.46\cdot10^3$	$1.63\cdot10^4$	$2.4\cdot10^4$
	$5.25\cdot10^3$	86					
COOMe	—		—	$3.25\cdot10^4$	$8.36\cdot10^3$	$2.77\cdot10^4$	—
NO_2	$3.09\cdot10^6$	86	—	—	—	—	—

[a] Allowing for the statistical factor of 6.

[b] For the ethoxycarbonyl group.

Table 26. Effect of solvent on rate of reaction of substituted pentafluorobenzenes C_6F_5R with sodium methoxide and piperidine[85,86,93,94].

Solvent	Relative rate of substitution of *p*-fluorine at 50°C*.									
	Me	H	COO–	F	Cl	Br	C_6F_5	COOMe	CF_3	COMe
	with sodium methoxide									
Methanol	1	1	1	1	—	1	—	1	—	—
Dioxan–methanol (5:1 by vol.)	6.73	46.1	47.6	69.7	—	37.5	—	—	—	—
	with piperidine									
n-Hexane	—	1	—	1	1	—	1	1	1	1
Methanol	—	5.11 (15)	—	4.46 (12)	3.02 (19)	—	0.59 (2)	7.35 (14)	4.3 (6)	6.0 (22)
Dioxan	—	43.6 (40)	—	27.5 (34)	17.3 (29)	—	6.6 (11)	—	11.9 (22)	13.1 (24)

* Parentheses enclose relative rates of substitution of the *para*-fluorine at 100°C.[93]

An interesting solvent effect has been detected in the reaction of hexafluorobenzene[93] or methyl pentafluorobenzoate[94] with sodium methoxide in methanol or in a binary methanol–benzene mixture (Table 26). Addition of benzene to methanol diminishes the reaction velocity, probably owing to weakening of electrostatic interaction of the reagent and the fluorine atoms *ortho* to the reaction centre (breakdown of the so called "built-in solvation") and the steric retarding effect of the methanol-solvated fluorine atoms located *ortho* to the reaction centre[93]. The solvation of these atoms increases their bulk and

intensifies their steric interaction with the substituent. Probably for this reason the Hammett correlations for the reactions of substituted pentafluorobenzenes with piperidine are satisfied with poorer indices in methanol than in aprotic solvents (Table 27).[92,93]

The effects of the fluorine atoms in the polarographic reduction of pentafluorohalogenobenzenes are satisfactorily additive[99]. Whereas their contributions to the half-wave reduction potentials of pentafluorophenyl bromide and iodide decrease in the sequence $o > m > p$, in the case of the chloride and hexafluorobenzene the contributions are independent of the positions of the fluorine atoms in the benzene ring. These results suggest that the mechanism of the electrochemical detachment of fluorine and chlorine is different from that for bromine and iodine in pentafluorohalogenobenzene derivatives[100].

Several quantitative data have been published on the reactions of polyfluorinated aromatic compounds with radical agents. Thus the ratio of the rate constants for the phenylation of hexafluorobenzene and benzene by phenyl radicals generated by the decomposition of benzoyl peroxide is 0.44. The rate-determining stage of the process is probably addition of the phenyl radical to the aromatic substrate with formation of a radical σ-complex[101].

Table 27. Correlation between the rate constants of the reactions of substituted pentafluorobenzenes C_6F_5R with nucleophilic reagents and the σ_p^--constants of the substituents.

Reagent	Solvent	Temp., °C	ρ	r	s	$-\lg k_0$	Ref.
Piperidine	n-hexane	50	5.4	0.989	0.33	7.10	92,93
		100	4.8	0.990	0.27	6.15	
Piperidine	dioxan	50	4.9	0.992	0.29	5.66	92,93
		100	4.4	0.994	0.22	4.58	
Piperidine	methanol	50	5.8	0.986	0.41	6.57	92,93
		100	4.8	0.991	0.27	4.98	
Na methoxide	methanol	50	5.3	0.993	0.34	3.89	92,93
		100	4.7	0.994	0.29	1.94	
Na methoxide*	16% methanol + 84% dioxan	50	6.9	0.999	0.08	2.34	84
		100	6.1	0.998	0.18	0.51	
Na pentafluorophenoxide	*NN*-dimethylacetamide	106	5.7	0.986	0.34	—	92,93

* Correlation with σ_m^--constants.

VIII. EFFECTIVENESS OF FLUORINE ATOMS

The effectiveness of fluorine atoms at different positions of the pentafluorophenyl group in influencing the reaction centre can be assessed both from thermodynamic data (ratio of ΔpK_a values for pentafluorophenyl- and *m*-fluorophenyl-benzene derivatives) and from kinetic data (ratio of reaction rate constants for these derivatives) (Table 28).

Table 28. Relative effects of fluorine atoms on reactivity of pentafluorobenzene derivatives.

No.	Reaction	Solvent	Temp., °C	$\frac{\Delta pK_a(C_6F_5\text{—Ph})}{\Delta pK_a(m\text{-}FC_6H_4\text{—Ph})}$	$\frac{k(C_6F_5)}{k(m\text{-}FC_6H_4)}$	Sequence of effects	Additivity F atoms	Ref.
1	$ArT + MeOH \xrightarrow{MeONa} ArH + CH_3OT$	MeOH	40	7.62	—	$o>m>p$	yes	13,14
2	$ArT + NH_2C_6H_{13} \xrightarrow{LiNHC_6H_{13}} ArH + \underset{\displaystyle T}{NHC_6H_{13}}$	$NH_2C_6H_{13}$	25	8.1	—	$o>m>p$	yes	11,14
3	$ArH + R^-Cs^+ \rightleftarrows Ar^-Cs^+ + RH$	$NH_2C_6H_{13}$	34	7.44	—	$o>m>p$	yes	14
4	$ArF + CH_3ONa \rightarrow ArOCH_3 + NaF$	MeOH	50	—	$4.27\cdot10^6$	$m>o>p$	no	[a]
5	$ArCl + 2e \rightarrow ArH$	DMF	25	4.77[b]	—	$p\sim o\sim m$	yes	99
6	$ArBr + 2e \rightarrow ArH$	DMF	25	6.45[b]	—	$o>m>p$	yes	99
7	$ArI + 2e \rightarrow ArH$	DMF	25	6.95[b]	—	$o>m>p$	yes	99
8	$ArC(CF_3)_2OCH_2CH(O)CH_2 + (n\text{-}Bu)_2NH \rightarrow ArC(CF_3)_2OCH_2CH(OH)CH_2NBu_2$	$C_5H_{11}OH$	60	—	1.85	$o>m\sim p$	no	102
9	$ArSnMe_3 \xrightarrow{HClO_4} ArH$	H_2O, MeOH	50	—	1.34	$p>o>m$	no	25
10	$ArSnMe_3 \xrightarrow{H_2SO_4} ArH$	H_2O, AcOH	50	—	$6.84\cdot10^{-4}$	$p>o>m$	no	25
11	$Ar\text{—}CH(Me)\text{—}OCOMe \rightarrow ArCH{=}CH_2 + MeCOOH$	—	352	—	0.364	$p>m\sim o$	no	56
12	$Ar\text{—}C_6H_4T\text{-}p \xrightarrow[CF_3COOH]{HClO_4} Ar\text{—}Ph$	H_2O	70	—	$3.49\cdot10^{-3}$	$p>o>m$	no	57
13	$Ar\text{—}C_6H_4T\text{-}o \xrightarrow[CF_3COOH]{HClO_4} Ar\text{—}Ph$	H_2O	70	—	$2.56\cdot10^{-3}$	$o>m$	no	57
14	$Ar_3COH \overset{+H^+}{\rightleftarrows} Ar_3C^+ + H_2O$	H_2SO_4, H_2O	25	2.81[c]	—	$p\gg o>m$	yes	60
15	$ArCOOH + H_3O \rightleftarrows ArCOO^- + H_3O^+$	H_2O	25	7.65	—	$o>m>p$	yes	9
16	$ArCH_2COOH + H_2O \rightleftarrows ArCH_2COO^- + H_3O^+$	H_2O	25	4.6	—	$o>m>p$	yes	9
17	$ArCH_2\underset{\displaystyle NH_2}{CH}\text{—}COOH \rightleftarrows ArCH_2\underset{\displaystyle \underline{\underline{NH_3^+}}}{CH}\text{—}\underline{COO^-}$	H_2O	25	<u>4.67</u>	—	$m\sim o\sim p$	yes	9
18				<u><u>4.64</u></u>	—	$m\sim o\sim p$	yes	9
19	$\overset{+}{Ar}NH_3 + H_2O \rightleftarrows ArNH_2 + H_3O^+$	H_2O, H_2SO_4	25	4.91	—	$o>m>p$	yes	9
20	$ArCH_2\overset{+}{N}H_3 + H_2O \rightleftarrows ArCH_2NH_2 + H_3O^+$	—	—	3.9	—		—	49
21	$ArOH + H_2O \rightleftarrows ArO^- + H_3O^+$	H_2O	25	6.36	—	$o>m>p$	yes	9
22	$ArCH_2OH + H_2O \rightleftarrows ArCH_2O^- + H_3O^+$	—	—	4.0	—	$m>p$	—	49

[a] Present work. [b] Ratio of differences in half-wave potentials $-E_{\frac{1}{2}}$. [c] Ratio of values of ΔpK_{R^+}.

These ratios show that the effects of *o*-, *m*-, and *p*-fluorine atoms depend on the nature of the reaction centre[9]. The efficiencies of the fluorine atoms in the pentafluorophenyl group are about the same—*o* > *m* > *p*—for reactions 16—18, 20, and 22 (Table 28), since they are governed solely by the inductive effect of the pentafluorophenyl group. The same sequence applies to reactions 1—3, 6, 7, 15, 19, and 21, in which the electron-accepting inductive character of the fluorine atoms also prevails. With all these reactions the effects of the

Table 29. σ-Constants of substituents.

Reaction series	Solvent	Temp. °C	Substituent	σ-Constants of substituent								Ref.
				σ_m	σ_p	σ_m^+	σ_p^+	σ_p^-	σ^*	σ_I	σ_R^0	
1	2	3	4	5	6	7	8	9	10	11	12	13
pK_a	75% CH_3OH —	39.8	C_6F_5	−0.12	−0.03	—	—	—	—	—	—	66
m-, *p*-RC_6H_4COOH	25% H_2O		CF_3	+0.48	+0.48	—	—	—	—	—	—	66
	50% butoxyethanol	25	Ph	+0.06	−0.01	—	—	—	—	—	—	67
pK_a	CCl_4	—	C_6F_5	—	+0.45	—	—	—	—	—	—	— a
m-,*p*-RC_6F_4COOH			Ph	—	−0.01	—	—	—	—	—	—	— a
			CF_3	—	+0.70	—	—	—	—	—	—	— a
pK_a	H_2O	25	C_6F_5	—	—	—	—	—	2.0	—	—	— b
RCOOH			Ph	—	—	—	—	—	0.6	—	—	78
			CF_3	—	—	—	—	—	2.6	—	—	78
pK_a	H_2O	25	C_6F_5	—	—	—	—	—	—	0.31	—	9
RCH_2COOH			Ph	—	—	—	—	—	—	0.10	—	103
			CF_3	—	—	—	—	—	—	0.42	—	103
			$COOEt$	—	—	—	—	—	—	0.34	—	103
pK_a	45% dioxan	25	C_6F_5	+0.34	+0.41	—	—	—	—	—	—	66
m-,*p*-$RC_6H_4\overset{+}{N}H(Me)_2$	+ 55% water		CF_3	+0.48	+0.60	—	—	—	—	—	—	71
pK_a { $RRC(CF_3)OH$	H_2O	25	C_6F_5	—	—	—	—	—	1.3	—	—	81
{ $RC(CF_3)_2OH$			C_6F_5	—	—	—	—	—	0.9	—	—	81
			Ph	—	—	—	—	—	0.26	—	—	— c
			CF_3	—	—	—	—	—	2.6	—	—	80
Rate of detritiation	H_2O	70	C_6F_5	—	—	+0.285	+0.255	—	—	—	—	57
$RC_6H_4T \xrightarrow[CF_3COOH]{HClO_4} RPh$			Ph	—	—	+0.012	−0.2	—	—	—	—	57
Rate of nucleophilic substitution	n-hexane	50	C_6F_5	—	—	—	—	0.66	—	—	—	— d
$RC_6F_5 + NHC_5H_{10} \longrightarrow$			CF_3	—	—	—	—	0.74	—	—	—	92,93
		100	C_6F_5	—	—	—	—	0.66	—	—	—	— d
$\longrightarrow$ *p*-$RC_6F_4NC_5H_{10}$	dioxan	50	C_6F_5	—	—	—	—	0.60	—	—	—	— d
		100		—	—	—	—	0.57	—	—	—	
	MeOH	50	C_6F_5	—	—	—	—	0.48	—	—	—	— d
		100		—	—	—	—	0.47	—	—	—	
Rate of nucleophilic substitution	$CH_3CON(CH_3)_2$	106	C_6F_5	—	—	—	—	0.50	—	—	—	— d
$RC_6F_5 + C_6F_5ONa \longrightarrow$				—	+0.42	—	—	—	—	—	—	95
			CF_3	—	—	—	—	0.74	—	—	—	92,93
$\longrightarrow$ *p*-$RC_6F_4OC_6F_5$				—	+0.58	—	—	—	—	—	—	95
^{19}F n.m.r.	CF_3Cl	—	C_6F_5	+0.26	+0.27	—	—	—	—	0.25	0.02	66
m-,*p*-RC_6H_4F			C_6Cl_5	+0.25	+0.24	—	—	—	—	0.25	−0.01	66
			Ph	+0.04	0	—	—	—	—	0.08	−0.09	104
			CF_3	+0.44	+0.49	—	—	—	—	0.39	0.10	71
^{19}F n.m.r.	CF_3Cl	—	C_6F_5	—	—	—	—	—	—	0.15	0.00	66
RC_6F_5			Ph	—	—	—	—	—	—	−0.03	−0.07	66
			CF_3	—	—	—	—	—	—	0.33	0.01	66
^{19}F n.m.r.												
C_6F_5RXY			C_6F_5	+0.22	—	—	—	—	—	—	—	105
^{35}Cl n.q.r.			C_6F_5	—	—	—	—	—	1.93	—	—	49
				—	—	—	—	—	—	—	−0.12	— e

a Calculated from data of Ref. 63.

b Calculated by means of the equation[78,63]

$$pK_a\ (RCOOH) = -1.795\ \sigma^*(R) + 5.275\ ,$$

$$pK_a\ (C_6F_5COOH) = 1.67\ .$$

c Calculated by means of the equation[80]

$$pK_a = -1.44\ \Sigma\sigma^* + 16.67\ ,$$

with pK_a = 8.80 for $C_6H_5C(CF_3)_2OH$ [81] and σ* = 2.6 for the trifluoromethyl group[80].

d Calculated from data of Refs. 92 and 93.

e Calculated by means of the equation

$$\sigma_R^0 = (-2.44 + 0.0521\ \nu + 0.132\ pK_a)\ ,$$

from data of Ref. 106 with pK_a = 3.48 for $C_6F_5CH_2COOH$ [9] and ν = 35.76 MHz for $C_6F_5CH_2Cl$.[49]

fluorine atoms of the pentafluorophenyl group exhibit satisfactory additivity. Such additivity may thus be expected in nucleophilic reactions such as 1, 2, 3, 6, and 7 and in the dissociation of various acidic groups, e.g. reactions 15—22, involving a transition state or intermediate product without a significant contribution by *p*-electrons of lone pairs on the fluorine atoms, when the predominant stabilising effect will be the electron-accepting inductive effect in the sequence $o > m > p$.

The distribution of negative charge in the intermediate σ-complex in nucleophilic substitutions (reaction 4 in Table 28) depends to a considerable extent on the position of the fluorine atoms in the ring, since the participation of *p*-electrons of the fluorine atoms in this process is very substantial. Here, therefore, the stabilising effects of the fluorine atoms vary in the sequence $m > o > p$, and are non-additive.

Reaction 8 (Table 28) probably involves formation of a hydrogen bond between the reagent and an *ortho*-fluorine atom of the substrate, which accelerates the reaction[102]. In this case, of course, additivity of the effects of the fluorine atoms cannot be expected.

Electrophilic reactions such as 9—14 (Table 28), involving transition states or intermediate compounds with a significant contribution by *p*-electrons of lone pairs on fluorine atoms, exhibit the sequence $p > o > m$, corresponding to the predominant contribution by the positive conjugation effect of *ortho*- and *para*-fluorine atoms in the benzene ring. As with aromatic nucleophilic substitution, the effects of the fluorine atoms in the pentafluorophenyl group are not additive. An exception is reaction 14, for reasons discussed above (Section III).

Directly opposite requirements must obviously be met for resonance stabilisation of the σ-complexes in nucleophilic and in electrophilic aromatic substitution. Hence the former reactions become relatively slower (Section VII), and electrophilic substitutions relatively faster (Section II), than the additive rates to be expected with increasing degree of fluorination of the benzene ring.

IX. ANALYSIS OF σ-CONSTANTS OF PENTAFLUOROPHENYL GROUP

Quantitative data on the electronic effects of the pentafluorophenyl group can be derived as various σ-constants from thermodynamic measurements of pK_a or reaction velocities, as well as from the fluorine-19 n.m.r. chemical shifts of the corresponding pentafluorobiphenyl derivatives. Table 29 gives various σ-constants of the pentafluorophenyl group obtained for various reaction series. These data show that, with respect to its inductive effect (σ_m, σ^*, and σ_I constants), this group is a strong electron-accepting substituent in comparison with phenyl, but is weaker than trifluoromethyl. Its electron-accepting inductive effect is closely similar to those of ethoxycarbonyl and pentachlorophenyl. It is significant that the σ_I^*-constants of the pentafluorophenyl and phenyl groups, obtained from the ionisation constants of tertiary alcohols[81], are only about one-third of the analogous σ^*-constants deduced from the ionisation constants of carboxylic acids, and that the σ^*-constant in a tertiary alcohol containing two pentafluorophenyl groups is larger than that in the corresponding alcohol containing only one such group[81]. This effect (Section VI) may be attributed to $p-\pi$ interaction of trifluoromethyl groups and the benzene ring, which weakens the acceptor properties of phenyl and pentafluorophenyl groups[71]. Introduction of a second pentafluorophenyl group into the tertiary alcohol weakens the $p-\pi$ interaction owing to the increased *I*-effect of the field due to this group. It is significant that chlorine-35 nuclear quadrupole resonance has revealed an increase in the electron-accepting *I*-effect of pentafluorophenyl also in compounds of the type C_6F_5CHClR (R = Cl, CH_3, $COOC_2H_5$, C_6F_5).[49] The change in ^{35}Cl n.q.r. frequency in the compound $C_6F_5CHClCF_3$ might give information on the $p-\pi$ interaction of trifluoromethyl and pentafluorophenyl groups. The value of the σ_I-constant for the latter (and other groups) deduced from the fluorine-19 n.m.r. shifts of the pentafluorophenyl ring are usually 0.1 below the corresponding values obtained by Taft's method[66]. Nevertheless, Taft's method for estimating the σ-constants of a substituent, involving the ^{19}F n.m.r. chemical shifts of monofluorobenzene derivatives[104], will give values close to the σ-constants determined from other reaction series.

The σ_m-constants are smaller than the σ_p-constants for various reaction series, although it would appear that the opposite relation should apply, since the resonance effect of pentafluorophenyl expressed as the σ_R^0-constant is very slight. However, this last constant disregards direct polar conjugation of the substituent with the reaction centre, which is very important for the pentafluorophenyl group, as the preceding discussion has shown, for instance, in electrophilic and nucleophilic aromatic substitutions. It is highly probable that a constant effect of a *p*-pentafluorophenyl group cannot be expected, expressed as a narrow range of values of the σ_p-constant: rather a considerable range may be expected depending on the conditions of stabilisation of the transition state or the intermediate compound in various reactions. Whereas the values σ_m and σ_m^+ lie in the range 0.22—0.34, the corresponding range for σ_p, σ_p^+, and σ_p^- is 0.255—0.66. The relation $\sigma_m^+ > \sigma_p^+$ reflects the effective resonance participation of the pentafluorophenyl group in the distribution of positive charge in electrophilic reactions[57].

The very low values of the σ_m- and σ_p-constants derived from the ionisation of benzoic acids in 75% aqueous methanol, and also the decrease in the σ_p^--constant obtained from the correlation with the rate constants of nucleophilic aromatic substitution in methanol[92,93], are due (Section VII) to solvation by the alcohol of the fluorine atoms in the pentafluorophenyl group, which becomes less strongly accepting.

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Thus the survey of the effect of the pentafluorophenyl ring on the reactivity of various functional groups has revealed an interesting combination of acceptor and donor properties of the fluorine atoms, which interact specifically with various functional groups. The effects of the pentafluorophenyl group connected predominantly with $p-p$ interaction of the fluorine atoms and the reaction centre are especially interesting.

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The Chemistry of Unsubstituted Mono- and Di-amidrazones

A.L.Rusanov

The literature data on the methods of preparation and the reactions of unsubstituted mono- and di-amidrazones are discussed. Particular attention has been devoted to the employment of di-amidrazones in the synthesis of heterochain polymers. The bibliography includes 111 references.

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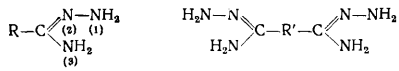
I. INTRODUCTION

Unsubstituted mono- and di-amidrazones, which can be represented by the general formulae



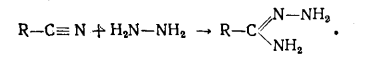
are finding increasing applications in the synthesis of monomeric and high-molecular-weight organic compounds. However, there are virtually no systematic literature data on the synthesis, properties, and applications of these compounds, since the reviews published previously were devoted mainly to the chemistry of substituted amidrazones[1,2] in which at least one of the hydrogen atoms at the nitrogen atoms was substituted by some group and also to the chemistry of compounds (for example, aminoguanidine) containing, together with amidrazone groups, other functional groups[3-5]. Moreover, the advances in the field of high-molecular compounds obtained on the basis of unsubstituted diamidrazones were not considered in any of the earlier reviews.

The present survey deals mainly with problems associated with the methods of synthesis, principal reactions, and applications of unsubstituted mono- and di-amidrazones, the employment of diamidrazones in the chemistry of high-molecular-weight compounds being analysed in greatest detail.

II. METHODS OF SYNTHESIS

1. Interaction of Nitriles with Hydrazine

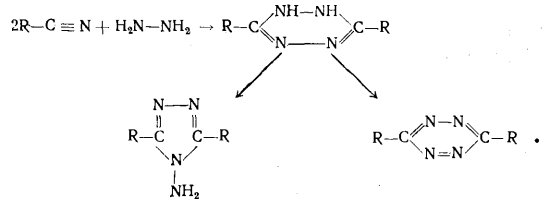
The simplest method for the preparation of amidrazones involves the interaction of nitriles with hydrazine or hydrazine hydrate[6]:



This reaction involves in its first stage nucleophilic attack by hydrazine on the carbon atoms of tne nitrile group and therefore its feasibility is to a large extent determined by the positive charge on the carbon atom of the nitrile group. The reaction of nitriles with hydrazine under mild conditions has been used successfully to synthesise unsubstituted amidrazones with one heterocyclic substituent: 2-thiazolylamidrazone, unsubstituted amidrazone[7], 4-alkyl- and phenyl-2-pyridylamidrazones[8,9], 2-quinolylamidrazone[8], 2-pyrimidinylamidrazone[8], 2-(1,10-phenanthrolinyl)-amidrazone[8], 3-isoquinolylamidrazone[10], and pteridinylamidrazones[11,12]. A number of perfluoroalkylamidrazones have been obtained in high yields by this method[13-15].

Certain unsubstituted diamidrazones have been synthesised by the reaction of hydrazine with dinitriles. Oxalodiamidrazone has been obtained from dicyanogen and hydrazine at room temperature[16-19]. Diamidrazones have been obtained under analogous conditions from the corresponding dinitriles of perfluoro-derivatives of dicarboxylic acids[13] and 2,6-dicyanopyridine[20].

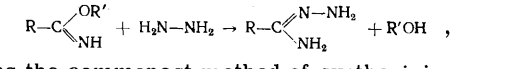
In some cases the reaction requires an increase of temperature, frequently to 100°C and above. Under these conditions, side products may be formed, including derivatives of 4-amino-1,2,4-triazole, dihydrotetrazine, and *s*-tetrazine[21]:



In order to synthesise amidrazones under the mildest possible conditions to avoid the occurrence of side reactions, one of the reaction components is frequently activated. Thus the "activated" state of nitriles is achieved by converting them into imidoesters, amidines, and thioamides.

2. Interaction of Imidoesters, Amidines, and Thioamides with Hydrazine

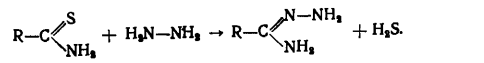
The reaction of imidoesters or their salts with hydrazine, which takes place according to the Scheme



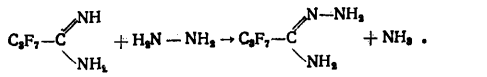
constitutes the commonest method of synthesising unsubstituted amidrazones. In a series of classical studies by

Pinner[22-27] amidrazones were synthesised from carbocyclic and heterocyclic aromatic acid imidoesters. In most cases amidrazones were not obtained in the form of free bases, but as their more stable salts. Subsequent investigations[28-31] demonstrated the applicability of this reaction to derivatives of a number of aromatic and aliphatic-aromatic acids, although the amidrazones were not isolated but were used *in situ* for further reactions. Subsequent studies of this reaction showed that it can be applied successfully to derivatives of aliphatic acids[32,33]. The extension of this method to the synthesis of unsubstituted diamidrazones made it possible to obtain the corresponding derivatives of isophthalic[34], terephthalic[35], pyridine-2,6-dicarboxylic[36], and oxalic[37] acids.

The method of synthesis of unsubstituted amidrazones based on the interaction of acid thioamides with hydrazine, has been widely used:



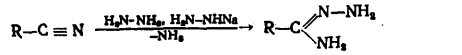
This reaction can be successfully employed to prepare various pyridylamidrazones[38,39] and benzamidrazone[38]. Oxalodiamidrazone has been synthesised in high yield by the reaction of dithioxamide with hydrazine[18,40]. The employment of the corresponding amidines as the "activated nitriles" for the synthesis of unsubstituted amidrazones is much less common. Nevertheless, Brown and coworkers[13] succeeded in synthesising perfluorobutyramidrazone by the reaction of perfluorobutyramidine with anhydrous hydrazine according to the following Scheme:



Together with the substitution of the cyano-group by more reactive functional groups, attempts were made to activate hydrazine. The employment of sodium hydrazide in place of hydrazine proved to be the most effective.

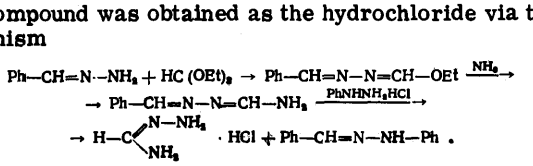
3. Interaction of Nitriles with Sodium Hydrazide

The synthesis of unsubstituted amidrazones from nitriles and sodium hydrazide via the mechanism



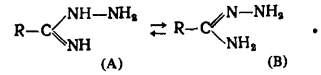
is a reaction common to many nitriles and takes place under mild conditions with high yields. It can be used successfully to synthesise unsubstituted monoamidrazones[41,42]—acetamidrazone, caprinamidrazone, myristamidrazone, heptadecanecarboxamidrazone, stearamidrazone, benzamidrazone, salicylamidrazone, α-naphthamidrazone and β-naphthamidrazone—and also for the synthesis of a number of unsubstituted diamidrazones of aliphatic dicarboxylic acids[43]—dodecanedicarboxylic, sebacic, suberic, pimelic, adipic, and glutaric.

A specific method of synthesis, differing from the processes described previously, has been proposed for the preparation of the first member of the homologous series of unsubstituted monoamidrazones—formamidrazone[44]. This compound was obtained as the hydrochloride via the mechanism



Other synthetic pathways, frequently used to prepare substituted amidrazones and discussed by Neilson et al.,[2] have not found extensive applications in the synthesis of unsubstituted amidrazones.

When the methods of their synthesis were considered, the structure proposed by Pinner[25] was attributed to all amidrazones. Nevertheless, many investigators[2,45] acknowledge the possibility of the tautomerism



There are at present no data confirming unambiguously the validity of any particular view, but study of the structures of certain substituted and unsubstituted amidrazones by infrared spectroscopy and NMR showed that structure (B) is preferable[46,47]. On the other hand, the infrared spectra of perfluoroalkylamidrazones contain three absorption bands in the range 3100–3500 cm^{-1} due to the stretching vibrations of the NH and NH_2 groups[13]; two other intense absorption maxima are associated with the vibrations of the C=N bond (1600–1700 cm^{-1}) and the deformation vibrations of the NH_2 groups (1655 cm^{-1}). Weak absorption maxima in the region of 1590 cm^{-1}, which are characteristic of NH deformation vibrations, have also been noted in the spectra of the products.

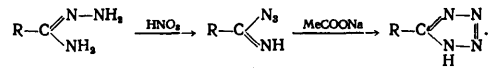
III. REACTIONS

1. Homocondensation of Amidrazones

Typical reactions of amidrazones, which greatly hinder their synthesis, are homocondensation processes, proceeding, according to Pinner's data[23,26] via the formation of dihydrotetrazines subsequently converted into compounds similar to those described above.

2. Interaction of Amidrazones with Nitrous Acid and Its Esters

When amidrazones are treated with nitrous acid or its esters, tetrazoles are formed[48,49]. This reaction proceeds via the formation of an azide imide, which subsequently rearranges to the tetrazole:

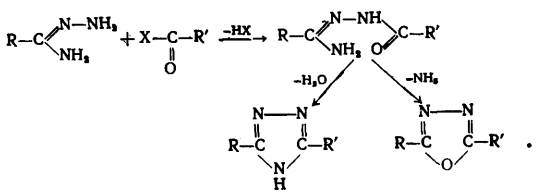


This reaction has been used successfully to synthesise tetrazoles containing alkyl[42], aryl[23,25,26], heterocyclic[24,38], and other substituents[50] in the 5-position and also to synthesise a number of bistetrazoles[43]. In all cases the tetrazoles were synthesised smoothly and the final products were obtained in nearly quantitative yields. An exception is acetamidrazone, which decomposes under the usual diazotisation conditions in an acid medium with formation of acetic acid, ammonium chloride, and hydrazoic acid; 5-methyltetrazole was synthesised successfully by the reaction of acetamidrazone with ethyl nitrite in ethanol[32,33].

3. Interaction of Amidrazones with Carboxylic Acids and Their Derivatives

The reaction of unsubstituted amidrazones with carboxylic acids and their derivatives (esters, anhydrides, and chlorides) leads to the formation of acylamidrazones,

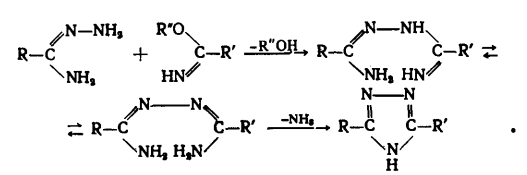
which are then converted into either 1,2,4-triazoles or 1,3,4-oxadiazoles, depending on the conditions in their subsequent treatment:



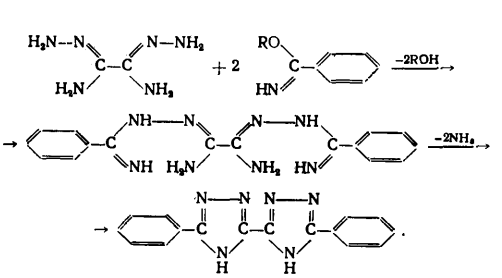
1,2,4-Triazoles are synthesised[51,52] by the above method via the thermal cyclodehydration of acylamidrazones in the absence of solvent or in *m*-cresol, *N*-methyl-2-pyrrolidinone, and hexamethylphosphoramide[53]. This reaction has been used successfully to synthesise 1,2,4-triazoles from aromatic acid amidrazones[26,53-55]. Mono- and arylbis-[3-(*o*-nitrophenyl)-1,2,4-triazoles], which are intermediates in the synthesis of triazoloquinazoline systems, have been obtained under analogous conditions[56-62].

1,2,4-Triazoles have been synthesised under the same conditions from the amidrazones of aliphatic monocarboxylic acids[42] and oxalodiamidrazone[63,64]. However, the cyclisation of acylamidrazones in the presence of strong acids (dichloroacetic[53,63-65], trifluoroacetic, phosphoric, and sulphuric[53]) is accompanied by the liberation of ammonia and the conversion of the acylamidrazone moieties into 1,3,4-oxadiazole moieties.

The possibility of the alternative formation of 1,2,4-triazole and 1,3,4-oxadiazole rings disappears when imidoesters are used as the carboxylic acid derivatives, since the "dihydrazidines" formed in the first stage of the reaction are converted only into the corresponding 3,5-disubstituted 1,2,4-triazoles[22-27]:



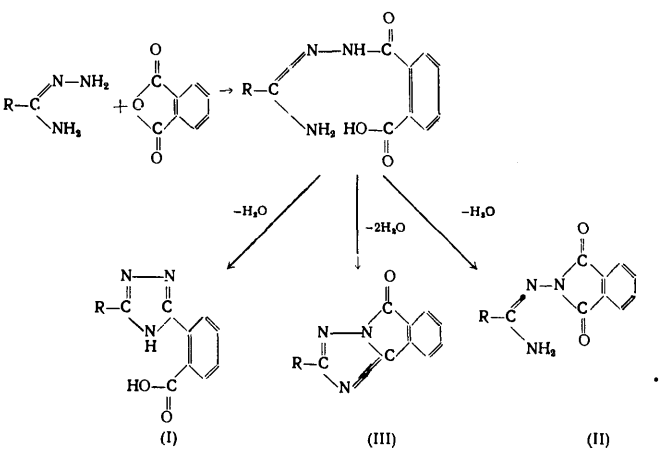
The above reaction, like the homocondensation of amidrazones discussed previously, greatly hinders their synthesis from imidoesters. This synthetic method has been used to prepare bi-5-phenyl-1,2,4-triazol-3-yl by the reaction of oxalodiamidrazone with ethyl benzimidate or its hydrochloride[66,67]:



4. Interaction of Amidrazones with Cyclic Anhydrides of Aromatic Di- and Tetra-carboxylic Acids

In contrast to the reactions of amidrazones with carboxylic acid derivatives, their interaction with aromatic *ortho*- and peri-dicarboxylic acids and their derivatives (particularly anhydrides) was investigated comparatively recently in connection with research in the field of thermostable heterocyclic polymers[34,67-78].

According to the results of the majority of investigators[34,67-73], the first stage of the reaction of unsubstituted amidrazones with phthalic anhydride involves the formation of *o*-carboxybenzamidrazones, the subsequent cyclodehydration of which gives rise to compounds having the structures, according to the data of various workers, of *o*-carboxyphenyl-1,2,4-triazoles (I)[67], *N*-phthalimidoamidines (II)[72], and isoindolo[1,2-]-*s*-triazol-5-ones (III)[34,68-71]:

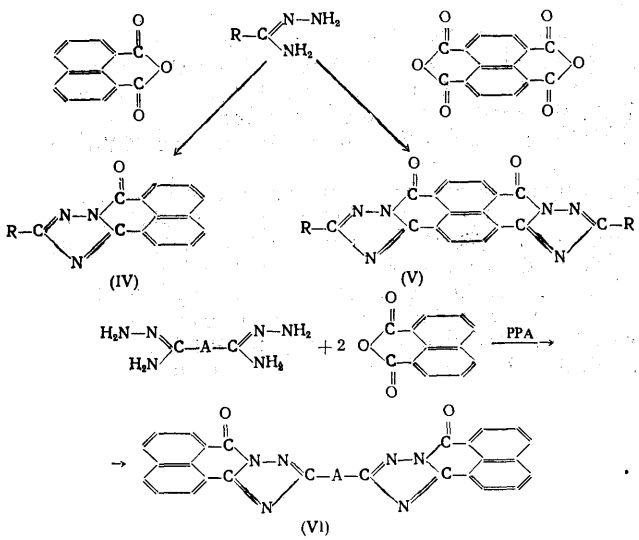


(I) (III) (II)

Subsequent studies on these reactions[73-75] established unambiguously that the final products have isoindolo[1,2]-*s*-triazol-5-one structures of type (III), while *o*-carboxyphenyl-1,2,4-triazoles and *N*-phthalimidoamidines are intermediates. The process takes place via the interaction of the initial amidrazones with phthalic anhydride in polar aprotic solvents and subsequent heating of the resulting *o*-carboxybenzamidrazones. It could not be carried out in polyphosphoric acid (PPA)[79], probably because of the possible interaction of the final heterocycle with the amidrazone (which has not yet reacted) via the O=C–N< linkage[71,75].

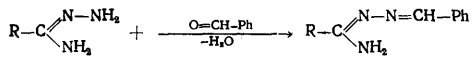
In contrast to the reaction of amidrazones with phthalic anhydride, their reaction with naphthalic anhydride takes place most successfully in PPA[71,74-78]. Condensation of monoamidrazones with the anhydrides of naphthalic and naphthalene-1,4,5,8-tetracarboxylic acids and also of diamidrazones with naphthalic acid anhydride in PPA gave nearly quantitative yields of substituted benzo-*s*-triazoloisoquinolinones (IV), bis(benzo-*s*-triazoloquinazolinones)

(V), and also benzobis-1,2,4-triazolophenanthrolinediones (VI):

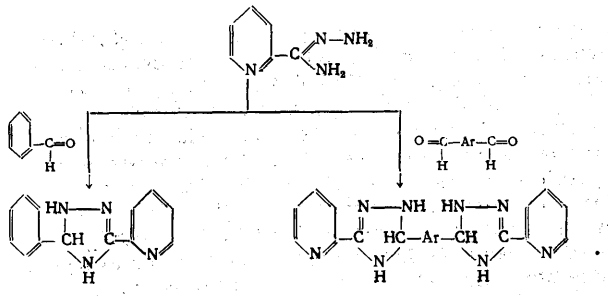


5. Interaction of Amidrazones with Aldehydes and Ketones

This reaction was first investigated by Pinner[23,24], who showed that, when unsubstituted amidrazones interact with benzaldehyde in an acid medium, Schiff bases are formed:



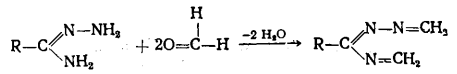
By extending this reaction to fluorinated monoamidrazones[15], it was possible to obtain *N*-benzylideneheptafluorobutyramidrazone whose subsequent treatment with I_2 and then $NaHSO_3$ led to the formation of 2-(heptafluoropropyl)-5-phenyl-1,2,4-triazole. According to Hergenrother and Carlson[80], who investigated the reaction of 2-pyridylamidrazone with aromatic mono- and di-aldehydes, the cyclic products of this reaction are disubstituted mono- and bis-triazolines:



These are not converted into the corresponding 1,2,4-triazoles on treatment with sulphur, chloranil, dimethyl sulphoxide (DMSO), and $FeCl_3$ under different conditions.

These workers carried out the reaction of 2-pyridylamidrazone with a number of mono- and di-ketones: acetophenone, *pp'*-diacetylbiphenyl, *p*-diacetylbenzene and 2,6-diacetylpyridine; the corresponding 3-methyl-substituted mono- and bis-triazolines were obtained[80].

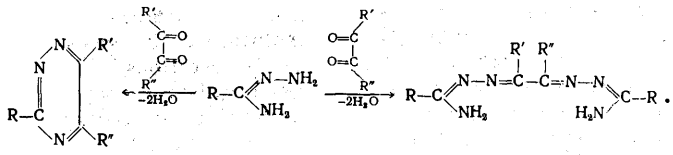
The condensation of amidrazones with an excess of highly reactive carbonyl compounds, for example with formaldehyde, involves both $N_{(1)}$ and $N_{(3)}$ atoms of the amidrazone group[27]:



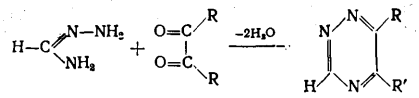
The possibility, in principle, of the interaction of both reaction centres with the carbonyl compounds led to a successful reaction between unsubstituted amidrazones and α-dicarbonyl compounds.

6. Interaction of Unsubstituted Amidrazones with α-Dicarbonyl and Polycarbonyl Compounds

This reaction results in the formation of 1,2,4-triazines[26] or acyclic products[81]:

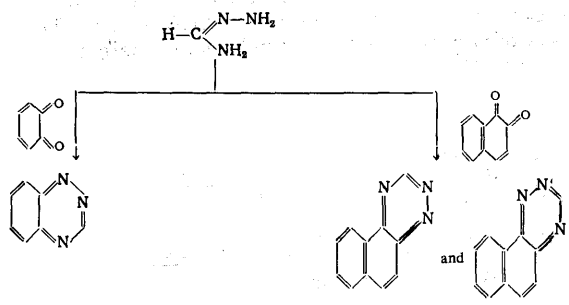


It has been widely used to synthesise a number of 1,2,4-triazines by the interaction of monoamidrazones with α-dicarbonyl and bis-α-dicarbonyl compounds and also of diamidrazones with α-dicarbonyl compounds. Thus the reaction of formamidrazone with various α-dicarbonyl compounds yielded mono- and di-substituted 1,2,4-triazines[82]:



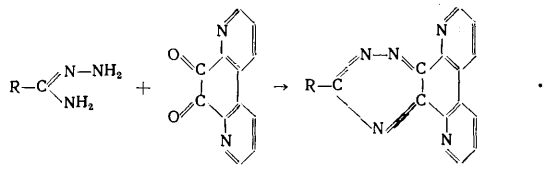
A series of 1,2,4-triazines with aromatic carbocyclic and heterocyclic substituents were synthesised from unsubstituted mono- and di-amidrazones by Case[8,9], Culbertson[83,84], and Hergenrother[85-87].

The syntheses of condensed systems incorporating 1,2,4-triazine rings, based on the interaction of unsubstituted amidrazones with *o*-quinones and related systems, are widely used[8,9,82]. Thus the reaction of formamidrazone with *o*-benzoquinone and 1,2-naphthoquinone gave rise to 1,2,4-benzotriazine and two isomeric naphthotriazines[82]:

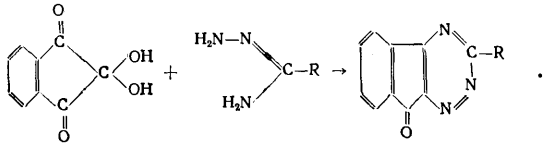


Even more condensed systems—substituted 1,2,4-triazino[5,6-*f*]-4,7-phenanthrolines—were obtained by Case

by the reaction of a number of amidrazones with 4,7-phenanthroline-5,6-dione[8,9]:



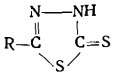
Together with α-dicarbonyl compounds, polycarbonyl compounds can also be made to react with amidrazones; thus triketones or their hydrates condense with amidrazones to form condensed heterocycles, incorporating 1,2,4-triazine moieties[35]:



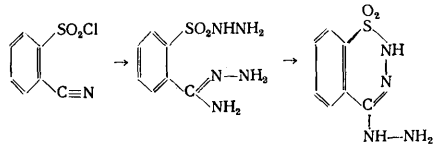
Ketoacids and ketoesters having the general formula RO–CO–CO–CO–CO–OR can also be employed as polycarbonyl compounds in condensation reactions with amidrazones[88,89]. The products of their condensation with amidrazones are 1,2,4-triazinepolycarboxylic acids or their esters.

7. Other Reactions of Amidrazones

Together with the syntheses of heterocyclic compounds from amidrazones which were discussed above, other reactions of these compounds were investigated. Thus, when amidrazones derived from aromatic carbocyclic and heterocyclic acids were treated with CS_2, 1,3,4-thiadiazole-5-thiones were obtained in high yields (73–95%):

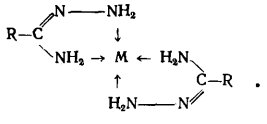


(R = phenyl, naphthyl, 2-, 3-, and 4-pyridyl, 2-quinolyl, etc.). Aromatic acid amidrazones containing a sulphonyl hydrazide group in the *o*-position, undergo intramolecular cyclisation; thus benzamidrazone-*o*-sulphonyl hydrazide—the product of the interaction of *o*-cyanobenzenesulphonyl chloride with hydrazine—readily cyclises to 4-hydrazino-1,2,3-thiadiazine 1,1-dioxide[91]:



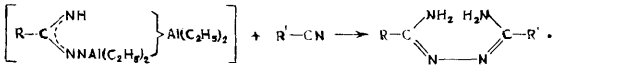
8. The Formation of Metal Complexes

Amidrazones form complexes with transition metal ions which are highly coloured with distinct melting points.



Complex formation proceeds so readily that it can serve as a basis of analytical methods for the determination of microamounts of both amidrazones and transition metal ions. In particular, it has been observed that oxalodiamidrazone can be used to detect microamounts of nickel[18].

The reaction of two equivalents of triethylaluminium with amidrazones in benzene results in the formation of tetrameric bis(diethylalumino)amidrazones[92]:



These compounds are soluble in benzene and on reaction with nitriles are converted into 1,4-disubstituted diazabuta-1,3-diene-1,4-diamines.

IV. UNSUBSTITUTED DIAMIDRAZONES IN THE SYNTHESIS OF HETEROCHAIN POLYMERS

Whereas unsubstituted monoamidrazones have found only limited applications (among derivatives of the pyridine series, several substances with pharmacological and antimicrobial activities were found[31,39,93–95]), unsubstituted diamidrazones of dicarboxylic acids have been assuming increasing importance as monomers for the synthesis of a number of heterochain and in particular heterocyclic polymers.

Examination of the reactions involving the formation of heterocycles from amidrazones which were discussed above shows that, like *o*-phenylenediamine, unsubstituted amidrazones readily react with (1) carboxylic acids and their derivatives forming on subsequent cyclisation 1,3,4-oxadiazole or 1,2,4-triazole rings (2-substituted benzimidazoles are formed from *o*-phenylenediamine), (2) with the cyclic anhydrides of aromatic *ortho*- or peri-dicarboxylic acids and subsequent formation of heterocycles which can be combined under the common name aroylene-*s*-triazoles (under analogous conditions, *o*-phenylenediamine gives rise to aroylenebenzimidazoles), and (3) with α-dicarbonyl compounds to form 1,2,4-triazines (under analogous conditions, *o*-phenylenediamine leads to the quinoxaline ring). Since bis-(*o*-phenylenediamines) have been widely used in recent years in the synthesis of thermostable heterocyclic polymers[96], their "analogues" (diamidrazones) have naturally also attracted attention as potential polyfunctional monomers.

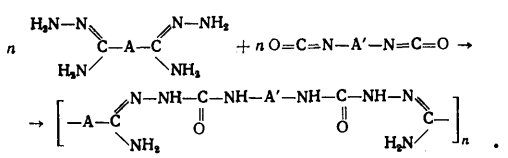
Since the nucleophilic reactivity of the hydrazine moieties of amidrazones is comparable to that of the imido-groups in *o*-phenylenediamine or is actually superior[80], polymers based on diamidrazones can be synthesised under the same conditions as the polymers based on bis-(*o*-phenylenediamines).

However, one should note that diamidrazones have one significant advantage over bis-(*o*-phenylenediamines). Thermostable heterocyclic polymers are usually synthesised[97] by a two-stage process involving polyfunctional monomers; linear prepolymers are synthesised in the first stage under mild conditions, which means that each monomer used in the process must have two functional groups. The linear polymers formed in the first stage have free functional groups distributed in such a way that in the second stage heterocycles can be formed under the influence of heat or chemical agents. The synthesis of linear polymers in the first stage entails the necessity for a selective polycondensation process, usually selective polyamidation. When the polyamidation is carried out by

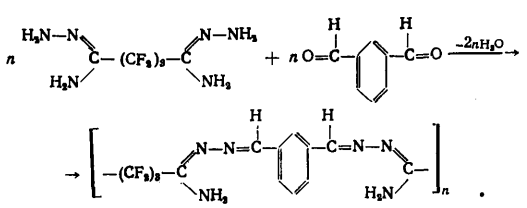
the interaction of polyfunctional nucleophilic compounds with polycarboxylic acid derivatives, process selectivity is achieved more readily the greater the difference between the nucleophilic reactivities of the reaction centres in the *o*- or α-positions relative to one another[98,99]. An alternative condition for selective polyamidation is rapid deactivation of the reaction centre after the group in the *o*- or α-position relative to it has entered into the amidation reaction. Since the amino-groups of bis-(*o*-phenylenediamines) exhibit comparatively similar nucleophilic reactivities, their reactions with highly reactive carboxylic acid derivatives frequently involve the breakdown of the selectivity of the processes, leading to gel formation and the prepolymers cannot therefore be converted into the desired products. In contrast to bis-(*o*-phenylenediamines), in diamidrazones the nucleophilic reactivities of the hydrazine and amidine centres differ sharply, which makes it possible to carry out polycondensation processes involving them with a high degree of selectivity. In combination with the relative availability of many diamidrazones and their resistance to oxidation, this factor makes these compounds extremely promising monomers.

All that has been said above applies not only to the reactions of diamidrazones with polycarboxylic acid derivatives but also to their reactions with dicarbonyl compounds and di-isocyanates.

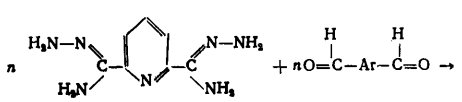
High-molecular-weight film- and fibre-forming poly-(carbamoylamidrazones) were obtained by the reaction of diamidrazones with di-isocyanates in aprotic dipolar solvents containing lithium chloride at 20–50°C:[100]

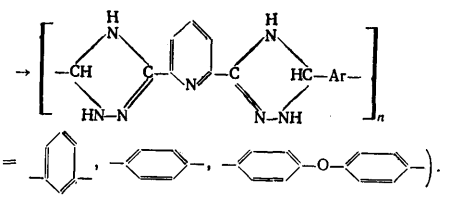


Polymers incorporating fragments of the Schiff base type (polyarylidene-amidrazones) have been obtained by the reaction of hexafluoroglutarodiamidrazone with isophthalaldehyde[101]:



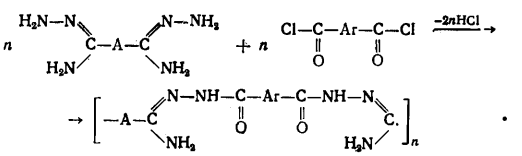
In both instances[100,101] there is a possibility of the conversion of the resulting polymers into heterocyclic systems, but there are no unambiguous data showing that this possibility is in fact realised. In contrast to these studies, Hergenrother and Carlson[80] showed unambiguously that the reaction of the diamidrazone of pyridine-2,6-dicarboxylic acid with aromatic dialdehydes leads to the formation of polytriazolines:





Polytriazolines are soluble to a limited extent in *m*-cresol, dimethylacetamide, dimethyl sulphoxide, and formic and trifluoroacetic acids. The intrinsic viscosities of solutions of these polymers are 0.51–0.61 dl g^{-1}, which makes it possible to obtain strong elastic films from their solutions in acids. According to the results of thermogravimetric analysis, the degradation of these polymers begins in the temperature range 280–400°C; attempts to convert them into the corresponding poly-1,2,4-triazoles were unsuccessful.

A number of studies were made on the interaction of diamidrazones with dicarboxylic acid dichlorides with consequent conversion of the resulting poly(acylamidrazones)[53-54,63,64,101-108]. Poly(acylamidrazones) were synthesised by the reaction of oxalic[63,64,103-108], isophthalic[102], terephthalic[102], and pyridine-2,6-dicarboxylic acid[53,54] diamidrazones with aromatic dicarboxylic acid dichlorides under the conditions of interfacial polycondensation[53,54,63,64,103-108] and low-temperature polycondensation in aprotic amide solvents[53,54,63,64,102,104]:

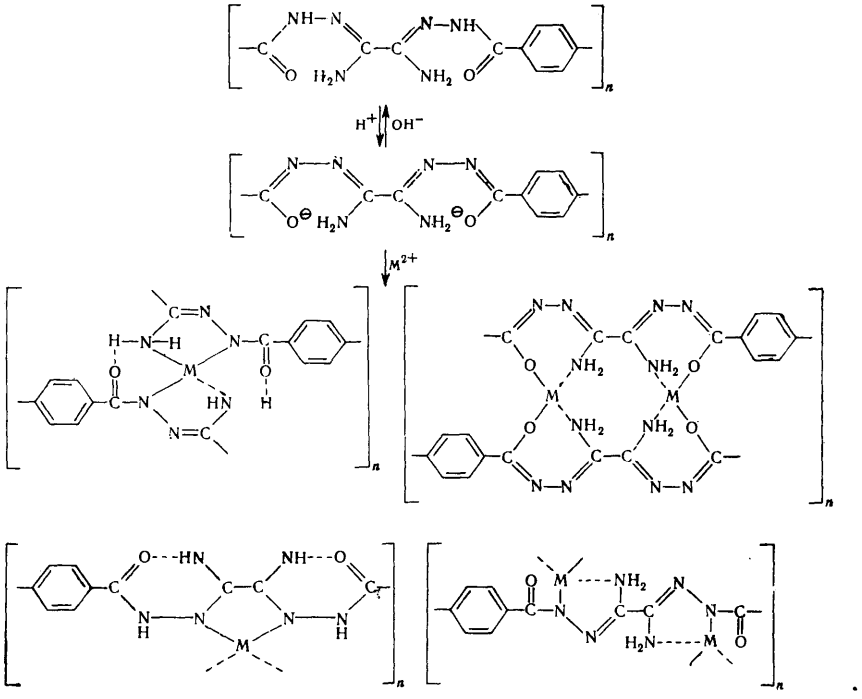


The poly(acylamidrazones) with the highest molecular weights among those obtained exhibit film- and fibre-forming properties[53,54,103,105,107-110].

The poly(acylamidrazones) were converted into the corresponding poly-1,2,4-triazoles by heating in high-boiling solvents, for example *m*-cresol[53,54], or by heat treatment in the solid phase at a temperature exceeding 250°C.[53,54,63,64,102,105,108] The polymers obtained by the solid-phase heat treatment of poly(acylamidrazones) contain 1.4–4% of oxadiazole rings according to the analysis of the products formed[53,54]. The cyclisation of poly(acylamidrazones) in strong acids (dichloroacetic[63,64], trifluoroacetic[53,54], PPA[53,54], and sulphuric[53,54]) was accompanied by the formation of poly-1,3,4-oxadiazoles.

The poly-1,2,4-triazoles and poly-1,3,4-oxadiazoles obtained in this way are soluble in concentrated sulphuric acid and, according to the results of dynamic thermogravimetric analysis, begin to undergo degradation in air at about 420°C.

Chelate polymers, produced by the interaction of poly-(acylamidrazones) with various metal cations (Ca^{2+}, Ba^{2+}, Sn^{2+}, Zr^{2+}, Zn^{2+}, Cd^{2+}, Bi^{2+}, Pb^{2+}, Cu^{2+}, Fe^{2+}, Au^{+}, etc.), are of exceptional interest in connection with the urgent problem of the synthesis of fire-resistant polymers[103,109]. Chelate polymers have been most widely synthesised from poly(acylamidrazones) based on oxalodiamidrazones and terephthaloyl chloride and the following structure has been proposed for them[103]:



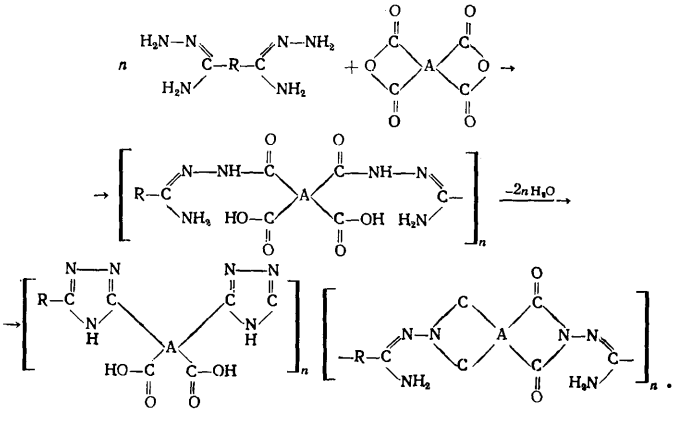
These polymers are highly fire-resistant and are used as the fire-resistant fibre Enkatherm[103]. The Table presents the comparative oxygen indices of various fibres, demonstrating the appreciable advantage of Enkatherm over other fibres.

Characteristics of the fire resistance of a number of fibres.

Polymer fibre	Temp. of spontaneous inflammation, °C	Oxygen index	Polymer fibre	Temp. of spontaneous inflammation, °C	Oxygen index
Cotton	400	0.18	Polyacrylonitrile	560	0.18
Polypropylene	440	0.18	Wool	590	0.25
Acetate	480	0.18	Nomex	—	0.28
Polyester	510	0.20	Polybenzimidazole	—	0.41
Nylon	530	0.22	Enkatherm	—	0.52

Among the series of other attempts at the synthesis of polymers based on diamidrazones and dicarboxylic acid derivatives, special mention should be made of the work of Ried and Giesse[67], who achieved the reaction of oxalo- and terephthalo-diamidrazones with the ethyl bisimidoesters of the same acids in lower alcohols with subsequent heat treatment. According to the authors[67], the reaction products are low-molecular-weight poly-1,2,4-triazoles.

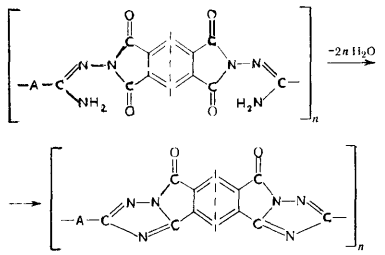
The synthesis of partly "ladder-types" polymers based on the diamidrazones of dicarboxylic acids has been attracting increasing attention recently. The interaction of diamidrazones with dianhydrides was achieved for the first time by Ried and Giesse[67] in the specific instance of the reaction of oxalodiamidrazones and pyromellitic and cyclopentanetetracarboxylic acid dianhydrides in pyridine. The structure of polytriazoles containing carboxylic acid side chains was attributed to the products. Another structure (polyamidinoimide) was proposed for the products of the reaction of diamidrazones with pyromellitic acid dianhydride[72]:



The first stage of the process—the synthesis of poly-(*o*-carboxy)acylamidrazones—was carried out in dimethyl sulphoxide. The resulting high-molecular-weight polymers were converted into films and subjected to polycyclodehydration.

In the course of subsequent investigations[34,68-71] it was shown that poly(amidinoimides) are merely intermediates formed under comparatively mild cyclisation conditions;

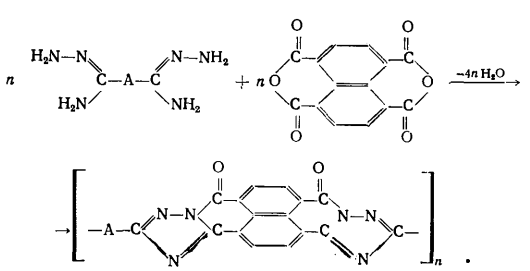
at higher temperatures they are converted into polytriazoloisoindolones:



In the spectroscopic study of the structures of the polymers obtained the authors[67,72] probably failed to take into account the fact that polytriazoloisoindolones, like many other heterocyclic polymers, are incompletely cyclised polymeric structures and contain a considerable number of defective units, which are responsible for the appearance of additional absorption bands in the infrared spectra of the polymers.

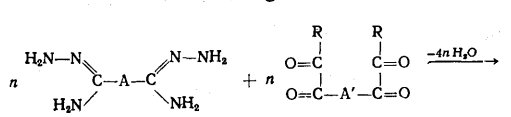
The presence of defective units in the polymeric structures under consideration and also the tendency of the isoindolotriazolone rings themselves to undergo degradation at the $\rangle C-CO-$ and $-OC-N\langle$ bonds and to hydrolyse are responsible for the comparatively poor thermal characteristic of these polymers—the majority of polytriazoloisoindolones begin to undergo degradation at temperatures not exceeding 400°C.[69-71]

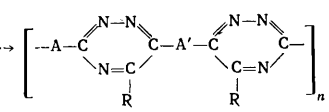
Polybenzobistriazolophenanthrolines (polynaphthoylenetriazoles), produced by the reaction of dicarboxylic acid diamidrazones with naphthalene-1,4,5,8-tetracarboxylic acid or its dianhydride, have a much higher thermal stability[71,73,76-78]. They are synthesised by single-stage polycyclocondensation in PPA or by two-stage polycyclocondensation with the first stage carried out in hexamethylphosphoramide in accordance with the following scheme:



The single-stage process in PPA, whereby film-forming polymers with a logarithmic viscosity of the solutions of about 2.5 dl g^{-1} may be obtained, is more effective in relation to the above polymers. Polybenzobistriazolophenanthrolines, which are soluble in sulphuric and methanesulphonic acids, begin to lose weight appreciably in air at 500°C under the conditions of dynamic thermogravimetric analysis and at a temperature in excess of 400°C under the conditions of isothermal thermogravimetric analysis.

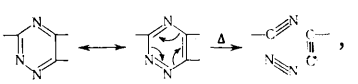
A number of high-molecular-weight poly-1,2,4-triazines have been obtained by the reaction of dicarboxylic acid diamidrazones with bis-(α-dicarbonyl) compounds[85-87,111] in accordance with the following scheme:





The reaction of dicarboxylic acid diamidrazones with diglyoxals was achieved by Hergenrother[85,87] and Culbertson[111] in polar organic solvents (*m*-cresol[85,87], hexamethylphosphoramide[111], etc.) between 0°C and the boiling point of the solvent with subsequent heat treatment of the polymers or without it. The initial diamidrazones were derived from pyridine-2,6-dicarboxylic[85,111], oxalic[87,111], and also malonic, succinic, glutaric, adipic, sebacic, isophthalic and terephthalic acids[111]. The diglyoxals employed were *pp'*-oxybis(phenyleneglyoxal) hydrate[85,87,111], 1,4-diglyoxaloylbenzene, *pp'*-thiobis(phenyleneglyoxal)[87,111], 1,2-diglyoxaloylnaphthalene, 2-chloro-1,3-dioxalylbenzene, etc.[111]

The fully aromatic poly-1,2,4-triazines exhibit limited or partial solubility in polar solvents of the type of *m*-cresol, dimethyl sulphoxide, dimethyl acetamide, and hexamethylphosphoramide. According to the results of dynamic thermogravimetric and differential thermal analyses, they begin to undergo intense degradation at about 400°C in air and at 450°C in an inert medium. The comparatively low thermo-oxidative and thermal stability of these polymers can be accounted for by the ease of liberation of nitrogen,



and the oxidation of the $\rangle C-H$ fragment of the triazine ring[85].

Poly-1,2,4-triazines, which are much more soluble in polar solvents and have a much higher thermo-oxidative stability compared with the polymers discussed above, were obtained by the reaction of dicarboxylic acid diamidrazones with dibenzils. The dicarboxylic acid diamidrazones employed were derived from pyridine-2,6-dicarboxylic[85,86] and oxalic[87] acids and the dibenzils were *pp'*-oxydibenzil[85-87] 1,3- and 1,4-bis(phenylglyoxaloyl)benzenes, *pp'*-thiodibenzil[86,87], as well as *pp'*-methylenedibenzil, and *pp'*-carbonyldibenzil[86]. The resulting polymers soften at 270–330°C, in contrast to unsubstituted poly-1,2,4-triazines, and exhibit a high resistance to isothermal heat-induced ageing in air at 260°C in the course of 1000 h[87]; at 290°C these polymers lose 20–25% of the initial weight in the course of 45 h. The polymers can be used as thermostable adhesive films and binders for fibreglass[86].

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Mutual Influence of Ligands in Complexes

Yu.N.Kukushkin

The review deals with the theoretical concepts and experimental data on the mutual influence of ligands in complexes. Studies published after 1952 are covered.
The bibliography includes 166 references.

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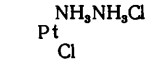
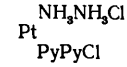
I. INTRODUCTION

The problems of the mutual influences of atoms was raised by Chernyaev in relation to inorganic chemistry. In 1925 he formulated the *trans*-influence rule [1], which, after Werner's coordination theory had been devised, became the most important generalisation in the chemistry of complexes. In recent years certain non-Soviet scientists have tended to attribute the discovery of the trans-*influence* to Werner. This tendency began with the review of Quagliano and Schubert [2], who, referring to Werner's paper [3], claimed that Werner introduced the concept of the elimination of groups in the *trans*-position.

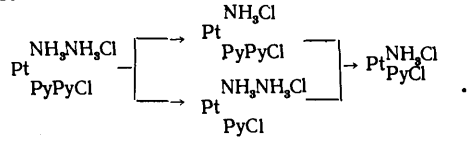
This situation apparently arose because Jørgensen, who supported Blomstrand's views on the structure of complexes, assumed that Peyrone's chloride has the structure



When it reacts with pyridine, the product is a mixed tetrabase complex to which the following structure was attributed



Its cleavage by hydrochloric acid proceeds via the following stages:



Werner laid the foundations of coordination theory [3]. In his communication he explained the isomerism of dichlorodibaseplatinum(II) complexes from the standpoint of the hypothesis, which he put forward for the first time, that platinum(II) complexes have a planar structure. He developed his planar structure hypothesis on the basis of

Jørgensen's experimental data[4]. He introduced the concept of the planar configuration of platinum(II) complexes and concluded that, when $[Pt(NH_3)_4]^{2+}$ reacts with hydrochloric acid, the complex $[Pt(NH_3)_2Cl_2]$ with the *trans*-configuration is obtained. However, the *trans*-cleavage rule (Jørgensen's rule) can in no way be regarded as the *trans*-influence rule. Chernyaev's *trans*-influence rule includes not only Jørgensen's rule but also Peyrone's and Kurnakov's rules. Thus there are no grounds for attributing to Werner the discovery of the *trans*-influence rule.

In March 1952 a conference was held on the *trans*-influence rule[5], where 25 years of the study and refinement of Chernyaev generalisation were assessed. This review presents the main achievements in this field during the last two decades.

In 1952 the *trans*-influence rule was based on complexes of bivalent and quadrivalent platinum and partly bivalent palladium[6,7]. Lebedinskii's preparative studies demonstrated *trans*-influence in compounds of tervalent rhodium and iridium (Ref. 5, p. 95). On the other hand, Ablov merely posed the question of *trans*-influence in tervalent cobalt complexes and Volshtein did the same in relation to tervalent chromium complexes. In summarising the conference proceedings, Chernyaev expressed his confidence that the *trans*-influence rule would be extended to many other elements in Mendeleev's Periodic System.

One may say that at present the vast majority of studies on *trans*-influence are carried out with platinum compounds. However, investigations of *trans*-influence in cobalt complexes have developed on a large scale and this problem is dealt with in a special review[8] published in 1969. Many studies have been made on *trans*-influence in rhodium(III) complexes and others on tervalent gold and ruthenium have been published. Isolated investigations have been made on *trans*-influence in gallium, tin, chromium, rhenium, and iron compounds.

A characteristic feature of the studies after 1952 is the change from a qualitative approach to quantitative investigation of the phenomenon. The first attempt at a quantitative characterisation of *trans*-influence was made by Gel'man and Karandasheva[9]. The development of these investigations enabled Zvyagintsev and Karandasheva to devise a quantitative *trans*-influence scale for individual ligands[10,11]. Kinetic studies on substitution reactions involving platinum(II) complexes enabled Grinberg and Kukushkin to discover in 1957 the *cis*-influence of ligands in complexes[12].

II. THEORY OF *TRANS*- AND *CIS*-INFLUENCE

The theories of *trans*-influence have been described in detail in a number of books and reviews[13-17]. Therefore they need not be considered in detail and only those which constituted important stages in the development of the *trans*-influence rule need be enumerated.

The Grinberg–Nekrasov polarisation theory[18,19] must be regarded as the first theory of this kind. Grinberg's interpretation of *trans*-influence on the basis of the oxidation-reduction interaction of the ligand with the central atom[20] extended the applicability of the polarisation theory. This theory has a considerable predictive power and is still used to account for the σ-*trans*-influence of ligands.

The next stage was Syrkin's explanation of *trans*-influence[21] on the assumption of ds-hybridisation in complexes. In recent years these views have again attracted the attention of theoreticians in relation to the phenomenon of "rehybridisation" of the hybrid dsp^2 orbitals of the central atom[22-24].

An important stage in the development of the theory of *trans*-influence was the high trans-influence of unsaturated ligands such as ethylene and carbon monoxide established by Gel'man[25]. The polarisation theory proved incapable of accounting for these facts. However, they served as the foundation for the development of the theory which was proposed almost simultaneously by Chatt and coworkers[26,27] and by Orgel[28]. The Chatt–Orgel theory refers to ligands with pronounced π-acceptor properties, such as ethylene, phosphines, or carbon monoxide. Owing to the π-acceptor properties of these ligands, the formation of metal–ligand double bonds becomes possible. A σ-bond is formed via the donor–acceptor mechanism and a π-bond is formed as a result of the overlapping of the filled d orbital of platinum having appropriate symmetry with the vacant orbital of the π acceptor (Fig. 1).

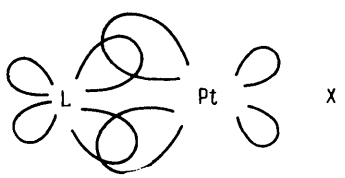


Figure 1. Schematic illustration of the formation of a metal–ligand π-bond.

In this case the ligand L can be phosphine or a sulphur-containing species. This scheme (Fig. 1) explains the enhanced rate of substitution of the ligand X. When a π-bond is formed, the attack on the Pt–X bond is facilitated and the transition state, which is an intermediate having a trigonal bipyramidal configuration, is stabilised (Fig. 2).

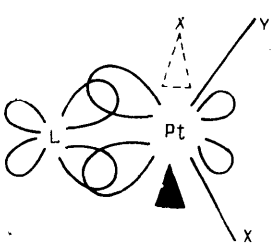


Figure 2. Schematic illustration of the stabilisation by the ligand of the intermediate with a trigonal bipyramidal configuration.

Bersuker pointed out a very significant feature of the Chatt–Orgel theory, namely he stressed the inter-relation between the σ-donor and π-acceptor properties of ligands[29]. In the donor–acceptor interaction the ligand gives up its σ electrons to the central atom and thereby reduces the

energies of its own π orbitals. As a result it becomes a stronger π-acceptor. It is thus found that the more marked the σ-donor properties the greater the possibilities of the reverse charge transfer from the central atom to the π orbitals of this ligand (Fig. 3).

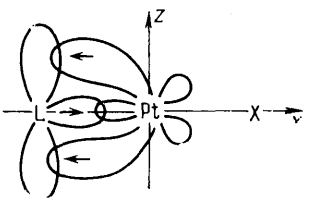


Figure 3. Schematic illustration of the σ- and π-type interactions of the orbitals of the ligand and the central atom.

Baranovskii and Sizova, who refined Bersuker's views, note[30] that the enhancement of the electron-donating capacity of the ligand in the *trans*-position with respect to L stimulates the transfer of electron density to the π^* orbital of the ligand L and at the same time hinders the shift of electrons from L to the central atom via the σ-bond. Thus, in considering the relative contributions of the donor–acceptor and dative components of the metal–ligand bond, one must also take into account the electron-donating properties of the ligand in the *trans*-position with respect to L.

On the basis of σ- and π-electronic effects, Langford and Gray[31] suggested that *trans*-influence be subdivided into σ- and π-trans-influences. Accordingly two series of ligand were obtained:

Ligand series based on the σ-effect

$$\underset{0.5169}{H^-} > \underset{0.3770}{PR_3} > \underset{0.360}{DMSO} \sim \underset{0.3574}{SCN^-} > \underset{0.3494}{CH_3^-, CO, CN^-} > \underset{0.3357}{Br^-} > \underset{0.3332}{Cl^-} > \underset{0.3139}{NH_3} > \underset{0.2877}{OH^-} > \underset{0.189}{C_2H_4}$$

Ligand series based on the π-effect

$$\underset{0.136}{DMSO} > \underset{0.096\ 0.124}{C_2H_4} > \underset{0.093}{CO} > \underset{0.088}{CN^-} > \underset{0.066}{NO_2^-} > \underset{0.052}{SCN^-}$$

The relative positions of the ligands in these series were established on the basis of the corresponding overlap integrals. The ligands in the σ-*trans*-influence series were arranged in sequence on the basis of the overlap integrals between the $6p$ orbital of platinum and the corresponding $p\sigma$ valence orbital of the ligand $[\int(6p\sigma/np\sigma)]$. The relative positions of the ligands in the π-*trans*-influence series were estimated from the overlap integrals between the $5d\pi$ orbital of platinum and the free π^* molecular orbital of the ligand. Mathematical radical functions for platinum were taken from Basch and Gray[32] and those for the ligand atoms from Clementi[33].

It has been shown[34–37] that the *trans*-influence of dimethyl sulphoxide (DMSO) in platinum(II) complexes is very close to that of ethylene. The properties of the complex ion $[Pt(DMSO)Cl_3]^-$ resemble those of the ion $[Pt(C_2H_4)Cl_3]^-$.[35,38] Baranovskii et al. calculated the corresponding overlap integrals and established the positions of DMSO and ethylene in the ligand σ- and π-*trans*-influence series[39]. The molecular orbitals of DMSO and ethylene were calculated by the LCAO-MO SCF method in terms of the CNDO approximation[40,41].

These values are indicated in the corresponding series. The overlap integral $\int(5d\pi/\pi^*C_2H_4)$ is close to the value obtained by Langford and Gray[31]. The difference between them can be explained by the different choice of the radial component of the p-function of carbon and the fact that Langford and Gray estimated the bond lengths on the basis of covalent radii, while Baranovskii et al.[39] used neutron diffraction data for the complex $K[Pt(C_2H_4)Cl_3].H_2O$.[42]

The calculations of the overlap integrals led to the conclusion that DMSO has a much greater σ-*trans*-influence than ethylene. It was concluded on the basis of the overlap integrals $\int(5d^{Pt}_{\pi}/\pi^*)$ for DMSO and ethylene that their π-*trans*-influences are similar and it is difficult to determine unambiguously their relative positions in the *trans*-influence series.

Bersuker's scheme[29,43] explains the *cis*-influence of ligands which was observed for platinum(II) compounds. Indeed, the shift of σ-electrons from the ligand L to the central atom should depend on the σ-donor properties of the ligands in the *cis*-position with respect to the given ligand (Fig. 3), If the σ-donor properties of the *cis*-neighbours are pronounced, the result should be a smaller shift of σ electrons from L to the central atom and this in turn should lead to a decrease of the π-acceptor interaction of the ligand with the central atom and hence to a decrease of the *trans*-influence of L. This mechanism of *cis*-influence explains satisfactorily the experimental observation that the *cis*- and *trans*-influence series are opposed. The view that the ligand which labilises the substituent on the opposite side stabilises the adjacent substituent and conversely was put forward in an earlier investigation[12]. Indeed, ammonia and pyridine have small *trans*-influences compared with chlorine, but they exhibit a marked *cis*-influence[44,45]. The studies of Grinberg and Kuz'mina on the exchange of chlorine in the complex ion $[Pt(C_2H_4)Cl_3]^-$ occupy a special place among these investigations. They showed that ethylene, which has a large *trans*-influence, fixes the *cis*-disposition of the chlorine atoms in the complex[46,47]. The opposed *trans*- and *cis*-influence series of the ligands C_2H_4, Cl^-, NH_3, and Py follows clearly from data for the rates of chlorine isotope exchange compared in Table 1.

Table 1. Rate constants for the exchange of chlorine in platinum(II) complexes.

Complex ion	Cl–Pt–Cl	L–Pt–Cl	Refs.	Complex ion	Cl–Pt–Cl	L–Pt–Cl	Refs.
$Cl\ Cl^{2-}$ Pt $Cl\ Cl$	$1.04\cdot10^{-5}$	$1.04\cdot10^{-5}$	44	$C_2H_4\ Cl^-$ Pt $Cl\ Cl$	$4.92\cdot10^{-6}$	Very rapid	46
$NH_3\ Cl^-$ Pt $Cl\ Cl$	$2.91\cdot10^{-5}$	$4.16\cdot10^{-6}$	45	$DMSO\ Cl^-$ Pt $Cl\ Cl$	$4.96\cdot10^{-4}$	Very rapid	33
$Py\ Cl^-$ Pt $Cl\ Cl$	$3.82\cdot10^{-5}$	$2.87\cdot10^{-6}$	45	$DMSO\ Cl^-$ Pt $Cl\ Cl$	$1.55\cdot10^{-4}$	Very rapid	48

Together with Kuz'mina and other coworkers, the author investigated the *cis*-influence of dialkyl sulphoxides on the rate of exchange of chlorine[35,48,49]. These studies

established that the chloride ion located in the opposite position relative to a dialkyl sulphoxide exchanges almost instantaneously, i.e. at the "zero exchange" rate. This behaviour of complex ions of the type $[Pt(R_2SO)Cl_3]^-$ in relation to the exchange of the chloride ion in the *trans*-position is analogous to the behaviour of $[Pt(C_2H_4)Cl_3]^-$.[46] This is also evidence for the closeness of the *trans*-influences of DMSO and ethylene.

The rate of exchange of the *cis*-chloride ions in the complexes $[Pt(R_2SO)Cl_3]^-$ proved to be unexpectedly high. Despite their large *trans*-influence, dialkyl sulphoxides do not fix the chloride ions in the *cis*-positions, but actually labilise them. The chloride ions on the Cl–Pt–Cl axis in the diethyl sulphoxide complex are extremely mobile, but are nevertheless approximately three times less mobile than in the dimethyl sulphoxide compound. This is probably related to the increase of the size of the alkyl groups, which should lead to the "screening" of the chloride ions.

It follows from the calculation on the electronic structure of the DMSO molecule by the LCAO-MO SCF method in terms of the CNDO approximation[49] that the oxygen $p\pi$ orbitals have a marked electron-donating capacity. The *cis*-influence of DMSO in complex ions of the type $[Pt(DMSO)Cl_3]^-$ can be accounted for by the interaction of the p_y orbitals of oxygen and the central atom, which labilises the bond between platinum and the chlorine in the *cis*-position (Fig. 4).

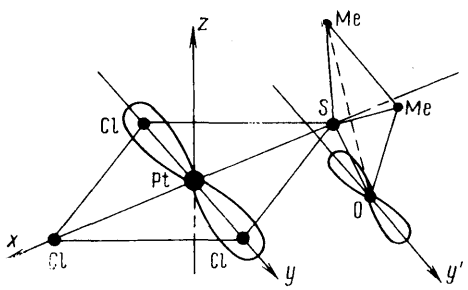


Figure 4. Schematic illustration of the interaction of the p_y orbitals of the central atom and the oxygen atom of the coordinated sulphoxide.

The majority of theories have been devised to account for the kinetic aspect of *trans*-influence. However, numerous data have now accumulated, which permits the consideration of *trans*-influence in the ground and not the transition state of the complex. Thus techniques such as X-ray diffraction, vibrational spectroscopy, NMR, etc. permit the detection of the *trans*-influence in the static state of the complex. A clear tendency to distinguish the trans-influences in the static and dynamic states has arisen in the world literature. To distinguish them, the first is referred to as the *trans*-influence and the second as the *trans*-effect. In addition one should add that two cases are also investigated in the dynamic state: on the one hand the rate of reaction and on the other the position of the reaction equilibrium. Thus in the dynamic state two aspects of the *trans*-effect are considered: the kinetic and thermodynamic aspects.

The investigation of Zumdahl and Drago[24] occupies a special place among studies on the theory of *trans*-influence. Using Hoffmann's modification of the extended Hückel methods, these workers calculated the electronic structures of a number of complexes of the type *trans*-$[PtL(NH_3)Cl_2]$. The complexes are arranged in Table 2 in order of increasing *trans*-influence of the ligand L which had been determined earlier. Some of the ligands in this series are hypothetical, for example, H_2S or PH_3. The hydrocarbon groups in these ligands have been replaced by the hydrogen atom to simplify the calculations and economise computer time. The authors[24] assume that all the ligands considered behave as σ-donors only; their π-acceptor properties are neglected.

Table 2. Overlap populations for the complexes *trans*-$[PtL(NH_3)Cl_2]$.

L	Pt–L bond length, Å	Overlap populations						
		Pt–N	Pt–Cl	Pt–L	$Pt(6p_y)$–L	$Pt(6p_y)$–N	Pt(6s)–N	$Pt(5d_{x^2-y^2})$–N
H_2O	2.00	0.3370	0.3909	0.2406	0.1114	0.1235	0.1205	0.1275
NH_3	2.00	0.3221	0.3832	0.3221	0.1313	0.1313	0.1139	0.1145
Cl^-	2.33	0.3240	0.3843	0.3322	0.1759	0.1212	0.1181	0.1225
H_2S	2.30	0.3244	0.3745	0.4235	0.2070	0.1320	0.1158	0.1154
CH_3^-	2.15	0.3009	0.3724	0.4637	0.1945	0.1431	0.1036	0.0349
PH_3	2.25	0.3032	0.3569	0.5585	0.2435	0.1490	0.1054	0.0366
H^-	1.06	0.3074	0.3641	0.6069	0.2603	0.1415	0.1046	0.1009

One of the first tasks formulated by the authors[24] was to determine the relative bond strengths. They obtained this information by analysing the Mulliken orbital populations. Analysis of the populations yields two criteria for measuring the relative bond strengths in molecules: (1) overlap populations; 2) overlap energies. We may recall that the overlap population is a measure of electron density in the region between two atomic orbitals. It follows from a consideration of the populations (Table 2) that the more marked the *trans*-influence of the ligand L the weaker the opposite Pt–N bond. This is consistent with the *trans*-influence for σ-ligands. It is interesting that the decrease of the population of the Pt–N bond is not due to the decrease of the involvement of the platinum 6*s* and $5d_{x^2-y^2}$ orbitals. Calculation shows that the involvement of this orbital in the platinum–nitrogen bond also increases when the *trans*-influence of the ligands is enhanced. On the other hand, the decrease of the population of the platinum–nitrogen bond is due to the reduced involvement of the platinum 6*s* and $5d_{x^2-y^2}$ orbitals. A similar conclusion concerning the decrease of the involvement of the 6*s* and $5d_{x^2-y^2}$ orbitals with enhancement of the *trans*-influence of the opposite substituent was reached[22] on the basis of the ^{195}Pt–^{31}P interaction constant. We may appropriately recall that the important role of the 6*s* and $5d_{x^2-y^2}$ orbitals in the transmission of *trans*-influence was first pointed out by Syrkin[21].

Another interesting conclusion is that the Pt–Cl bonds in the *cis*-position are also weakened with enhancement of the *trans*-influence of L. Both conclusions refer to molecules in the static state.

Table 2 shows that, on passing from a ligand with a weak *trans*-influence (H_2O) to one with a strong *trans*-influence (H^-), the bond is weakened only to the extent of 10%. This finding suggests that the weakening of the bond is not the fundamental cause of *trans*-influence in the kinetics of substitution reactions at least for σ-linked ligands. Therefore, like Langford and Gray[31], Zumdahl and Drago[24] conclude that the reasons for the difference between the rates of substitution over a wide range is different degrees of stabilisation of the transition state.

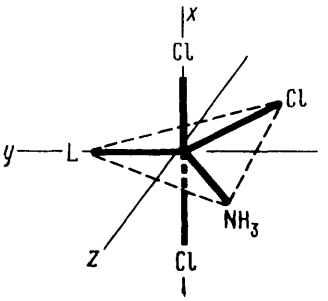


Figure 5. The directions of the Cartesian coordinate axes in the trigonal bipyramidal intermediate.

Zumdahl and Drago explained the *trans*-influence of σ-linked ligands in the following way. In the ground state the ligand L and the leaving group (NH_3) share the same platinum orbital ($6p_y$). We shall assume that Cl^- enters into the complex and that the intermediate has the trigonal bipyramidal structure illustrated in Fig. 5. In this structure the entering and leaving groups (Cl^- and NH_3) lie on either side of the Pt($6p_y$) orbital and employ both p_y and p_z orbitals for the formation of bonds. Thus L occupies more than half of the $6p_y$ orbital. This implies that, when L is a powerful σ-donor and can effectively occupy part of the vacant p_y orbital, the transition complex will be stabilised. Thus the difference between the energies of the ground and transition states will be relatively small for ligands which can effectively interact with the p_y orbital. Powerful σ-donors should behave as ligands of this kind. The calculated Pt($6p_y$)–L overlap populations (Table 2) show that there is an almost exact agreement between the capacity of the ligand to interact with the $6p_y$ orbital of platinum and its position in the experimental *trans*-influence series. The calculated overlap populations are listed in Table 3, which shows that, on passing from H_2O to H^-, the Pt–L bond is indeed strengthened, while the other bonds are weakened. The most interesting result are presented in Table 4, which includes the differences between the overlap populations of the individual bonds and orbitals in a tetracoordinate planar complex and a pentacoordinate bipyramidal complex. The difference shows that, on passing from H_2O to H^-, all the bonds are weakened to approximately the same extent. The Pt–Cl bond within the plane is missing in the ground state. Therefore, Table 4 in fact gives for it not the difference but the actual overlap population in this transition state. It is seen from Table 4 that, when L = H^-, the weakening of the Pt–L bond is much smaller than for L = H_2O. The difference refers almost completely to the Pt(6s)–L and Pt($d_{x^2-y^2}$)–L interactions. The sums of these reductions in strength are almost the same in the two cases.

Zumdahl and Drago[24] also calculated the difference between the activation energies for the transition from planar to pyramidal complexes for L = H^- and L = H_2O:

$$E_a = E_{H^-} - E_{H_2O} \ .$$

They found that the difference between the activation energies should be about 8 kcal mole^{-1}. Thus, for a ligand with a high *trans*-influence such as H^-, about 8 kcal mole^{-1} less is needed to pass from the planar to the trigonal bipyramidal configuration than for a ligand with a weak *trans*-influence (H_2O).

Table 3. Overlap populations in trigonal bipyramidal complexes.

Complex	Pt($6p_y$)–L	Pt–L
$PtH_2O(NH_3)Cl_3^-$	0.1602	0.1895
$PtH(NH_3)Cl_3^{2-}$	0.3356	0.5868
Pt–Cl (on *x* axis)	Pt–Cl (in the plane)	Pt–N
0.3441	0.3117	0.2920
0.3198	0.2859	0.2674

Table 4. Differences between overlap populations.

L	Pt($6p_y$)–L	Pt(6s)–L	Pt($5d_{x^2-y^2}$)–L
H_2O	0.0488	–0.0071	–0.0447
H^-	0.0753	–0.0142	–0.0382
Pt–L	Pt–Cl (on *x* axis)	Pt–Cl (in the plane)	Pt–N
–0,0511	–0.0468	0.3117	–0.0450
–0,0213	–0.0443	0.2859	–0.0400

Yatsimirskii recently examined the possible types of ligand interactions in complexes[50]. The analysis of the σ-type and π-type interactions of metal and ligand orbitals for the molecular fragment LMX in the *xy* plane is interesting. Tables 5 and 6 list the squares of the coefficients of the linear combinations of the corresponding atomic orbitals.

Table 5 shows that, for the *trans*-disposition of the ligands L and X, there is almost 100% orbital overlapping. On the other hand, for the *cis*-disposition, the orbital overlap is only to the extent of 50%. The same situation obtains also when π-bonds are formed.

Thus, when the dissociation of M–X bonds is considered, it follows from Tables 5 and 6 that the ligands with pronounced σ- and π-donor properties should have a labilising effect directed mainly to the *trans*-partner. With reference to the work of Zumdahl and Drago[24], one may mention that, for unequal overlap populations of the atomic orbitals, this conclusion is no longer so evident.

For ligands with electron-accepting properties, the M–X bonds should be strengthened. The ligand in the *trans*-position has greater influence than the ligand in the *cis*-position. The conclusions which follow from Chatt's Orgel's and Bersuker's ideas remain valid for the associative mechanism.

Table 5. Characteristics of the σ-type interaction of the metal orbitals with the orbitals of ligands in the *xy* plane.

Metal orbitals	*trans*-L	X	*cis*-L
$d_{x^2-y^2}$	1/4	1/4	1/4
S	1/6	1/6	1/6
P_x	1/2	1/2	0
P_y	0	0	1/2
d_{z^2}	1/12	1/12	1/12
P_z	0	0	0
Common orbitals with X	100%	—	50%

Table 6. Characteristics of the π-type interaction of the metal orbitals with the orbitals of ligands in the *xy* plane.

Metal orbitals	*trans*-L	X	*cis*-L
d_{xy}	1/4	1/4	1/4
d_{xz}	1/4	1/4	0
d_{yz}	0	0	1/4
Common orbitals with X	100%	—	50%

An important result of Yatsimirskii's study [50] is the conclusion that the *trans*- and *cis*-influence series may be reversed, depending on the reaction mechanism (dissociative or associative).

Yatsimirskii's remark [50] that, apart from the formation of common orbitals, Coulombic interactions between the ligands and the central atom are important is also significant. Naturally the Coulombic interaction is more marked the more effective the charges on the central atom in the ligand. This interaction leads to non-directional effects. The decrease of the effective charge on the central atom of the complex should facilitate dissociation and weaken association and conversely.

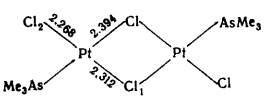
III. CRYSTAL-CHEMICAL MANIFESTATION OF *TRANS*-INFLUENCE

The number of studies undertaken to establish a relation between the *trans*-influence of individual ligands and the corresponding bond lengths increased considerably in recent years. The earlier investigations in this field were carried out exclusively on platinum complexes. The studies carried out up to 1962 have been analysed in Kukina's review [51]. Later studies are described in other reviews [52,53]. Bokii and Kukin's study [54] is one of the first where it was shown convincingly that interatomic distances depend on the nature of the ligand in the *trans*-position. In the complex $K[Pt(C_2H_4)Br_3].H_2O$ the bromine atom in the *trans*-position relative to ethylene is approximately 0.1 Å further away from the platinum atom than the bromine atom located opposite another bromine atom. A difference between the Pt–Br distances was observed also in the salt *cis*-$[Pt(C_2H_4)(NH_3)Br_2]$. Here too the platinum–bromine bond length on the C_2H_4–Pt–Br axis is greater by approximately 0.1 Å than that on the NH_3–Pt–Br axis [55,56].

A change in interatomic distances probably occurs only for a large difference between the *trans*-influences of the inner-sphere ligands. Thus the Pt–Cl interatomic distances in the complex $K[Pt(NH_3)Cl_3]$ cannot be inferred. The differences are within the limits of experimental error [57,58]. It has been shown [59] that the Pt–Cl and Pt–N bond lengths in *cis*- and *trans*-$[Pt(NH_3)_2Cl_2]$ are almost the same.

The Pt–Cl and Pt–Br bond lengths in complexes usually vary within fairly narrow limits. It has been found that in the hydride compounds *trans*-$[Pt(PEt_3)_2BrH]$ [60] and *trans*-$[Pt(PPh_2Et)_2ClH]$ [61] the above bond lengths are unusually large. The authors explained this by the strong *trans*-influence of the ligand H^-. An increase in the lengths of the Pt–X bonds located opposite trialkylphosphine has been observed in the trialkylphosphine complexes *trans*- and *cis*-$[Pt(PR_3)_2X_2]$ where X is a halide ion. The Pt–Cl bond length in the *trans*-isomer is 2.30 Å, while in the *cis*-isomer it increases to 2.37 Å. [62,63] From this it follows that the phosphine groups have a fairly marked *trans*-influence.

The interatomic distances and valence angles in the bridged compound $Pt_2Cl_4[As(CH_3)_3]_2$ have been determined [64,65]. It has been established that the Pt–Cl distance in the *trans*-position relative to arsenic is greater than the normal distance approximately by 0.1 Å.



These data are regarded as evidence for a marked *trans*-influence of trimethylarsine. A similar situation is observed in the dimeric tripropylphosphine complex *trans*-$PtCl_4(PPr_3)_2$. [66] We may mention that the Pt–Br distances involving the bridge and terminal bromine in $[N(C_2H_5)_4]_2[Pt_2Br_6]$ differ by 0.04 Å. [67] The difference is of the same order of magnitude as that between the Pt–Cl_1 and Pt–Cl_2 distances in $Pt_2Cl_4[AsMe_3]_2$.

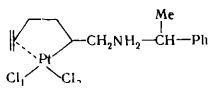
The Pt–Cl bond lengths in certain platinum(II) complexes have been compiled in the review of McWeeny et al. [68] It is interesting to quote this Table in a somewhat extended form (Table 7).

It is clear from Table 7 that the atoms can be arranged in the following sequence in terms of the *trans*-influence in platinum(II) complexes:

$$Si > C \sim H^- > P > C = C,\ Cl > O\ .$$

The much greater *trans*-influence of the σ-linked carbon atom compared with that of the olefinic π-bond merits attention. Apart from the data in Table 7, this is also indicated by the results of other investigations [72,73]. Bombieri et al. [73] studied the cyclic platinum complex [PtLPyCl], where L is methoxycyclo-octa-1,5-diene. This ligand undergoes ring closure via the σ-linked carbon atom on one side and the olefinic π-bond on the other. It was established that the Pt–N bond located opposite the Pt–C bond is unusually long (2.02 Å). This can be regarded as evidence in support of the strong *trans*-influence of the carbon atom.

It has been shown [74] that the Pt–Cl_1 bond located opposite the σ-linked carbon atom in the complex



is longer by 0.09 Å than the Pt–Cl_2 bond in the *trans*-position relative to the olefinic π-bond. A similar situation has been observed in dimeric μ-acetate complexes of palladium [75]. The Pd–O bonds located opposite the σ-linked carbon atom are longer than the Pd–O bonds located opposite the olefinic π-bond. The difference between the *trans*-influences of the olefinic π-bond and the σ-linked carbon atom has also been discussed in other reports [76,77]. Two studies in recent years established a marked *trans*-influence of the hydrocarbon groups in rhodium complexes. Thus the length of the rhodium–nitrogen bonds located opposite the ethyl group in the complex ion $[Rh(C_2H_5)(NH_3)_5]^{2+}$ is 2.256 Å, while the length of the remaining rhodium–nitrogen bonds are 2.072 Å. [78]

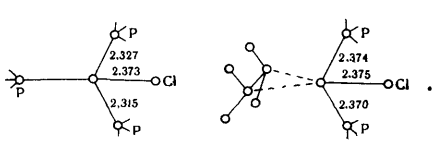
Table 7. Pt–Cl distances in the certain platinum(II) complexes.

Complex	*trans*-Ligand	Bond length, Å	Refs.
$[Pt(acac^*)_3Cl]^-$	O	2.28±0.01	69
trans- $[Pt(PEt_3)_2Cl_2]$	Cl	2.30±0.01	62
$[(C_{15}H_{17})_2Pt_2Cl_3]$	C=C	2.31±0.01	70
cis- $[Pt(PEt_3)_2Cl_2]$	P	2.37±0.01	63
trans- $[Pt(PMe_2Ph)_2Cl(CH_2SiMe)]$	C	2.415±0.005	71
trans- $[Pt(PPh_2Et)_2ClH]$	H	2.42±0.01	61
trans- $[Pt(PPhMe_2)_2(SiPh_2Me)Cl]$	Si	2.45±0.01	68

*acac = acetylacetonate ion.

A study of the structure of $\{RhPy_2Cl_2[P(o\text{-}C_6H_4CH_3)_2.(o\text{-}C_6H_4ClH_2)]\}$ showed that the Rh–Cl bond length is 2.399 Å on the Py–Rh–Cl axis and 2.531 Å on the C–Rh–Cl axis [79]. Thus, like the ethyl group, the benzyl group has a powerful *trans*-influence.

X-Ray diffraction studies on $[Rh(PPh_3)_3Cl]$ and $[Rh(PPh_3)_2(CF_2{=}CF_2)Cl]$ showed that, when triphenylphosphine is replaced by tetrafluoroethylene, there is no significant change in the Rh–Cl bond in the *trans*-position but the Rh–P bond in the *cis*-position relative to tetrafluoroethylene increases appreciably [80].



It has been shown [81] that in the octahedral complexes ML_3Cl_3 of the meridian type, where L = dimethylphenylphosphine and M = Re^{III}, Os^{III}, or Ir^{III}, the M–Cl and M–P bonds located opposite the phosphine groups are longer than those located opposite the chlorine atoms. The difference is approximately 0.1 Å (Table 8).

Very accurate measurements have shown [82] that the Ru–Cl bond in the *trans*-position relative to the water molecule in the complex $Cs[RuCl_5(H_2O)]$ is shorter than the other bonds. Presumably this is a consequence of the weak *trans*-influence of the water molecule.

Table 8. Bond lengths in compounds of the type ML_3Cl_3.

Bond	Re^{III}	Os^{III}	Ir^{III}
M–Cl (*trans* w.r.t. Cl)	2.353 (6)	2.347 (6)	2.361 (6)
M–Cl (*trans*-w.r.t. P)	2.454 (6)	2.439 (6)	2.429 (6)
M–P (*trans* w.r.t.Cl)	2.401 (6)	2.350 (6)	2.277 (6)
M–P (*trans* w.r.t.P)	2.458 (6)	2.408 (6)	2.363 (6)

It has been established [83] that the dimeric complex $[Ir_2(CO)_4Me_2Cl_4]$ is formed via a double chloride bridge. It is noteworthy that the Ir–Cl bridging bonds are marked non-equivalent. The length of the Ir–Cl bond in the *trans*-position relative to Me is 2.52 Å and the length of the bond in the *trans*-position relative to CO is 2.38 Å. These results can be regarded as supporting the much greater *trans*-influence of the alkyl group compared with that of the CO molecule.

In his review [53] Porai-Koshits quotes interesting data on the influence of the Rh–Rh bond in dimeric formate and acetate complexes resulting in an increase in the length of the Rh–H_2O, Rh–Cl, and Rh–Br bonds in the *trans*-positions. In addition he notes that the *trans*-ligands in their turn also affect the Rh–Rh bond length. In halide complexes this bond is much longer than in hydride complexes (2.45–2.47 and 2.35–2.38 Å respectively).

Porai-Koshits [53] notes that the structural manifestation of the *trans*-influence of ligands are extremely delicate and depend on many factors. It is still not always possible to take into account all these factors. Thus there are very conflicting manifestations of the *trans*-influence of a multiple bond. In molybdenum compounds the Mo=O double bond causes an appreciable lengthening of the *trans*-bond with any ligand. In rhenium and ruthenium complexes the increase in the length of the bond in the *trans*-position relative to M=O occurs only for neutral ligands but not for acido-ligands. The Os=N triple bond constitutes a special case. In the complex $K_2[OsNCl_5]$ the length of the Os–Cl bond on the N≡Os–Cl axis is increased to 2.60 Å compared with the other bonds, whose length is 2.32–2.37 Å. The problem of the dependence of the strength of the metal–ligand bond located opposite a multiply-linked ligand in hexacoordinate compounds has been examined theoretically [84]. The influence of the yl oxygen on the inner-sphere fluoride ions in Group V and VI transition metal complexes has been investigated by NMR. [85,86]

The structure of the octahedral terpyridyl complex of gallium $GaCl_3.2,2',2''$-terpyridyl has been investigated [87] and it has been established that the length of the Ga–Cl bond located opposite nitrogen is much smaller than that of the other two bonds on the Cl–Ga–Cl axis. The authors [87] attribute this finding to *trans*-influence.

IV. *TRANS*-INFLUENCE IN VIBRATIONAL SPECTROSCOPY

Force constants can serve as a measure of the strength of a chemical bond. When complexes of the same type are compared, the stretching vibration frequencies of chemical bonds are frequently used instead of force constants as a measure of the strengthening or weakening of the bonds.

We shall not consider here studies in which the relative strength of a metal–ligand bond was inferred from indirect data. They have been analysed in a monograph[16] (p. 315). Although the sensitivity of the metal ligand bond stretching vibrations to the type of ligand in the *trans*-position was established initially for Pt–H [88] and Pt–C bonds [89], it is nevertheless useful to begin the consideration of these data with studies where Pt–Cl vibrations were investigated.

Much information based on extensive experimental data concerning the influence of inner-sphere ligands on the Pt–Cl bonds was obtained by Chatt and coworkers[90]. Like Bersuker[29], the authors of this investigation concluded that there are at least two causes of *trans*-influence: the σ-electron shift from the ligand to the central atom and the π-electron shift from the central atom to the ligand. The σ-electron shift is probably the main cause of the strong *trans*-influence of hydrides and alkyl and aryl carbonions and the π-electron shift is characteristic of olefins. The σ-electronic mechanism of the transmission of *trans*-influence should weaken the bond in the *trans*-position for the molecule in the static state. On the other hand, the π-electronic mechanism should strengthen the bond in the opposite position.

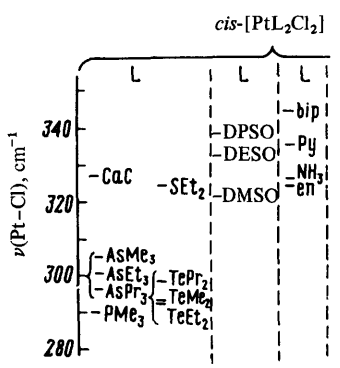


Figure 6. The spectroscopic *trans*-influence scale for ligands based on complexes of the type *cis*-$[PtL_2Cl_2]$.

A *trans*-influence scale has been set up for ligands on the basis of the Pt–Cl and Pt–Br stretching vibration frequencies[90]. The scale, supplemented by other data [91–93], is presented in Fig. 6. Compared with ammonia and pyridine (ligands with a weak *trans*-influence) phosphines and arsines lower the strength of the bonds in the opposite positions. It is claimed[23] that the *trans*-influence of phosphines is caused mainly by the σ-component, the π-component of phosphines being insignificant. Diethyl sulphide, diethyl selenide, and particularly cacodyl, which exhibit a powerful dynamic *trans*-effect (unlike phosphines), do not weaken but actually stabilise the bond in the opposite position. Basolo and Pearson[16] regard this finding as inconsistent with other experimental data (Basolo and Pearson[16], p. 316). However, bearing in mind that this scale refers to the *trans*-influence in the static state of the molecule, there is no inconsistency. Owing to the π-acceptor properties of sulphides and particularly of olefins, the effective charge on the platinum atom should increase and this should intensify the Coulombic interaction between the central atom and the ligand.

It has been shown by calculations and experimentally [36–38, 94, 95] that dialkyl sulphoxides have fairly pronounced π-acceptor properties. It was therefore interesting to establish their position in Chatt's *trans*-influence scale. Table 9 lists the vibration wave-numbers of the Pt–Cl bond in complexes of the type *cis*- and *trans*-$[Pt(R_2SO)_2Cl_2]$.

A similar Table has been compiled on the basis of studies [92, 93] on *cis*- and *trans*-$[Pt(DMSO)Cl_2L]$, where L represents amines or olefins (Table 10).

Table 9. The vibrational wavenumbers (cm^{-1}) of the Pt–Cl bond in the *cis*- and *trans*-complexes $[Pt(R_2SO)_2Cl_2]$.

Type of vibration	R_2SO				
	DMSO	DESO	DPSO		DiPSO
	cis	*cis*	*cis*	*trans*	*trans*
Pt–Cl	333 s. 309 s.	342 s. 322 s.	350 s. 326 s.	355 s.	353 s.

Table 10. The vibrational wavenumbers (cm^{-1}) of the Pt–Cl bonds in the *cis*- and *trans*-complexes $[PtL(DMSO)Cl_2]$.

Type of vibration	L							
	NH_3		NH_2CH_3		NH_2Et		C_2H_4	C_2H_6
	cis	*trans*	*cis*	*trans*	*cis*	*trans*	*cis*	*cis*
Pt–Cl	346 s. 312 s.	344 s.	334 s. 313 s.	348 s.	338 312	349	338 s. 311 s.	334 306

Chatt's *trans*-influence scale (Fig. 6) was established on the basis of data for complexes with a *cis*-configuration. The value of ν(Pt–Cl) on this scale is the average of the values for two Pt–Cl bands. The scale for compounds with a *trans*-configuration might characterise the *cis*-influence, but in fact it essentially reflects the non-directional influence of the effective charge of the central atom on the ligands having the opposite charge. The *trans*-influence scale leads to the following conclusions.

1. In terms of the overall influence of the σ-donor and π-acceptor properties, sulphoxides are close to olefins, particularly to cyclo-octadiene. The similarity of the properties of olefin and sulphoxide complexes has been frequently pointed out [32, 33, 36, 37, 47, 48].

2. Comparison of the positions of diethyl sulphide and diethyl sulphoxide shows that sulphoxides tend to fix chlorine in the *trans*-position to a greater extent. The presence of oxygen at the sulphur atom should enhance the effective charge of the sulphoxide sulphur atom compared with the sulphide sulphur atom. It has indeed been shown by X-ray emission spectroscopy [96, 97] that the effective positive

charge on the sulphur atom in a sulphoxide is higher than in a sulphide. The same conclusion was reached[95] on the basis of the acid properties of analogous sulphide and sulphoxide compounds. The higher effective positive charge may be the reason for the somewhat more marked π-acceptor properties of sulphoxides compared with the corresponding sulphides.

3. In mixed dimethyl sulphoxide–amine and dimethyl sulphoxide–olefin compounds with the *cis*-configuration the arithmetical mean of the Pt–Cl bond stretching vibration frequencies is approximately the same as for the disulphoxide compounds. When two strong π-acceptors are present in the complex, the involvement of each in the interaction with the *d* orbitals of platinum probably decreases to such an extent that the effective charge of the central atom remains approximately the same.

It is interesting to note that, despite the appreciable difference between the type of ligands, the Pt–Cl bond stretching vibration wavenumbers in the spectra of compounds having the *trans*-configuration remain virtually constant and are in the range 339 ± 3 cm^{-1}.[90,91,98,99] Since *trans*-diolefine compounds are unknown, they cannot be represented on this scale. It would be interesting to supplement the series of compounds by complexes of the type *trans*-$[PtA(C_2H_4)Cl_2]$.

In the series of compounds with the *trans*-configuration, disulphoxide complexes occupy an anomalously high position. Mixed sulphoxide–amine compounds have somewhat lower Pt–Cl bond vibration frequencies. One should note that in all the compounds investigated, the Pt–Cl stretching vibration frequencies are higher for compounds with the trans-configuration than for the corresponding *cis*-compounds. This may be related to the higher symmetry of charge distribution. The ligands L in the complexes *trans*-$[Pt(PMe_2Ph)_2LCl]$ have been arranged in the following series in terms of *trans*-influence on the basis of the Pt–Cl bond vibrations: Cl^-, Me^-, Me_2SiCH_2, Ph_2MeSi.[71] On passing from Cl^- to Ph_2MeSi, the vibration wavenumber of the bond in the *trans*-position falls from 370 to 242 cm^{-1}. This series is satisfactorily consistent with data for the *trans*-influence of the given ligands obtained by ^1H NMR and X-ray diffraction. The following *trans*-influence series has been established[100] on the basis of the Pt–Cl stretching vibration frequencies in the complexes $[Pt(AsEt_3)_2LCl]ClO_4$: $CO > RNC > ArNC > P(OPh)_3 \simeq \simeq P(PMe)_3 > AsEt_3 \simeq PEt_3$.

The Pt–H bond vibration wave-numbers in the spectra of the complexes *trans*-$[PtA_2LH]$, where A = PEt_3 or $AsET_3$, which have been determined by Chatt and Shaw[101], made it possible to arrange ligands in the following series in terms of the strength of the *trans*-influence:

$$NO_3^- < Cl^- < Br^- < I^- < NO_2^- < SCN^- < SnCl_3^- < CN^- \ .$$

It is interesting that it coincides almost completely with the series of ligands based on the Pt–C bond stretching vibration frequencies in the compounds *trans*-$[Pt(PR_3)_2(CH_3)L]$.[102] The series is $NO_3^- < SCN^- < Cl^- < Br^- < I^- < NO_2^-$. They are both analogous to the *trans*-influence series established at an early stage by the discoverer of *trans*-influence–Chernyaev. Only the thiocyanate ion deviates from the second series. The authors[102] suggested that in this case it may be coordinated via the nitrogen atom and not via the sulphur atom.

The *trans*-influence in iridium(III) compounds has been detected[103] by infrared spectroscopy. The study of the spectra of the meridional compounds $[Ir(PMe_3Ph)_3LCl_2]$ showed that in the series L = Cl^-, PR_3, or AsR_3, H^- there is a steady decrease of the Ir–Cl frequency, which can indicate a relative decrease of the strength of this bond. This is consistent with the variation of the *trans*-influence of the ligands:

$$H^- > PR_3 \simeq AsR_3 > Cl^- \ .$$

It was established in the same study that in the series of ligands L = Cl^-, H^-, Br^-, I^-, SCN^-, CN^- there is virtually no change in the vibration frequencies of the Ir–Cl bonds in the *cis*-positions.

A study of octahedral complexes of tervalent rhodium and iridium[104] established that the stretching vibration frequencies of the Rh–Cl and Ir–Cl bonds depend mainly on the nature of the ligands in the *trans*-positions. The ν(M–Cl) frequencies increase in the following sequence of ligands:

$$Cl^- < Br^- < I^- \sim CO < Me^- \simeq PR_3 \simeq AsR_3 < H^- \ .$$

A study of the Au–C bond vibration frequencies and the deformation frequencies of the methyl group in the ion $[Me_2AuX_2]^-$ showed[105] that the *trans*-influence series for gold(III) complexes is the same as for platinum(II):

$$Me_2S > Br^- > Cl^- > en > OH^- > H_2O \ .$$

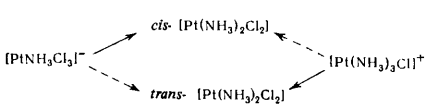
The substitution of two halide ions in the square planar ion AuX_4^- (X = Cl or Br) by two Me^- carbanions leads to the formation of complexes with the *cis*-configuration only and reduces the force constant of the bond Au–X by more than 30%.[105] Thus these data also indicate a much more marked *trans*-influence of the Me^- group compared with Cl^- or Br^-.

The infrared and Raman spectra of the complexes $Me_2SnX_4^{2-}$, where X = F, Cl or Br, have been investigated[106]. It was established that these compounds have the *trans*-configuration. After the substitution of two fluoride ions in SnF_6^{4-} by Me^-, there is some decrease of the force constant of the Sn–F bond. This happens to a smaller extent when a chloride ion is substituted and is altogether negligible in bromide compounds. The authors attribute this variation to the enhancement of the covalence of the tin–halogen bonds. They note that in transition metal compounds the bonds in the *trans*-position relative to the alkyl group are weakened, while in tin compounds the weakening is observed in the *cis*-position.

In contrast to other investigators, Ivannikova et al.[107] concluded that there is no correlation between ν(Pt–Cl) and the ligand *trans*-influence series for complexes of the type $[Pt(NH_3)_2LCl]X$. In most of the studies where such correlation has been established non-electolytic complexes were investigated. Possibly the results of Ivannikova et al.[107] can be accounted for by the fact that they employed compounds containing outer-sphere anions.

V. *TRANS*-INFLUENCE IN THE KINETICS OF SUBSTITUTION REACTIONS

The kinetic aspect of *trans*-influence follows clearly from the classical reactions of ammonia with chloroplatinate(II) to form *cis*-$[Pt(NH_3)_2Cl_2]$ and the cleavage of the tetrammine $[Pt(NH_3)_4]Cl_2$ by hydrochloric acid with formation of *trans*-$[Pt(NH_3)_2Cl_2]$. After excluding reaction stages without fundamental importance, these transformations can be represented schematically as follows:



It is difficult to imagine that the isomeric complexes *cis*-$[Pt(NH_3)_2Cl_2]$ and *trans*-$[Pt(NH_3)_2Cl_2]$ have the same free energy. Indeed, according to the literature[108] the difference between the total energies of these isomers is 3 kcal mole^{-1}, that of the *trans*-isomer being lower. It was established even earlier[109] that the *trans*-isomer is more stable from the energy standpoint, since dry solid *cis*-$[Pt(NH_3)_2Cl_2]$ is converted at 230°C into the corresponding *trans*-isomer as well as being decomposed. Thus the cleavage of the triammine by hydrochloric acid is consistent with thermodynamics and the interaction of the monoammine and ammonia with formation of *cis*-$[Pt(NH_3)_2Cl_2]$ follows the thermodynamically less favourable pathway. Consequently, kinetic factors play the main role in determining the direction of the reaction $[Pt(NH_3)Cl_3]^- + NH_3 = cis\text{-}[Pt(NH_3)_2Cl_2] + Cl^-$.[110,111] Subsequently others reached a similar conclusion[112]. It has been established[111] that a very small amount of *trans*-$[Pt(NH_3)_2Cl_2]$ is formed in the reaction between ammonia and chloroplatinate(II) in addition to *cis*-$[Pt(NH_3)_2Cl_2]$, and after the cleavage of the tetrammine the *trans*-isomer contains a small amount of *cis*-$[Pt(NH_3)_2Cl_2]$.

Subsequently it was shown[113,114] that the compounds *cis*-$[PtA_2X_2]$, where A = amine and X = Br or I, have a higher free energy than the corresponding *trans*-isomers, since on heating in the dry state the *cis* → *trans* isomerisation takes place with energy evolution. Depending on the nature of the amine, the isomerisation energies of the iodide and bromide complexes are 4–6 and 2–3 kcal mole^{-1} respectively.

The occurrence of the reaction via the thermodynamically less favourable pathway but in conformity with the *trans*-influence is probably a common phenomenon. It has been established in a number of studies[32,34,115–117] that the sulphoxide compounds *trans*-$[Pt(R_2SO)ACl_2]$ isomerise in the dry state to the more stable *cis*-isomers with energy liberation. However, the reaction of the ion $[Pt(R_2SO)Cl_3]^-$ with amines does not proceed via the thermodynamically more favourable pathway with formation of *cis*-$[Pt(R_2SO)ACl_2]$, but follows the kinetically more favourable pathway with formation of *trans*-$[Pt(R_2SO)ACl_2]$:

$$[Pt(R_2SO)Cl_3]^- \xrightarrow{+A} \begin{matrix} trans\text{-}[Pt(R_2SO)ACl_2] \\ \downarrow \\ cis\text{-}[Pt(R_2SO)ACl_2] \end{matrix}.$$

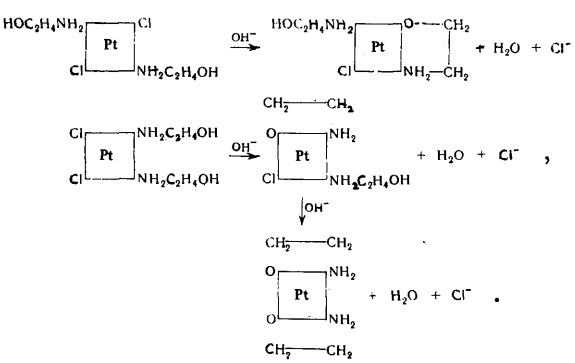
The kinetic manifestation of the *trans*-influence has been satisfactorily described in a number of books and reviews[13–16,30]. In recent years most kinetic studies of the *trans*-influence were made, as before, on platinum complexes. The exchange of labelled [^{14}C] diethylamine in complexes of the type *trans*-$\{PtL[^{14}C](NHEt_2)Cl_2\}$ in methanol and other non-aqueous solvents has been investigated[118]. The authors reached a number of interesting conclusions. Thus they established that triethylphosphine, arsine, and stibine can be arranged in the following sequence in terms of their *trans*-influence: $R_3Sb > R_3P > > R_3As$. The *trans*-influence of the alkyl derivatives of phosphorus, arsenic, and antimony in the reactions investigated is always greater than that of the aryl derivatives. The series $C_2H_4 \simeq$ i-PrCH=CHMe $\simeq Me_2C(OH)C{\equiv}CC(OH)Me_2 \gg Et_3Sb > Ph_3Sb > Me_3P > Et_3P >$ n-$Pr_3P > > Ph_3P > Et_3As \gg$ n-Pr_2S shows that the *trans*-influence of dipropyl sulphide is much smaller than that of phosphines, arsines, and stibines.

A major and interesting study[119] dealt with the kinetics of substitution in complexes of the type *trans*-$[PtL_2Cl_2]$ as a function of the nature of the inner-sphere ligand L and the entering ligand. It might have been expected that the results would make it possible to establish the ligand series in terms of the strength of the *cis*-influence. Unfortunately the rate constants are sometimes so close that the adjacent ligands in the series change places depending on the compounds investigated. For this reason, it was impossible to establish a rigorous *cis*-influence series. Nevertheless, an investigation[119] demonstrated unambiguously a greater *cis*-influence of triethylarsine compared with triethylphosphine, i.e. the opposite variation of the *trans*- and *cis*-influences of ligands was again confirmed. One should note that, among the ligands investigated, organic dialkyl sulphides exhibit both a weak *trans*-influence and a weak *cis*-influence.

Ammonia and aliphatic amines have a much weaker *trans*-influence than phosphines. It has been shown[120] that the *cis*-influence of ammonia and diethylbenzylamine greatly exceeds that of triethylphosphine. This applies both to the solvation of the complexes *trans*-$[Pt(PEt_3)_2Cl_2]$, *trans*-$[Pt(PEt_3)(NH_3)Cl_2]$, and *trans*-$[Pt(PEt_3).(NEt_2CH_2Ph)Cl_2]$ in methanol and to the chlorine isotope exchange reactions in these complexes.

Clear-cut findings indicating the manifestation of *trans*-influence were obtained in a study of the exchange of diethyl sulphoxide in the complex ions $[Pt(DESO)Cl_3]^-$ and $[Pten(DESO)Cl]^+$.[121,122] While the DESO exchange in the first complex is relatively rapid ($k = 7.6 \times 10^{-2}$ litre mole^{-1} s^{-1}), in the ion $[Pten(DESO)Cl]^+$ there is virtually no exchange. This can be undoubtedly attributed to a much weaker *trans*-influence of the amino-groups of ethylenediamine compared with the *trans*-influence of the chloride ion.

Stephen and Basolo established[123] that in the interaction of *trans*-$[Pt(NH_2C_2H_4OH)_2Cl_2]$ with alkali one of the ethanolamine molecules undergoes ring closure faster than the other. Studies have been made[124,125] on the rate of closure of ethanolamine rings in the isomeric *cis*- and *trans*-complexes $[Pt(NH_2C_2H_4OH)_2Cl_2]$. As a result, data were obtained showing that the closure of the first ring in the *trans*-complex is much faster than in the *cis*-complex. On the other hand, the second ring is formed much faster in the *cis*-complex than in the isomeric compound. This fact indicates the manifestation of *trans*-influence, which clearly follows from the following schemes.



Owing to the comparatively powerful *trans*-influence of chlorine, substitution on the Cl–Pt–Cl axis is much easier than on the Cl–Pt–NH_2R axis. Therefore, the closure of the first ring in *trans*-$[Pt(NH_2C_2H_4OH)_2Cl_2]$ is much faster. For the closure of the second ring in the *trans*- and *cis*-isomers of $[Pt(NH_2C_2H_4OH)(NH_2C_2H_4O)Cl]$, substitution on the Cl–Pt–OR and Cl–Pt–NH_2R axes respectively is necessary. The much higher rate of substitution of the second ring in the *cis*-complex is probably a consequence

of the greater *trans*-influence of the amino-group compared with the OR^- group. One may mention that in platinum(II) complexes the *trans*-influence of the amino-group of alanine bound in a cyclic form is somewhat greater than the *trans*-influence of the carboxy-group[126].

In thioethers forming metal complexes the sulphur atom is at the apex of a trigonal pyramid. Consequently there should be three conformers of platinum and palladium complexes of the type $[Pt(RSC_2H_4SR)X_2]$. An ^1H NMR study[127] has been made of the interconversion of these conformers, involving the inversion of the molecular structures relative to the sulphur atom. It was established that the rate of inversion in the complexes $[Pt(RSC_2H_4SR)X_2]$ and $[Pd(RSC_2H_4SR)X_2]$ depends on the *trans*-influence of the ligands X. The ligands X can be arranged in the following series in terms of their facilitating influence on the inversion process: $Cl^- < Br^- < I^- \ll Ph^-$. It has been shown that the inversion in the palladium complexes is much easier than in the corresponding platinum compounds.

The first kinetic study of the substitution reactions in rhodium(III) complexes was made by Zvyagintsev and Shubochkina[128]. Unfortunately, this study was not developed further subsequently. Systematic investigations, which clearly revealed *trans*-influence in complexes, were also made by Poë and coworkers[129–134]. They investigated extensively the kinetics of substitution reactions of the type

$$trans\text{-}[Rhen_2LY] + Z \rightarrow trans\text{-}[Rhen_2LZ] + Y \quad .$$

According to the results of these studies, the *trans*-influence series for rhodium(III) is as follows: $H_2O < OH^- \simeq \simeq NH_3 \leqslant Cl^- < Br^- < I^-$. In many respects it agrees with the corresponding *trans*-influence series for platinum(II).

It has been established[135] that the rate constants for the substitution of ammonia by water in the complexes $[RhEt(NH_3)_5]^{2+}$ and $[Rh(C_2F_2H)(NH_3)_5]^{2+}$ are smaller by several powers of ten than the rate constant for the substitution of ammonia in the ion $[RhH(NH_3)_5]^{2+}$. However, the analogous substitution in the ion $[RhCl(NH_3)_5]^{2+}$ is slower still. Thus the ligands investigated can be arranged in the following series in terms of their *trans*-influence in rhodium(III) complexes: $H^- \gg Et^- > C_2F_4H^- \gg Cl^-$.

It has been shown[131] that the relative *trans*-influence of ligands depends on the nature of the ligand eliminated from the complex.

The rates of substitution reactions in the iridium complexes *trans*-$[Iren_2X_2]^+$ (X = Cl, Br, or I) and *trans*-$[Iren_2LCl]^+$ (L = NO_2, Br, or I) with various nucleophiles were investigated spectrophotometrically[136]. It was established that these reactions are complicated neither by catalysis nor by stereochemical rearrangements. Their rates are independent of the nature and concentration of the entering ligand. This suggests that the reaction proceeds via a rate-determining stage:

$$trans\text{-}[Iren_2LX]^+ + H_2O \underset{\text{fast}}{\overset{\text{slow}}{\rightleftharpoons}} trans\text{-}[Iren_2LH_2O]^{2+} + X^- \quad ,$$
$$trans\text{-}[Iren_2LH_2O]^{2+} + Y^- \longrightarrow trans\text{-}[Iren_2LY]^+ + H_2O \quad .$$

It follows from the results[136] that the *trans*-influence increases in the series $NCS^- < Cl^- < Br^- < NO_2^- < I^-$. The position of the thiocyanate ion is different from that in the corresponding series for platinum(II). This is because in the iridium(III) complexes the thiocyanate ion is bound to the central atom via nitrogen[137].

The strong *trans*-influence of the hydride ion compared with the chloride ion can be inferred from the finding[138] that, when the complex $[PtH_2Cl(PEt_2Ph)_3]$ reacts with sodium iodide, the chloride ion is readily substituted by iodide. However, it has been established that the substitution for iodide of the chloride ion located opposite another chloride ion requires high temperatures and a long reaction time. The strong *trans*-influence of tertiary phosphines is indicated by the very rapid substitution of the chloride ion located opposite the phosphine in the meridional complex $[Ir(PEt_3)_3Cl_3]$. In hot acetone the substitution takes place in 3 min. On the other hand, the substitution of the two other chloride ions requires boiling for 3.5 h.

The hydrolysis of *cis*-$[Ruen_2X_2]^+$, *cis*-$[Ruen_2(OH)Cl]^+$, and $[Ru(NH_3)_5X]^{2+}$ has been investigated[139]. It was established that the hydrolysis does not entail stereochemical changes in the complexes. The authors put forward a mechanism involving a conjugate base in which *trans*-influence plays a significant role. They assumed that the rapid substitution of the halogen is associated with the *trans*-influence of the amido-group as a result of its interaction of the $p\pi$–$d\pi$ type.

A study[140] where the aquation of the ion $[Cr(H_2O)_5I]^{2+}$ in the presence of Cl^- ions was investigated is of interest. It was established that the main reaction products are $[Cr(H_2O)_6]^{3+}$, while $[Cr(H_2O)_5Cl]^{2+}$ is obtained in a yield of only 10–20%. In another study[141] this reaction was investigated using labelled [^{18}O] water. It was possible to show that the elimination of the ion from the complex is preceded by an appreciable exchange of water in the ion $[Cr(H_2O)_5I]^{2+}$. These findings together with the observation that the exchange of water in the ion $[Cr(H_2O)_5Cl]^{2+}$ is very slow led to the conclusion that the inner-sphere iodide ion has a labilising influence on the water molecule in the opposite position. This conclusion is quite likely and, if it is true, then the above observation can be regarded as the first reliable evidence in support of the occurrence of *trans*-influence in chromium(III) complexes.

trans-Influence in the iron(II)-phthalocyanine complex has been suggested by Jones and Twigg[142], who investigated the rate of substitution of DMSO by imidazole in the axial position in the complex $FePc(DMSO)_2$. The reaction was carried out in DMSO. It was found that the rate-determining stage is the substitution of the first DMSO molecule:

$$FePc(DMSO)_2 + Imid \rightleftharpoons FePc(DMSO)(Imid) + DMSO,$$
$$FePc(DMSO)(Imid) + Imid \rightleftharpoons FePc(Imid)_2 + DMSO.$$

The second molecule is substituted at a higher rate owing to the greater *trans*-influence of imidazole compared with DMSO.

One should note that, when there is only one possibility of substitution, (in the *trans*- or *cis*-position), it is dangerous to reach conclusions concerning directional intramolecular interaction.

Cobalt complexes undoubtedly occupy the first place as regards the number of kinetic studies on substitution reactions. Nevertheless, the problem of the applicability of the *trans*-influence rule to cobalt complexes has not been completely resolved. It is interesting that Basolo and Pearson, who contributed much to the study of the kinetics of substitution reactions in cobalt complexes, did not devote even a single chapter or paragraph to this problem in their book[16]. Although the review of Pratt and Thorp[8] is devoted to the *cis*- and *trans*-effects in cobalt complexes, it fails to elucidate this problem completely. They quote the following ligand series based on the *trans*-influence:

$$\text{alkyls, } SO_3^{2-} \gg \begin{matrix} CN^-,\ N_3^-,\ NO_2^-,\ NH_3 \\ HO^-,\ Cl^-,\ Br^-,\ I^- \end{matrix} > H_2O > NSC^- \quad .$$

Unfortunately, the *trans*-influence series for cobalt complexes depends on the type of complex used as a basis for the substitution reaction series. Any rule must have predictive power. However, for cobalt complexes the above series has so far had a comparatively low predictive power.

VI. THE MUTUAL INFLUENCE OF LIGANDS AND ACID PROPERTIES OF COMPLEXES

A great contribution to the study of the problem of the influence of inner-sphere ligands on the acid properties of complexes was made by Grinberg, who describes them in a monograph[13] (p. 388). As early as 1935, Grinberg and Ryabchikov showed[143] that in platinum(II) complexes ligands with a strong *trans*-influence reduce the acid dissociation of proton-containing groups located in the opposite positions. They studied the acid properties of the isomeric *cis*- and *trans*- complexes $[Pt(NH_3)_2(H_2O)_2]^{2+}$ and established that the first acid dissociation constant of the *trans*-isomer is higher than that of the *cis*-isomer. The second acid dissociation constants are close, but K_2 for the *cis*-isomer is somewhat higher. These findings were explained from the standpoint of the enhancement of the *trans*-influence of the ligands in the series $OH^- > NH_3 > H_2O$. According to the polarisation model of *trans*-influence, with increase of the σ-donor properties of the ligand the *trans*-ligand is depolarised with a consequent weakening of its acid properties. Since the *trans*-influence of water is weaker than that of ammonia, the first acid dissociation constant of the ion $\begin{bmatrix} NH_3 & & H_2O \\ & Pt & \\ H_2O & & NH_3 \end{bmatrix}^{2+}$ should indeed be higher than that of the ion $\begin{bmatrix} NH_3 & & H_2O \\ & Pt & \\ NH_3 & & H_2O \end{bmatrix}^{2+}$. The second dissociation constants are those of the ions $\begin{bmatrix} NH_3 & & OH \\ & Pt & \\ H_2O & & NH_3 \end{bmatrix}^{+}$ and $\begin{bmatrix} NH_3 & & OH \\ & Pt & \\ NH_3 & & H_2O \end{bmatrix}^{+}$. Since the *trans*-influence of the hydroxy-group is somewhat greater than that of ammonia, K_2 for the *cis*-isomer proved to be somewhat higher than for the *trans*-isomer.

This variation of the acid properties was confirmed[144,145] for other pairs of isomeric diaquo-complexes. A similar behaviour was discovered also for octahedral cobalt(III) and chromium(III) complexes[146]. Apart from the influence of the *trans*-ligands on the properties of inner-sphere proton-containing molecules, Grinberg and coworkers discovered the influence of the ligands in the *cis*-position with respect to the dissociating molecule[144]. In particular, they established that an inner-sphere pyridine molecule enhances the acid properties of H_2O molecules in platinum(II) complexes[144,147] and NH_3 molecules in platinum(IV) complexes[148-150]. Stetsenko systematically arranged the available information about the *trans*- and *cis*-influence of ligands on the acid properties of platinum complexes and demonstrated convincingly[151] that, following the replacement of NH_3 by another ligand, the acid properties of the *cis*- and *trans*-complexes $[PtA_2B_2]^{2+}$ change in the same direction (become stronger or weaker). However, the change in the acid properties of the *cis*-isomer is as a rule greater.

The hypothesis of the weakening of the acid properties of inner-sphere proton-containing molecules in both *trans*- and *cis*-positions with increase of the *trans*-influence of ligands is valid only for σ-donors. In 1955 Leden and Chatt[152] estimated the acid dissociation constant of the complex $[Pt(C_2H_4)(H_2O)Cl_2]$ and found it to be approximately 10^{-5}. Thus, despite the very strong *trans*-influence of ethylene, it does not weaken but actually enhances the acid properties of the inner-sphere water molecule. Grinberg postulated that *trans*-active ligands with pronounced π-acceptor properties can intensify the acid dissociation of inner-sphere ligands by increasing the effective positive charge on bivalent platinum[13] (p. 391). Numerous findings confirming this view have now been obtained[94,95,153-158]. The comparatively weak influence on the acid properties of the aquo-complexes of platinum(II) following the substitution of the ammonia molecule in the ion $[Pt(NH_3)_3(H_2O)]^{2+}$ by triphenylphosphine or triphenylstibine was somewhat unexpected[158].

The overall experimental data show that the mutual influence of ligands, shown by a change in acid properties, is relatively non-directional. If the proton-donating molecule is a σ-donor alone, then in principle the influence of the ligands on its acid properties may be reduced to the following cases (Fig. 7): I. by direct transmission of the influence of one ligand to another in the *cis*-position; II. by the transmission of the influence of σ-donors to the trans-position via the p_y orbital; III. by the transmission of the electron density of σ-donors in the *cis*-position via the $d_{x^2-y^2}$ orbital. Thus the increase of *trans*- or *cis*-influence, leading to an increase of electron density in the Pt–Rh bond, should weaken the acid properties of the coordinated molecule RH.

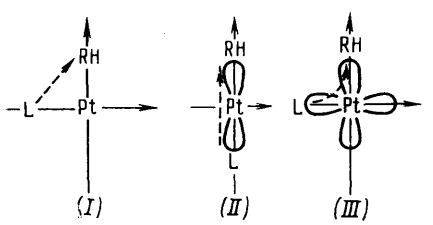


Figure 7. Schematic illustration of the transmission of the influence of a ligand with σ-donor properties.

A different situation should arise for ligands with π-acceptor properties (Fig. 8). If it is assumed that RH exhibits neither π-acceptor nor π-donor properties, then the influence of π-ligands on its acid properties can only be electrostatic. The effective charge of the central atom consists of the nuclear charge and the charges of the electrons in its orbitals. Since a limited number of orbitals are involved in interactions of the π-type, it is useful to infer the change of the effective charge from the shift of electron density in the corresponding orbitals. If the ligand L with π-acceptor properties is fixed on the *X* axis and the location of the ligand RH relative to it is varied, then mainly the d_{xy} and d_{xz} orbitals of the central atom will be involved in the interaction with L. When the ligands are in the *trans*-positions, the centres of gravity of the electron densities of the d_{xy} and d_{xz} orbitals will shift by a distance *l* to the π-acceptor and will be located on the *X* axis (IV*a*, IV*b*).

It is evident from Schemes V*a* and V*b* that for ligands in the *cis*-positions the centres of gravity of the d_{xy} and d_{xz} orbitals are also remote from RH but less so than for the *trans*-positions. Thus, in consequence of the π-acceptor properties of the ligand L, the acid properties of the RH molecule should be enhanced in both the *cis*- and *trans*-positions. However, the influence should be somewhat more marked for ligands in the *trans*-positions.

If the ligand L exhibits π-donor properties, then it should weaken the acid properties of RH in both the *trans*- and *cis*-positions and to a somewhat greater extent in the former case.

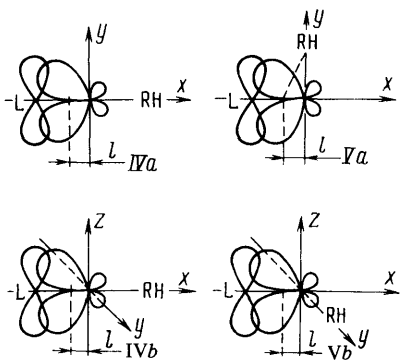


Figure 8. Schematic illustration of the transmission of the influence of a ligand with π-acceptor properties.

The mutual influence of ligands in relation to the acid properties of octahedral complexes, in particular platinum(II) complexes, is less definite. Grinberg and Gil'dengershel' established that the acid dissociation constant of the bromo-complex $[Pt(NH_3)_5Br]^{3+}$ is 5.6×10^{-9} and that of the chloro-analogue $[Pt(NH_3)_5Cl]^{3+}$ is 7.9×10^{-9}.[160] This is consistent with the polarisation model of *trans*-influence. The bromide ion, which has a stronger *trans*-influence than the chloride ion, causes a greater counter-polarisation of the ammonia molecule in the opposite position. As a result the acid properties of the bromo-complex are weaker than those of the chloro-complex. However, from this point of view the acid properties of *cis*-$[Pt(NH_3)_4Cl_2]^{2+}$ should be weaker than the acid properties of *trans*-$[Pt(NH_3)_4Cl_2]^{2+}$, since in the first case two of the four ammonia molecules are in the *trans*-positions with respect to the chloride ions. On the other hand, experimental data indicate more marked acid properties of the *cis*-isomer[161]. From this, it follows that the difference between the *trans*-influences of chlorine and ammonia in platinum(IV) complexes is less important than the repulsion of the protons of the molecules in the *cis*-positions or the polarity of the complex ion.

Spitsyn et al. established that the ligands can be arranged in a definite series in terms of their influence on the acid properties of certain platinum(IV) aquo-complexes. On this basis, they proposed a *trans*-influence scale for ligands[162].

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In conclusion, one must say that so far there is no theory which explains all the experimental facts and which embraces all the aspects of the mutual influence of ligands in complexes. One of the problems which still awaits solution is the manifestation (or absence) of the mutual influence of ligands in equilibrium systems involving ligand substitution. Systematic studies on this problem are being made by Peshchevitskii[112,163-166].

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The Reactions of Hydrocarbons on Membrane Catalysts

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The reactions of different classes of hydrocarbons on catalysts selectively permeable with respect to hydrogen are considered. The possibilities of membrane catalysts to increase the rate and selectivity of reactions, to obtain incomplete hydrogenation products, and to decrease the competition between the adsorption of the substance hydrogenated and hydrogen are demonstrated. The coupling of reactions on membrane catalysts whereby it is possible to achieve a reaction, which does not occur spontaneously, as a result of the decrease of the free energy of the coupled reaction when the substance common to the two reactions passes through the membrane catalyst is discussed.
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1. INTRODUCTION

Membrane catalysts differ from other heterogeneous catalysts in that they exhibit selective permeability with respect to only one reactant. The principal metals investigated as membrane catalysts are those which are to some extent permeable to hydrogen. Such metals have been used as cathodes on one surface of which hydrogen was obtained electrochemically and on the other a reaction with the hydrogen diffusing through the metal was carried out. Studies have also been made on the hydrogenation of olefins and of other reactions on a palladium membrane with gaseous hydrogen on its other side.

Even before the appearance of membrane catalysts, catalytic hydrogen redistribution processes between the molecules of the same or different substances were discovered (see Section 8). It was established that the best catalyst for such reactions is palladium, but the reason for this and also the mechanism of the redistribution of hydrogen remained obscure.

Studies on the redistribution of hydrogen in unsaturated cyclic hydrocarbons on palladium and platinum films showed (see Gryaznov's review[1]) that the process consists of a set of dehydrogenation and hydrogenation reactions. The ratios of the rates of these reactions depend on the ability of the catalyst to absorb hydrogen removed from the dehydrogenated molecules, to maintain it in an active state for hydrogenation, and to supply it to the molecules undergoing hydrogenation. This idea explains the advantages of palladium over other metals as hydrogen redistribution catalysts as well as many other experimental results.

Subsequently the reactions of hydrocarbons involving the elimination and addition of hydrogen were studied on membrane catalysts permeable with respect to hydrogen alone. This made it possible to achieve coupled reactions[2-6], occurring on different sides of the membrane catalyst, as a result of the transport through the catalyst of a substance, for example hydrogen, which is formed on one surface of the catalyst and is consumed on the other. Two reactions coupled in this way accelerate one another without mixing all the reactants involved in them, which was inevitable in coupled reactions known previously, occurring in a single reaction volume in the absence of a catalyst or on the same catalyst surface. Similar results were obtained independently[7] in the USA. In recent years new membrane catalysts and methods for the preparation on them of olefinic dienes, cyclo-olefins, and aromatic hydrocarbons were developed in the USSR[8-15].

This review surveys the journal and patent literature dealing with the reactions of hydrocarbons on membrane catalysts and with the coupling of reactions on such catalysts.

2. EFFECT OF THE HYDROGEN SORBED BY THE CATALYST ON REDUCTION REACTIONS

The catalytic activation of hydrogen dissolved in palladium was noted in a report[16] on the diffusion of hydrogen through palladium. In contact with hydrogen-saturated palladium, iron(III) salts were converted into iron(II) salts and hydrogen halides were obtained from the halogens. Certain organic compounds were reduced on palladium[17]. Granular zinc coated with palladium black and treated with hydrochloric acid to saturate the palladium with hydrogen was used for this purpose[18]. Subsequently the total hydrogenation of benzene, toluene, xylenes, and ethylbenzene was achieved on palladium black[19]. It was noted[20] that benzobicyclononene is hydrogenated to dicyclohexylmethane on palladised activated charcoal both in the presence and absence of free hydrogen.

It was shown in 1934[21] that below room temperature the hydrogen sorbed by a palladium film hydrogenates olefins faster than the hydrogen entering from the gas phase. The rate of hydrogenation of ethylene or butene under the experimental conditions[22] was not limited by the rate of hydrogen

transfer from the bulk of the palladium layer onto its surface. In the course of hydrogenation hydrogen is extracted from palladium faster than on evacuation with a high-vacuum pump. At higher temperatures the rate of hydrogenation of benzene is independent of the partial pressures of the reactants. On this basis, it was postulated that the hydrogen dissolved in palladium participates in the reaction with adsorbed benzene[23]. The constancy of the rate of hydrogenation of benzene (on raising the temperature from 120° to 220°C in the presence of a palladium catalyst deposited on silica gel[24] and from 168° to 220°C on palladium black[25]) was interpreted[25] as a consequence of phase transitions in the palladium–hydrogen system. When the palladium catalyst is saturated by hydrogen at room temperature in the course of several tens of hours, its activity with respect to the hydrogenation of benzene falls sharply. On treatment with benzene vapour, the activity of the catalyst is gradually restored, which was interpreted[26] as proof that the hydrogen-rich β-phase of the palladium–hydrogen system is catalytically inactive. The increase of the activation energy for the hydrogenation of benzene with decrease of temperature leads to the same conclusion[27]. On the basis of all these data for the hydrogenation of benzene, it was concluded[28] that pure palladium and the α-phase of the palladium–hydrogen system are catalytically active and that on formation of considerable amounts of the β-phase the activity falls sharply.

Nickel, platinum, copper, and tungsten films obtained by the condensation of their vapours in a high vacuum are inactive with respect to the hydrogenation of ethylene, but films of these metals prepared in the presence of specific amounts of hydrogen, oxygen, or nitrogen are catalytically active[29]. The promotion of Raney nickel catalysts by hydrogen was discovered[30–32] in the hydrogenation of various substances by the hydrogen retained in the catalysts. The hydrogen adsorbed by the catalyst was removed reversibly and without an appreciable decrease of the activity of the catalyst. The removal of the hydrogen dissolved in the metal was irreversible with deactivation of the catalyst, since the consumption of structural hydrogen in hydrogenation alters the composition of the active surface. The activity was restored[33] by heating Raney nickel at 300°C in hydrogen.

In contrast to Raney nickel, palladium black retains its catalytic activity and the capacity to sorb hydrogen at room temperature after the removal on hydrogenation of the hydrogen retained by it[34].

As a result of several extractions of hydrogen from Raney nickel by the substance hydrogenated, the active structure of the catalyst is completely disrupted[35]. After this, the time required to saturate the catalyst surface by hydrogen until the attainment of the reversible hydrogen potential increases sharply and the hydrogen deposited on the surface is not involved in hydrogenation. The ability of palladium to give up comparatively readily the adsorbed and dissolved hydrogen makes it one of the best catalysts for low-temperature hydrogenation. The rate of reaction increases with increase of pressure to 3 atm, despite the fact that the catalyst surface is covered by hydrogen at a pressure as low as 1.5–2 atm. At low temperatures an increase of hydrogen pressure increases the degree of involvement in the reaction of the hydrogen dissolved in palladium. To elucidate the state of the hydrogen sorbed by Raney nickel, a potentiometric method was used[36]. In the course of the hydrogenation of acetylene a constant potential of the nickel catalyst was rapidly reached and the removal of hydrogen from the catalyst continued at a high rate, which the authors[37] regarded as proof that the hydrogen dissolved in the catalyst is also involved in the reaction.

With increase of the palladium content on the surface of the carrier, there is initially a slow and then a rapid increase of the rate of hydrogenation of unsaturated compounds in solution, which was explained by the appearance[38] of palladium crystals in which hydrogen is dissolved. This is consistent with the finding that in the region of low surface coverages of the carrier by palladium the rate of hydrogenation of triple bonds is lower than that of double bonds. When the coverage of the carrier corresponds to a sharp increase of the rates of both these processes, triple bonds are hydrogenated more readily than double bonds, as on massive palladium. In the latter case the author[38] assumes that triple bonds are hydrogenated mainly by the dissolved hydrogen, while in the presence of a catalyst with a low percentage of palladium it involves adsorbed hydrogen. A similar explanation of the increase of the specific activity of palladium with respect to hydrogenation for high surface coverages of the carrier by palladium was given in an earlier study[39], where it was suggested that the formation of the palladium crystal lattice and the dissolution of hydrogen in it lead to a type of activation of hydrogen different from that on catalysts with a low percentage of palladium. Such increase of the specific catalytic activity with increase of the degree of coverage has not been observed in catalytic oxidation[40].

In view of the foregoing findings, data on the catalytic activities of palladium hydride phases are interesting, but few such results are available. When the α- and β-phases of the palladium–hydrogen system coexist, the rate of hydrogenation of ethylene and propene on palladium hydride increases according to Wicke's data[41] by a factor of two with increase of the hydrogen: palladium atomic ratio from 0.1 to 0.4. Under these conditions, the surface concentration of hydrogen is not determined by its partial pressure but by its volume concentration in palladium. The rate of hydrogenation is not limited by the diffusion of hydrogen from the bulk phase to the catalyst surface and the rate of sorption of hydrogen at -78°C by palladium powder falls by a factor of 100 on passing from pure hydrogen to an equimolar ethylene–hydrogen mixture. Data for the hydrogenation kinetics and even the results of experiments with palladium deuteride show that atomic hydrogen adds to adsorbed olefin molecules on the palladium surface in the rate-limiting stage[42].

As already mentioned, it has been concluded[28] that the formation of considerable amounts of the β-phase of the palladium–hydrogen system reduces sharply the catalytic activity for the hydrogenation of benzene. The rate of hydrogenation of propene on the palladium catalyst decreases[43] after the catalyst has been treated with hydrogen. A similar effect has been observed[44] in the hydrogenation of ethylene on nickel. On the other hand, the catalytic activity of a nickel–copper alloy increases after treatment with hydrogen. The catalytic activity of nickel–palladium alloys containing between 9.5 and 25 wt.% of palladium changes little[45] after treatment with hydrogen, while the activity of nickel films for the ethylene hydrogenation reaction decreases after treatment with hydrogen. Evidence has been obtained[46,47] for the decrease of the catalytic activity of nickel and nickel–copper films on formation of hydride phases.

Thus the activity of many metallic hydrogenation catalysts increases following the sorption by the catalyst of specific amounts of hydrogen, while the formation of hydrogen-rich phases can reduce the catalytic activity.

3. HYDROGENATION BY HYDROGEN SUPPLIED THROUGH THE MEMBRANE CATALYST

In a number of studies hydrogenation reactions were investigated on a catalyst cathode through which hydrogen, obtained electrolytically on the other surface of the same cathode, passed to the reaction zone. The hydrogenation was then achieved either electrocatalytically or by the usual catalytic procedure.

A study[48] of the electrodiffusion of hydrogen through a palladium cathode showed that the rate of permeation by hydrogen increases after the addition of substances such as pyridine, sodium arsenite, and hydrogen sulphide to the electrolyte from which hydrogen passed to the cathode. On the other hand, the addition of the same substances to the electrolyte in contact with the outlet surface of the membrane electrode decreased the rate of diffusion of hydrogen. Electrochemical reduction of pyridine to piperidine on a nickel catalyst was accelerated by the addition of mercury(II) chloride, in contrast to the usual catalysis. This was explained[48,49] by the fact that the adsorption of the poison molecules on the surface of the cathode reduces sharply its adsorption potential and facilitates the transfer of the hydrogen atoms adsorbed on the cathode to the molecules undergoing hydrogenation.

The reduction of various substances on membrane steel, palladium, and platinum foil catalysts has been studied[50] with the aid of a nickel test tube part of the lateral surface of which had been replaced by the foil. Within the tube, there was an axial platinum anode and the electrolyte. The tube was immersed in a hot solution of the substance to be hydrogenated. The tube broke up fairly rapidly in the course of the experiment and the principal results were obtained for membranes welded to the edges of a slot in a copper disc to which two glass cylinders with reflux condensers were clamped via polyethylene washers. One cylinder, fitted with a platinum anode, contained the electrolyte and the other a solution of the substance hydrogenated. One surface of the membrane was the cathode and the hydrogen evolved on it passed to the other surface, where catalytic reduction took place. However, such steel and palladium membranes too worked for only a short time owing to recrystallisation and chemical effects leading to the formation of a leak. A platinum membrane could be used much longer. Partial hydrogenation of oleic acid to stearic acid and the reduction of nitrobenzene to aniline were carried out on a platinum membrane at a rate of hydrogen transfer of 6×10^{-6} g-atom cm^{-2} min^{-1}.

Subsequently a study was made[51] of the interaction of oxygen with electrolytic hydrogen diffusing through a steel membrane. It was found that at low current densities the oxygen adsorbed on the outlet surface of the membrane reduces the rate of permeation of hydrogen and at higher current densities it increases the rate of permeation compared with experiments in which the recombining hydrogen was desorbed into a vacuum. The formation of water in the interaction between adsorbed oxygen and hydrogen diffusing through the membrane was observed only in certain experiments at the maximum experimental temperature of 180°C. When a mixture of gaseous hydrogen and oxygen was supplied to the hydrogen-saturated surface of the membrane, water was not formed. At temperatures up to 190°C molecular nitrogen did not react with the hydrogen diffusing through a steel membrane and did not affect the rate of permeation of hydrogen through it.

Cyclohexene was hydrogenated within a palladium–silver alloy tube on the outer surface of which hydrogen was obtained electrochemically[53]. The hydrogenation of ethylene in a palladium tube through the walls of which diffused hydrogen obtained by the electrolysis of a solution of alkali on the outer surface of the tube proceeds much faster at 50°C than in the absence of the supply of hydrogen through the catalyst[53,54]. The hydrogenation of acetylene is accelerated even more as a result of the diffusion of hydrogen through the walls of a palladium tube[55]. However, an increase of the rate of reaction was not observed in the hydrogenation of maleic acid[56] where hydrogen diffused through both a smooth palladium membrane and one coated with palladium black. The authors[56] noted that these results confirmed the conclusion[57] that an electron is initially supplied to the molecule being reduced and then a proton, which can migrate from solution in cathodic reduction and from palladium in the usual catalytic hydrogenation.

It was shown[58] that hydrogen atoms from the palladium membrane are not involved in chain reactions of hydrogen with chlorine and with oxygen. Subsequently[59] a palladium membrane in contact with hydrogen on one side and with an ethylene–hydrogen mixture on the other was used to investigate the steady-states of the catalyst in heterogeneous reactions. A decrease of the concentration of hydrogen in the palladium foil was observed in the hydrogenation of ethylene compared with the concentration in equilibrium with the partial pressure of hydrogen in a mixture of ethylene. These results led to the conclusion that hydrogen atoms are involved in the reaction, but ethylene is hydrogenated simultaneously also by molecular hydrogen adsorbed on palladium. The exchange of hydrogen and deuterium, the interaction of hydrogen and oxygen, and the hydrogenation of ethylene on a palladium membrane were investigated by a similar method[60,61]. These reactions have radical mechanisms. If the amount of oxygen in the mixture with hydrogen is much greater than required by stoichiometry, the steady-state concentration of atomic hydrogen on the surface of the membrane catalyst is found to be smaller by a power of ten than the equilibrium concentration. No deviations from the steady-state concentration of atomic hydrogen from the equilibrium value were observed in the course of the hydrogenation of ethylene at temperatures from 200° to 300°C. This result, which differs sharply from that obtained at much lower temperatures[22], shows that at 200°C the rate of dissociation of hydrogen molecules and of recombination of hydrogen atoms on the palladium surface is greater by a power of ten than the rate of hydrogenation, while below room temperature the rates are comparable. A method has been developed[62,63] for the investigation of the mechanism of heterogeneous catalytic reactions with the supply and removal of hydrogen through a palladium capillary. In particular, the hydrogenation of ethylene in a gradient-free system was studied on the surface of this capillary. The kinetic data obtained at 200°C are consistent with the hypothesis of the consecutive addition of hydrogen atoms to the ethylene molecule. At higher temperatures the reaction mechanism changes.

A membrane consisting of a porous partition on which the catalytically active substance is deposited has been suggested for the liquid-phase hydrogenation of organic substances[64]. Hydrogen is supplied on one side of this partition, for example a glass sinter with a layer of nickel, and on the other side the substance to be hydrogenated, for example cottonseed oil, is present. The catalyst is not mixed with the hydrogenation products and the process can be made continuous and not cyclic. Later it was noted[65] that porous membrane catalysts can be used in principle also for the dehydrogenation and oxidation of organic compounds in the liquid phase. However, porous membrane catalysts are unsuitable for gas-phase processes, since

not only hydrogen but also the substance hydrogenated or oxidised can diffuse through the pores to the second reactor zone. Moreover, one loses an important advantage of non-porous membrane catalysts, namely that the hydrogen (or oxygen) transferred through them enters the reaction zone in the active, atomic state.

A study[66] of the diffusion of oxygen through a palladium membrane showed that the oxygen supplied via the membrane increases the catalytic and electrochemical activity of the membrane, in contrast to adsorbed oxygen, which inhibits electrochemical oxidation (for example of formic acid). The diffusion through the same membrane of part of the hydrogen formed in the dehydrogenation of formic acid decreases the oxidation current. It has been established[67,68] that, in the oxidation of hydrazine on a palladium membrane, the hydrogen formed as an intermediate in the electrochemical process is sorbed. Sorption of hydrogen can occur in the dissociation of the intermediates in the oxidation of hydrazine.

To transfer atomic hydrogen through palladium and palladium alloy partitions to the substance hydrogenated, a reactor with a spiral palladium tube was employed[69]. Hydrogen was supplied within the spiral and ethylene or styrene was hydrogenated on its outer surface by the hydrogen diffusing through palladium. A tube made of palladium alloy containing 23% silver, coated on the outside by a layer of gold 0.025 mm thick, served as the catalyst for the hydrogenation of cyclohexene[70]. The gold layer prevents the diffusion of hydrogen through the membrane from the side in contact with cyclohexene vapour, while hydrogen within the tube can diffuse through the walls. It was found that the rate of hydrogenation is proportional to the olefin pressure and the square of the degree of surface coverage of the catalyst by atomic hydrogen. The isomerisation of but-1-ene and *trans*-but-2-ene was not observed at 300°C on a palladium–silver tube which had no gold coating and was permeable to hydrogen from both sides[71], while the introduction of hydrogen into the tube caused rapid isomerisation of both hydrocarbons on the outer surface of the tube. With increase of the amount of hydrogen which has diffused, the hydrogenation of the butenes to butane became the dominant process. The removal of hydrogen via the membrane catalyst led to the dehydrogenation of butane, but the catalyst lost its activity after the complete removal of hydrogen. The supply of hydrogen through the membrane catalyst restored its activity, while gaseous hydrogen did not have this effect. The authors[71] explained this by the stable adsorption of olefins on the catalyst, which prevents the adsorption of hydrogen from the gas phase. According to their data[71], the first stage in the isomerisation of olefins is the addition of a hydrogen atom to the olefin molecule, after which hydrogen is split off. The diffusion of hydrogen formed in the dissociative adsorption of olefins on a palladium–silver alloy into the bulk of the alloy reduces the surface concentration of atomic hydrogen and the catalytic activity of the alloy with respect to isomerisation. The alloy consisting of 40% of palladium and 60% of gold, which dissolves much less hydrogen, exhibits a steady activity with respect to isomerisation.

The hydrogenation of but-1-ene and cyclohexene on the gold-plated surface of a palladium–silver tube with hydrogen supplied via its walls is slower by a factor of 60–200 than the diffusion of hydrogen through the same palladium alloy (with 23% of silver) alone. The rate of hydrogenation increases with increase of the rate of diffusion of hydrogen, which was explained[72] by a change in the distribution of hydrogen concentrations in the membrane.

Experiments with a thin-walled tube made of a palladium alloy containing 25% of silver, where the vapour of the substance to be hydrogenated was supplied inside the tube and hydrogen at a pressure of 3.5 atm was on the outside, showed[73] that, despite the low surface area of the membrane catalyst (9.8 cm^2), but-1-ene is hydrogenated to the extent of 82% at a temperature as low as 50°C. At this temperature the rate of diffusion of hydrogen through the catalyst (2.5 ml min^{-1}) does not reach the rate of supply of butene (3 ml min^{-1}). It is suggested[73] that in the presence of the olefin at the outlet surface of the membrane the permeability with respect to hydrogen may be enhanced by its rapid removal from the surface by the molecules being hydrogenated. After passing butene for 10 h, no decrease of catalytic activity was observed. At 250°C olefinic and acetylenic compounds, including even di-t-butylethylene which is sterically hindered, were hydrogenated quantitatively.

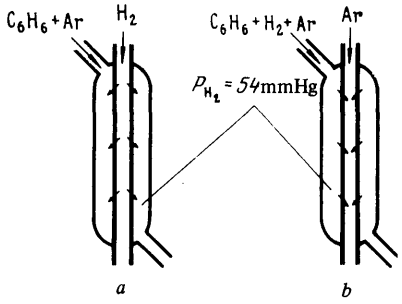

Figure 1. Schematic illustration of the supply (*a*) and removal (*b*) of hydrogen through a membrane catalyst in the course of the hydrogenation of benzene at a constant hydrogen partial pressure in the reaction zone.

The hydrogenation of benzene on the palladium alloy with 5% of nickel and the effect of the adsorption of benzene and cyclohexane vapours on the permeability of this membrane catalyst with respect to hydrogen and on its activity have been investigated[74,75]. It was established that the adsorption of cyclohexane vapour has little effect on the diffusion of hydrogen through the palladium–nickel alloy, while the adsorption of benzene vapour reduces the permeability. At a constant temperature and constant benzene and hydrogen partial pressures in the reaction zone the rates of hydrogenation are not the same for the supply and removal of hydrogen through the membrane catalyst (see the schematic arrangement in Fig. 1). This indicates the absence of equilibrium between the adsorbed hydrogen and the gas phase. The supply of hydrogen through the membrane catalyst increases the rate of hydrogenation of benzene only for a low ratio of the partial pressures of hydrogen and benzene in the reaction zone. If, on the other hand, the ratio is sufficiently high to ensure the required concentration of adsorbed hydrogen, then the supply of hydrogen via the membrane catalyst decreases the rate of hydrogenation, probably as a result of the displacement of some of the benzene molecules from the catalyst surface. The hydrogenation of benzene on the membrane catalyst leads not only to cyclohexane but also to cyclohexene, which is thermodynamically unstable under these conditions.

The high selectivity of hydrogenation on a membrane catalyst is due to the fact that the concentration of hydrogen adsorbed on its surface can be regulated by altering the hydrogen pressure on the opposite side. For this reason, membrane catalysts make it possible to obtain incomplete hydrogenation products and lead to new possibilities for reducing the competition between the adsorption of the substance hydrogenated and hydrogen, for estimating their surface concentrations, and for investigating the mechanism of reactions involving the addition of hydrogen.

4. HYDRODEALKYLATION OF BENZENE AND NAPHTHALENE HOMOLOGUES ON PALLADIUM ALLOYS

The hydrodealkylation reaction of benzene and naphthalene homologues is important not only in connection with the growing production of benzene from toluene and naphthalene derived from petroleum but also for the partial elimination of alkyl groups, for example in order to convert dimethylnaphthalenes into methylnaphthalenes. It was particularly important to elucidate the possibility of hydrodealkylation on palladium alloys suitable for use as membrane catalysts, because this is one of the few reactions involving the addition of hydrogen which is thermodynamically feasible at the temperatures of the dehydrogenation of alkanes and alkenes considered in the subsequent sections.

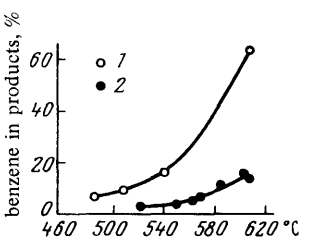

Figure 2. Variation of the benzene content in toluene hydrodealkylation products on the quenched (1) and unquenched (2) palladium–10% rhodium alloy.

It was found[76] that the rate of hydrodemethylation of toluene on the palladium alloy with 10% of rhodium increases by a factor of 6 with increase of temperature from 500° to 590°C. The activity of the catalyst can be increased by special heat treatment before the experiments, as was observed previously[77–79] for platinum films. Fig. 2 shows that after "quenching", the exposure of the palladium–rhodium alloy to a stream of hydrogen at 700°C for 20 min, and rapid cooling to the temperatures of the catalytic experiments, the rate of hydrodemethylation of toluene increases by a factor of 4 compared with the value before the heat treatment. The activity of the palladium alloy with 5.5% of nickel in relation to the hydrodemethylation of toluene proved to be lower than that of the alloy with 10% of rhodium, but after the above heat treatment of the catalyst the yield of benzene from toluene reaches 65% at 605°C.

The palladium alloy with 5% of rhenium catalyses the hydrodemethylation of toluene at a temperature as low as 320°C, but the yields are low and increase little with increase of temperature[80]. Toluene is converted into benzene to the extent of 21% at 547°C on the palladium alloy with 2% of molybdenum[81].

In a study of the effect of the substituent position in methyl- and dimethyl- naphthalenes on the rate of their hydrodemethylation binary alloys of palladium with molybdenum, rhenium, and nickel, consisting of solid solutions, were employed[82,83]. In the presence of alloys with 2.5 and 15% of molybdenum, 5% of rhenium, and 5% of nickel, the methyl groups of alkylnaphthalenes are eliminated more readily from the β-positions than from the α-positions. For example, at 527°C on the palladium–nickel alloy α-methylnaphthalene is converted into naphthalene to the extent of 29%, while the conversion of β-methylnaphthalene is 36%. Under the same conditions, the 1,6-dimethylnaphthalene conversion products were found to contain 1.5 times more α-methylnaphthalene than β-methylnaphthalene. These results are not complicated by isomerisation. In particular, the hydrodemethylation of 1,4- and 1,5-dimethylnaphthalene does not lead to the formation of β-methylnaphthalene.

The higher rate of elimination of groups in the β-positions and the absence of the isomerisation of α-methylnapthalene to β-methylnaphthalene were explained by postulating that alkylnaphthalene molecules are adsorbed via the plane of the ring on the flat sections of the catalyst surface. The carbon atoms of the methyl groups in the α-positions which deviate according to Coulson[84] from the plane of the naphthalene ring owing to the overlapping of the van der Waal's spheres of the methyl group and the hydrogen atom in the peri-position, are more remote under these conditions from the catalyst surface than the carbon atoms of the β-methyl groups in the plane of the naphthalene ring (Fig. 3).

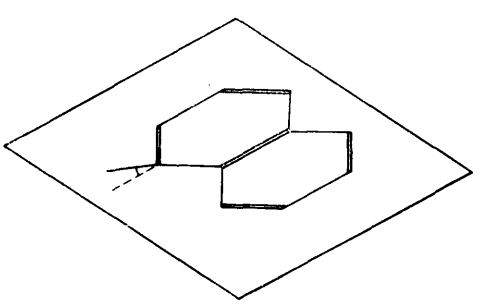

Figure 3. Schematic illustration of the adsorption of an α-methylnaphthalene molecule on a planar section of the catalyst surface.

This model suggests that the dimethylnaphthalenes in which the deviations of the methyl groups from the plane of the ring are particularly marked would be most difficult to demethylate. The available data[85] show that these deviations are maximum in 1,8-dimethylnaphthalene, the deviations of the two adjacent α- and β-methyl groups in 1,2-dimethylnaphthalene are somewhat smaller, and the deviations of the two adjacent β- and β′-methyl groups in 2,3-dimethylnaphthalene are smaller still. It has been stated[83] that the rate of hydrodemethylation should increase

in the following sequences of dimethylnaphthalenes: 1,8 < 1,2- < 2,3- < 1,4-, 1,5- < 1,3-, and 1,6- < 2,6- and 2,7-. The experimental data for the palladium alloy with 5% of nickel at 525°C are consistent with the above sequences (Table 1).

Table 1.

Dimethylnaphthalene	2,3-	1,4-	1,5-	1,6-	1,3-	2,6-
Yield of hydrodemethylation products, %	27,8	35,5	36,3	36,8	37,0	42,4

Experiments with dimethylnaphthalenes on the palladium–2% molybdenum alloy at 477°C also confirmed[81] the above reactivity series (Table 2).

Table 2.

Dimethylnaphthalene	1,8-	1,2-	2,3-	1,6-	2,6-
Yield of hydrodemethylation products, %	8	10	13	24	31

5. DEHYDROGENATION OF ALKANES AND ALKENES WITH ELIMINATION OF THE HYDROGEN FORMED THROUGH MEMBRANES

Many investigators attempted to increase the degree of dehydrogenation reactions by removing the hydrogen formed through membranes. Thin-walled platinum or palladium tubes, heated to 800°C, which were not used as dehydrogenation catalysts but merely as membranes permeable to hydrogen, were suggested for this purpose[86].

Porous partitions[87] obtained by subliming zinc from the walls of a brass tube were used as the catalytic membranes (cf. Warrick and Mack[88]). Palladium was also tested as the refractory component of the alloy; zinc was sublimed from a palladium–copper–zinc alloy. Such porous membranes were naturally not permeable to hydrogen alone and in addition they lost their permeability on contact with the vapours of hydrocarbons and other organic compounds. Porous tubes in which iron(III) and chromium oxides were deposited on the walls of the pores as well as perforated tubes where iron(III), molybdenum, aluminium, and chromium oxides were pressed into the apertures suffered from the same disadvantages[89].

Oxygen-permeable membranes have been proposed[90] to increase the degree of dehydrogenation of hydrocarbons. The reactor is divided into two zones by thin-walled silver tubes. The initial hydrocarbon is supplied to one zone filled with an alumina–chromium oxide catalyst or another dehydrogenation catalyst. The hydrogen formed on dehydrogenation is partly oxidised by the oxygen diffusing through the walls of the silver tubes from the other zone of the reactor where air is admitted. The decrease of the partial pressure of hydrogen achieved in this way in the dehydrogenation zone ensures a 20% conversion of butene into butadiene with a selectivity of 0.94 at 538°C and a pressure of 1.2 atm, whereas under the same conditions but in the absence of silver membranes dehydrogenation does not take place at all. It is noteworthy that the authors[90] failed to say anything about the diffusion of hydrogen from the dehydrogenation zone via the walls of the silver tubes, although the permeability of silver to hydrogen is greater by a factor of 3 than the permeability to oxygen. For this reason, the above effect might have been caused by the diffusion of hydrogen through the silver membranes and not of oxygen. The high selectivity, which is usually not observed in oxidative dehydrogenation, can also be explained from this point of view.

The method of preparation of hydrogen from hydrogen-containing substances[91], for example by the conversion of methane in a mixture with water vapour on a nickel catalyst at 450°C, provides for the removal of the hydrogen formed via the walls of tubes made of the palladium–25% silver alloy. The tubes are threaded through the catalyst bed in such a way that no point on the surface of the granular catalyst is further than 6 mm from the surface of the tubes. It is emphasised[91] that the tubes serve only as membranes permeable to hydrogen but do not exhibit a catalytic effect, since they cannot compete with the granular catalyst, which has a much greater surface area.

In contrast to the methods for the removal of hydrogen from the dehydrogenation zone[86–91], other workers[92,93] used foils made of binary alloys of palladium with nickel, ruthenium, rhodium, rhenium, silver, and platinum as membrane catalysts permeable to hydrogen alone. It was found[92] that, in the presence of the palladium alloy with 5.5 wt.% of nickel, isopentane is converted into isoprene and isopentenes. With increase of temperature to 558°C, the content of isoprene in the product reaches 18.6% and that of isopentenes 10.5%. On the palladium alloy with 10% of rhodium, 23.9% of isoprene and 6% of isopentenes were obtained from isopentane at 588°C. The dehydrogenation of 2-methylbut-1-ene on the palladium alloy with 5.5% of nickel at 287°C led to 81% of isoprene without side products[8]. A similar high activity and selectivity in the dehydrogenation of 2-methylbut-1-ene was shown by the palladium alloy with 10% of rhodium in the presence of which 78.7% of isoprene was obtained at 271°C.

The kinetics of the dehydrogenation of chromatographically pure 2-methylbut-1-ene, 2-methylbut-2-ene, and 3-methylbut-1-ene were investigated[93] on the palladium–5.89% nickel alloy. With increase of temperature from 340° to 400°C, the yield of isoprene from 3-methylbut-1-ene was found to be higher than for other isopentenes and to increase for a virtually constant content of the remaining isopentenes in the products. Consequently under these conditions isoprene is obtained from 3-methylbut-1-ene and not from its isomerisation products. At higher temperatures isoprene is formed mainly from 2-methylbut-2-ene produced by the isomerisation of 3-methylbut-1-ene. The dehydrogenation of pure 2-methylbut-2-ene to isoprene is complicated to a relatively small extent by isomerisation, since the change in the content of the 2-methylbut-2-ene isomerisation products is small compared with the increase in the content of isoprene when the temperature is increased. On the other hand, the isomerisation of 2-methylbut-1-ene to 2-methylbut-2-ene is much faster than dehydrogenation: the contents of 2-methylbut-2-ene and isoprene in the reaction products of 2-methylbut-1-ene and 2-methylbut-2-ene are almost the same.

A mixture of 95% of 2-methylbut-2-ene and 5% of 2-methylbut-1-ene was dehydrogenated at the Sterlitamak experimental SKI-3 synthetic rubber factory in enlarged reactors with membrane catalysts made of the same alloy[93]. At 430°C, a rate of supply of the mixture of the vapours of isopentenes and argon of 2.4 litre h^{-1}, and a partial pressure of isopentenes of 3 mmHg the yield of isoprene in the initial period of the experiment was 38.8%. The hydrogen evolved diffused through the membrane catalyst and was removed by the carrier gas. After 6 h of operation of the system, the yield of isoprene fell to 16.6%. Regeneration of the catalyst with air not only restored but also enhanced its activity. After operating for 20 h and four regenerations of the palladium–nickel foil catalyst, the maximum yield of isoprene at 430°C and a partial pressure of isopentenes of 3 mmHg was 54%.

The foregoing findings show that palladium alloy membrane catalysts exhibit a high activity and selectivity in the formation of isoprene and other dienes by dehydrogenation.

6. DEHYDROGENATION OF CYCLOHEXANE ON PALLADIUM AND PALLADIUM ALLOYS

The dehydrogenation of cyclohexane was investigated on palladium–ruthenium[94], palladium–silver[95,96], palladium–nickel and palladium–platinum[96], and palladium–tungsten and palladium–ruthenium[97] alloys, which are permeable to hydrogen alone, as well as on palladium foil[98]. Experiments[95] with a tube made of the palladium–23% silver alloy around which the required hydrogen pressure or a vacuum was established while the external surface served as the catalyst showed that the dehydrogenation of cyclohexane results in the formation of cyclohexene, the content of which increases at low hydrogen pressures in the reaction zone and at high rates of elimination of hydrogen from this zone. It is interesting that in the complete absence of hydrogen the catalyst did not show any activity in relation to the dehydrogenation of cyclohexane. The results led to the following mechanism for the dehydrogenation involving adsorbed hydrogen atoms and hydrogen atoms dissolved in the catalyst:

$$C_6H_{12} + H_{ads.} \xrightarrow{k_1} C_6H_{11}^{\cdot} + H_{ads.} + H_{soln.},$$

$$C_6H_{11}^{\cdot} + H_{ads.} \xrightarrow{k_2} C_6H_{12},$$

$$C_6H_{11}^{\cdot} \underset{k_4}{\overset{k_3}{\rightleftarrows}} C_6H_{10} + H_{ads.}.$$

Having assumed that cyclohexane molecules, the cyclohexyl radicals formed them, and cyclohexene molecules are adsorbed on the catalyst, it was found that in the steady state the concentration ratio $[C_6H_{10}]/[C_6H_{12}] = k_1k_3/k_2k_4[H_{ads}]$, i.e. is inversely proportional to the concentration of adsorbed hydrogen atoms. This is consistent with experimental data. After prolonged contact of the reaction mixture with the membrane catalyst, benzene was found in the products.

A study of the dehydrogenation of cyclohexane to benzene on palladium foil in a flow-circulation system showed[98] that the rate of reaction is described satisfactorily by the equation $w = kp^m_{C_6H_{12}}p^n_{H_2}$, where $m = 0.5$ and $n = 0.2$ at 250°C and $m = 0.6$ and $n = 0.5$ at 322°C. The fact that the p_{H_2} exponent is positive and does not exceed 0.5 under the conditions indicated suggests, in agreement with Gryaznov et al.[96], that hydrogen atoms adsorbed on the catalyst are involved in the dehydrogenation of cyclohexane. Together with hydrogen molecules, cyclohexane molecules, whose adsorption with the dissociation of one C–H bond can lead to the formation of cyclohexyl radicals, can serve as a source of hydrogen atoms. Further removal of hydrogen atoms led to the formation of species still more depleted in hydrogen until the formation of benzene molecules. Only benzene was found in the desorbed cyclohexane dehydrogenation products at temperatures below 350°C. If the rate-limiting stage is the conversion of the complex formed by a cyclohexane molecule from the gas phase and an adsorbed hydrogen atom into a hydrogen molecule and an adsorbed cyclohexyl radical and the subsequent conversion of the latter into benzene virtually corresponds to equilibrium (like the adsorption of cyclohexane molecules on hydrogen atoms), then the rate of dehydrogenation should be proportional to the degree of surface coverage of the catalyst by the complex $C_6H_{12}.H_{ads}$. Using the Langmuir equation, it is possible to obtain the following expression for the reaction rate:

$$w = \frac{k\,a\,a_{H_2}p_{C_6H_{12}}\sqrt{p_{H_2}}}{1 + a\,p_{C_6H_{12}} + a_{H_2}\sqrt{p_{H_2}}},$$

where k is the rate constant and a and a_{H_2} are the adsorption coefficients of cyclohexane and hydrogen respectively. The term including the partial pressure of benzene does not enter into the equation owing to the low degrees of dehydrogenation of cyclohexane. The linear relations between $p_{C_6H_{12}}/w$ and $p_{C_6H_{12}}$ and between $\sqrt{p_{H_2}}/w$ and $\sqrt{p_{H_2}}$ correspond to this equation. The experimental data, some of which are presented in Fig. 4, are indeed described by linear plots in terms of the above variables (Figs. 5 and 6). The kinetic equations derived on the assumption that the rate-limiting stage is the interaction of an adsorbed hydrogen atom and a cyclohexane molecule with formation of an adsorbed C_6H_{11} radical and an H_2 molecule are also consistent with the experimental data. On the other hand, if the rate-limiting stage is assumed to be, following Kiperman[99], the adsorption of cyclohexane molecule with elimination of a hydrogen atom or the interaction of an adsorbed hydrogen atom and one of the intermediates in the dehydrogenation of cyclohexane, then it follows from the resulting kinetic equations that the reaction should be inhibited by hydrogen. This has not been observed experimentally[98].

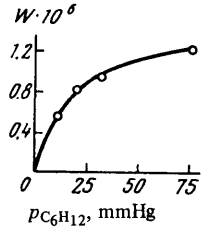

Figure 4. Variation of the rate of dehydrogenation of cyclohexane (C_6H_{12}) on palladium foil with its vapour pressure (250°C, hydrogen pressure 350 mmHg).

The catalytic activity of binary palladium alloys in relation to the dehydrogenation of cyclohexane depends in a complex manner on the nature and amount of the second alloy component[96]. Palladium alloys containing 20, 40, and 50% of silver are less active than pure palladium. The formation of the Kurnakov compounds Pd_3Ag_2 and PdAg does not

lead to an enhancement of catalytic activity. The introduction of between 0.1 and 1.5% of platinum into the palladium alloy results in an improvement of the catalytic activity of palladium at temperatures below 400°C and the palladium alloy with 5% of nickel is more active over the entire experimental temperature range than pure palladium. On the other hand, the alloy with 10% of nickel is inferior to pure palladium as regards activity. Consequently the catalytic activity of palladium–nickel alloys in the dehydrogenation of cyclohexane passes through a maximum as the nickel content in the solid solution is increased. A similar relation has been found[94] for palladium–ruthenium alloys: the most active alloy in the dehydrogenation of cyclohexane contains 8.36% of ruthenium, while those with 7.0 and 9.2% of ruthenium are somewhat less active.

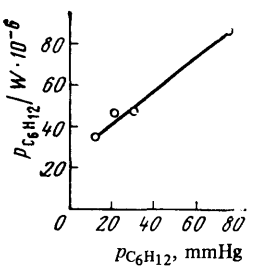

Figure 5. Variation of $p_{C_6H_{12}}/w$ with cyclohexane vapour pressure (250°C, hydrogen pressure 90 mmHg).

It has been noted that, with increase of the ruthenium content from 1 to 9%, the permeability of the palladium–ruthenium alloys to hydrogen, measured by the method of Mishchenko and Gryaznov[100], passes through a maximum for a ruthenium content of about 6%. The long-term tensile strength of this alloy at 550°C amounted to 11 kgf mm^{-2} over a period of 1000 h, [94] which is higher by a factor of almost 5 than that of pure palladium. The short-term tensile strength of deformed palladium–ruthenium alloys extended *in vacuo* increases with increase of the ruthenium content to 9% at 500° and 900°C. The above data lead to the conclusion that palladium alloys containing between 6 and 9% of ruthenium are optimal as regards catalytic activity in the dehydrogenation of cyclohexane, permeability to hydrogen, and mechanical properties. One must emphasize that, together with a high activity, the membrane catalyst must exhibit an adequate permeability to hydrogen and mechanical strength, so that thin-walled designs can be employed.

7. DEHYDROCYCLISATION OF *n*-ALKANES ON PALLADIUM ALLOYS

The dehydrocyclisation of straight-chain hexane, heptane, octane[9], and decane[82] under non-chromatographic pulse conditions was investigated on a foil made of the palladium alloy with 5.5% of nickel. At 618°C 9% of benzene was formed from hexane in a stream of hydrogen and cleavage to methane, which occurred at higher temperatures, was not observed. Heptane in a stream of argon at 587°C gave rise to 65% of aromatic hydrocarbons, including 50% toluene and 15% of benzene. The main octane dehydrocyclisation product on the same alloy proved to be *o*-xylene. *n*-Decane was converted into naphthalene to the extent of 3% at 553°C, while at higher and lower temperatures the yields of naphthalene were smaller.

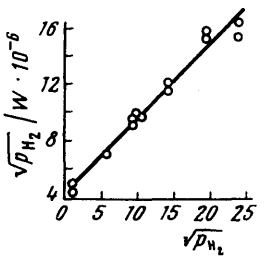

Figure 6. Variation of $\sqrt{p_{H_2}}/w$ with $\sqrt{p_{H_2}}$ at 250°C and a cyclohexane vapour pressure of 60 mmHg.

The palladium alloy with 10% of rhodium[76] showed a higher activity with respect to the dehydrocyclisation of *n*-heptane than the palladium alloy with 5.5% of nickel: 46% of toluene and 24% of benzene were obtained at 550°C on the palladium–rhodium, while on the palladium–nickel alloy under the same conditions the yields were 37% of toluene and 8% of benzene.

Palladium–rhenium alloys were tried as catalysts for the dehydrocyclisation of *n*-alkanes[101,102]. The product obtained from heptane at 625°C on the alloy containing 5% of rhenium consisted of 14% of toluene and 34% of benzene. The dehydrocyclisation of octane on the same catalyst is accompanied to an even greater extent by the hydrodealkylation of the aromatic hydrocarbon products to benzene.

The palladium alloy with 5% of ruthenium proved to be one of the most active catalysts of the dehydrocyclisation of *n*-alkanes[103]. Hexane, which, as shown by the experiments described previously, is dehydrocyclised with greater difficulty than *n*-alkanes with a higher molecular weight, gave rise to 58% of benzene at 575°C on a foil made of this alloy. In the presence of the palladium alloy containing 5% of tungsten and 1% of ruthenium, 54.7% of benzene and 2.6% of toluene were obtained from *n*-heptane at 590°C.

The high activity of palladium alloys used as hydrogen-permeable membrane dehydrocyclisation catalysts is particularly important, since alkanes widely occurring in different types of petroleum are converted by this reaction into more valuable aromatic hydrocarbons and the formation of one mole of such hydrocarbons is accompanied by the generation of four moles of hydrogen, which can be used on the other side of the same membrane catalyst for hydrodealkylation and other reactions.

8. THE COUPLING OF CATALYTIC HYDROGEN ELIMINATION AND ADDITION REACTIONS

By definition[104] coupled reactions consist of a system of two reactions occurring in the same medium the course of one of which depends on the other. A study of coupled oxidation reactions in solution showed[104] that coupling is possible only for complex processes with formation of an

intermediate which constitutes a link between the primary and secondary reactions. The conclusion reached in a monograph[104] that in coupled reactions chemical energy is transferred as such from one process to another must be regarded as even more general. We shall return to this conclusion after a brief survey of the results of studies of coupled reactions on the same surface of a heterogeneous catalyst.

The coupling of catalytic hydrogen elimination and addition reactions has been observed[105] in the hydrogenation of methyl tetrahydroterephthalate. It was found that at room temperature in the presence of palladium foil the hydrogenation process is accompanied by the dehydrogenation of part of the starting material to the terephthalate ester. The authors[105] noted that palladium black having lost its hydrogen in the hydrogenation reaction is again saturated with hydrogen from the tetrahydroterephthalate ester and not the hydrogen present in a free state. In the presence of a large amount of palladium black at room temperature the dehydrogenation of dihydronaphthalene predominates[106] over the thermodynamically unavoidable hydrogenation, since the absorption of hydrogen by palladium displaces the equilibrium. Cyclohexadiene has been converted into benzene and cyclohexene and the latter to benzene and cyclohexane on the palladised asbestos at temperatures below 130°C in a stream of carbon dioxide[107]. In these "irreversible catalytic" reactions (as defined by Zelinskii) hydrogen is not evolved, since the hydrogenation of one molecule of cyclohexene causes the hydrogenation of two other such molecules and the dehydrogenation of one cyclohexadiene molecule causes the hydrogenation of another such molecule. Similar reactions of hydrocarbons of different classes with double bonds in the rings and in side chains, with a triple bond in the side chain, and in bicyclic hydrocarbons with and without bridging groups have been investigated[108–124]. The conversion of ethylene into ethane and acetylene and of propene into propane and propyne has been observed[125] on palladium films and to a lesser extent on platinum films.

Various substances can serve as hydrogen donors and acceptors. In particular it has been stated[126] that between 240° and 260°C methylcyclohexane behaves as a donor and benzene as an acceptor of hydrogen. This pair of coupled reactions was subsequently investigated[127] on palladised silica gel. Petroleum naphthenes, which can be converted into valuable aromatic hydrocarbons, have been noted as particularly interesting hydrogen donors[126] and liquid vegetable oils have been noted as interesting hydrogen acceptors. However, this system has not been investigated and the possibility of the hydrogenation of unsaturated acids by the hydrogen obtained in the dehydrogenation of ethanol was confirmed by experiments using a nickel catalyst.

On the hypothesis that the energy required for the endothermic dehydrogenation of the hydrogen donor is provided by the exothermic hydrogenation of the hydrogen acceptor. Vesterberg and Braun[128] explained certain experimental data and calculated the ΔG°_{298} for pairs of coupled reactions: dehydrogenation of cyclohexane or methylcyclohexane–hydrogenation of maleic or fumaric acid, dehydrogenation of bibenzyl–hydrogenation of trimethylethylene. It was noted that the predominance of the maximum useful work obtained in the hydrogenation of the hydrogen acceptor over the corresponding quantity obtained in the dehydrogenation of the donor is a necessary but naturally not a sufficient condition for coupling. Another problem is to ensure a sufficient rate of the coupled reactions in the presence of the given catalyst.

The hydrodecyclisation (ring hydrogenolysis) of ethylcyclopentane coupled with the dehydrogenation of cyclohexane has been achieved[129,130] on platinised charcoal. The same hydrogen donor has been used[131] for the coupled hydrogenation of propenylbenzene to propylbenzene, of *trans*-stilbene to bibenzyl, of 1,1-diphenylethylene to 1,1-diphenylethane, etc. The use of ethylene as the acceptor of the hydrogen evolved in the dehydrogenation of n-butane on an alumina–chromium oxide catalyst increased[132] the yield of butadiene from 9.3 to 16.4%.

In all the studies described in this section the coupling of the reactions made it possible to increase their rate or selectivity. However, all the components of coupled reactions were present in the same volume and the separation of the resulting multicomponent mixtures frequently proved to be difficult and reduced the advantages of coupling.

9. THE COUPLING OF REACTIONS ON MEMBRANE CATALYSTS

It was suggested in 1964[2,3,5,11] that, in order to increase the efficiency of catalytic processes, two reactions be carried out on different sides of a partition made of a catalytically active substance or one coated by catalyst layers. Three types of coupling of catalytic reactions are then possible.

1. In the absence of the transfer of reactants through the catalyst the heat evolved in any exothermic reaction occurring on one catalyst surface can be used to carry out any endothermic reaction on the other catalyst surface. Any catalyst with adequate thermal conductivity can be used for such energy coupling of catalytic processes. Catalysts with low thermal conductivity can be deposited in the form of thin layers on the surface of a heat conducting partition.

2. When the substance formed as a result of the reaction on one catalyst surface and consumed in the reaction on the other surface is transferred through the catalyst, the thermodynamic equilibria in both reactions will be displaced and the degrees of conversion will increase. A catalyst permeable to the chosen substance alone is necessary for such thermodynamic coupling.

3. If the substance formed on one side of the catalyst and consumed on the other is transferred through the catalyst in an active, for example atomic, state, a specific (kinetic) coupling of the reactions is possible. To remove the substance from the catalyst surface where it is formed, the recombination and desorption stages are no longer required and its reaction on the other catalyst surface does not need activation.

The above types of coupling of catalytic processes can occur both separately and in combination with one another. The degree of coupling of two reactions is chosen in such a way that the steady-state process is stable. A distinctive feature of the coupling of reactions on a membrane catalyst is that the transfer of chemical energy from one process to the other[104] with minimal dissipation of energy is possible. The non-spontaneous reaction ($\Delta G_1^\circ > 0$) can be achieved as the result of the free energy of the other reaction ($\Delta G_2 < 0$), provided that $|\Delta G_2^\circ| > |\Delta G_1^\circ|$.

The use of hydrogen formed in the reaction on one side of the partition of a palladium or palladium alloy tube to carry out on the other side of the partition a reaction involving the addition of hydrogen is an example of the coupling of catalytic reactions. Thermodynamic calculations have shown[5] which hydrogen addition reactions are possible at temperatures sufficiently high for industrially important dehydrogenation reactions. In particular at 427°C (700°K)

ΔG° for the hydrodemethylation of toluene is negative and its absolute value is higher than the positive ΔG° for the dehydrogenation of butene to butadiene. Therefore thermodynamic limitations are lifted from the latter reaction when it is coupled with the hydrodemethylation of toluene.

The removal of hydrogen from the dehydrogenation of dehydrocyclisation zone via the membrane catalyst increases the equilibrium degree of conversion. At 527°C (800°K) and an overall pressure of 1 atm the equilibrium yield of butadiene from but-2-ene is 15%. If 90% of the hydrogen formed is removed from the reaction zone, the yield of butadiene increases to 38% and after the elimination of 98% of the hydrogen the equilibrium yield rises to 73%.

A palladium foil dividing the reactor in half can be used as the simplest example of a membrane catalyst. If the upper half of the reactor contains butene, the latter will be dehydrogenated to butadiene on the upper surface of the palladium foil, as shown in Fig. 7. The hydrogen formed in the dehydrogenation process dissolves in the palladium and migrates in an atomic form across the foil, whose cross-section is illustrated in Fig. 7 by a shaded band. On the lower surface of the palladium foil, atomic hydrogen can be used, for example, for the hydrodemethylation of toluene or for other hydrogen addition reactions.

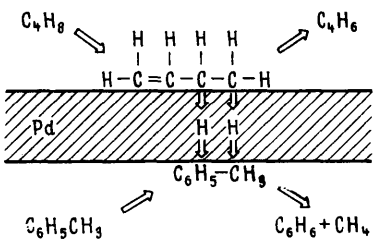

Figure 7. Schematic illustration of the coupling of butene dehydrogenation and toluene hydrodemethylation reactions on a palladium membrane catalyst.

In the general case any reaction involving the formation of hydrogen can take place on one surface of a membrane catalyst permeable to hydrogen alone:

$$A \rightarrow B + H_2 \quad , \qquad (1)$$

while on the other surface any hydrogen addition reaction can occur:

$$C + H_2 \rightarrow E \quad . \qquad (2)$$

It is of course necessary that reactions (1) and (2) should proceed at the same temperatures and pressures, since the thermal conductivity of a thin membrane is high and its strength is low. If reaction (1) is carried out separately from reaction (2), then a specific degree of surface coverage of the catalyst by hydrogen Θ_1^* is established under the specified conditions and, when reaction (2) takes place separately from reaction (1), the degree of surface coverage is Θ_2^*. The rates of these reactions can be expressed by the equation

$$w_i = k_i f_i(\mathbf{p}_j)\left[1 - \frac{\varphi_i(\mathbf{p}_j)}{K_{pi}}\right],$$

where i is the number of the reaction, j the reactant index, $\mathbf{p}_j$ the vector of the reaction mixture composition, $k_i f_i(\mathbf{p}_j)$ the rate of reaction disregarding its reversibility, $\varphi_i(\mathbf{p}_j)$ the expression of the law of mass action, and K_{pi} the equilibrium constant for the ith reaction.

If reactions (1) and (2) are carried out on a membrane catalyst, then under the same conditions the degree of surface converages of the two catalyst surfaces will be different (Θ_1 and Θ_2 respectively) owing to the transfer of hydrogen through the catalyst. The rate of transfer of hydrogen is determined by Θ_1 and Θ_2 and the coefficient β:

$$w_H = \beta(\theta_1 - \theta_2) \quad .$$

If the rate of transfer of hydrogen is higher than the rate of its formation by reaction (1), then the inequalities

$$\theta_1^* > \theta_1 > \theta_2 > \theta_2^*$$

constitute the main condition for the coupling of the reactions on a membrane catalyst permeable to hydrogen alone[133].

The three types of coupling discussed above involve (1) the maintenance of isothermal conditions owing to the transfer of heat from the exothermic hydrogen addition reaction zone to the endothermic hydrogen elimination reaction zone (energy effect), (2) an increase of the quantity $(1-\varphi_i(\mathbf{p}_j)/K_{pi})$ in consequence of changes in the equilibrium conditions (thermodynamic effect), and (3) an increase of the rate of reaction $k_i f_i(\mathbf{p}_j)$ when no account is taken of its reversibility (kinetic effect).

A mathematical model of the coupling of reactions on a membrane catalyst can be constructed taking into account three levels: (a) the molecular level including the stages of catalytic reactions; (b) the element of the membrane catalyst where catalytic reactions are combined with hydrogen and heat transfer through the catalyst; (c) the reactor with the membrane catalyst.

The first level is described by the kinetic equations for the corresponding reactions and the second level by a combination of these equations, the heat balance equation, and the equation for mass transfer through the catalyst. Analysis of these equations showed[133] that they have a steady-state solution characterising the stability of the coupling of the two reactions on the membrane catalyst.

The experimental evidence for the coupling of reactions, one of which involves the evolution and the other the addition of hydrogen, on different sides of a catalyst selectively permeable to hydrogen alone was obtained[4] in the dehydrogenation of cyclohexane within a palladium tube and in the hydrodealkylation of toluene or *o*-xylene on its outer surface by the diffusing hydrogen. Both reactions and hydrogen transfer are accelerated under the conditions of such coupling compared with the conditions where the reactions are carried out separately. The coupling of the dehydrogenation of *trans*-but-2-ene at 380°C and a pressure of 1.4 atm with the hydrogenation of benzene on the other surface of a palladium tube resulted in the formation of 6.1% of butadiene. This yield is three times higher than the equilibrium yield at the given temperature and a pressure of 1 atm without the removal of the hydrogen formed. The amount of butadiene collected from a unit geometrical surface area of the palladium membrane catalyst was 2000 times greater than for the K-16 industrial catalyst (according to Tyuryaev and Kolobikhin's data[134]).

The efficiency of the coupling of heterogeneous catalytic reactions is much higher than that of the simple removal of the hydrogen formed from the dehydrogenation zone. For example, the rate of formation of butadiene increases by a factor of five when a stream of argon onto the other side of

the membrane catalyst is replaced by a stream of a mixture of toluene vapour and argon, i.e. when the diffusing hydrogen is combined.

The use of membrane catalysts permeable to hydrogen in processes involving the evolution of hydrogen not only accelerates them but also suppresses side reactions. For example, in the dehydrogenation of isopentenes under flow conditions at 410°C on the surface of a thin-walled tube made of 94.5% palladium–5.5% nickel alloy with an inert gas flowing along its other surface, the yield of isoprene increases from 14 to 21%, without the formation of undesirable impurities (penta-1,3-diene and cyclopentadiene), as a result of the decrease of the partial pressure of hydrogen in the dehydrogenation zone from 15 to 5 mmHg.[133]

As shown in Sections 3–7, binary alloys of palladium with nickel, ruthenium, rhodium, rhenium, molybdenum, and other metals can be used as membrane catalysts permeable to hydrogen alone. These alloys exhibit a high permeability to hydrogen and are superior to pure palladium as regards catalytic activity with respect to dehydrogenation, dehydrocyclisation, hydrogenation, and hydrodealkylation of hydrocarbons.

For the continuous removal of the hydrogen formed in the dehydrogenation of alkanes, it has been suggested[7] that the hydrogen diffusing through a palladium or palladium alloy membrane be burnt. The heat of combustion of hydrogen makes it possible to reduce the supply of heat needed to carry out the endothermic dehydrogenation reaction. In the dehydrogenation of ethane under a pressure of 8.6 atm at 452°C up to 0.7 vol.% of ethylene was obtained on the inner walls of a palladium–25% – silver alloy tube when a mixture of nitrogen with 0.7 vol.% of oxygen was present outside the tube at a pressure of 7 atm. The combustion of the hydrogen removed from the dehydrogenation zone is not an optimal method for its combination, since the hydrogen which has migrated to the palladium alloy is extremely active in hydrogenation and other hydrogen addition reactions. Moreover the hydrogen obtained in the dehydrogenation of hydrocarbons on palladium membrane catalysts is sufficiently pure for the manufacture of semiconductor devices. Nowadays millions of cubic metres of hydrogen are purified daily for such purposes by diffusion through palladium without the synthesis of any other products.

In the industrial manufacture of vitamins and pharmaceutical preparations the hydrogenation or dehydrogenation processes are frequently carried out on porous (Raney) metals, blacks, and other catalysts whose fine particles contaminate the products. The greater mechanical strengths of membrane catalysts makes it possible to prevent the contamination of products by catalyst particles and to avoid the loss of catalysts, for example palladium.

It was discovered in recent years that catalysts for many industrial processes are best prepared by depositing the metals onto the surface of alumina or aluminium silicate blocks resembling honeycombs in shape. Such block catalyst offer a resistance to the flow of gas which is even lower than that of spherical catalysts, which were the best known previously. Block catalysts make it possible to reduce the volume of the reactor and the consumption of noble metals. A change from granulated catalysts in tubes or on reactor shelves to catalysts consisting of the constructional elements of the reactor has been suggested. It is easy to assess the prospects opened up by the next stage in this development— the creation of a reactor with a membrane catalyst for carrying out simultaneously two coupled processes.

Reactor designs with a membrane catalyst in the form of tubes have been proposed[135]. This system resembles a heat exchanger with a floating head, which eliminates the deformation of thin-walled palladium alloy tubes owing to differences between the thermal expansion coefficients of the alloy and the material of the reactor shell. Thin-walled tubes are welded to two collectors, one of which serves as the lid of the reactor shell and is fitted with a partition ensuring that the initial substance flows from above downwards in one half of the total number of tubes and from below upwards in the other half.

To increase the surface area of the membrane catalyst per unit volume of the reactor, reactors have been developed with a membrane catalyst in the form of flat or corrugated plates and also in the form of a double helix. To prevent the deformation of the membrane catalyst, specially corrugated sheets of a stronger material, inert with respect to hydrocarbons or coated by a thin layer of the catalytically active substance, can be inserted between the plates or the turns of the helix.

Membrane catalysts may consist of a combination of a selectively permeable but catalytically relatively inactive substance and the catalytically active component. When the active component (metal) is sufficiently dispersed and the reactant, for example hydrogen, is transferred from the metal to the carrier (membrane), the limitations due to the rate of diffusion of the given reactant through the massive metal are lifted. This can ensure the operation of membrane catalysts at low temperatures. Moreover, a membrane with different metal or alloy particles attached to its two sides makes it possible to extend the range of reactions capable of being coupled. Such a membrane can serve as a model for biological membrane-enzyme system.

Membrane catalysts make it possible to investigate heterogeneous catalysts in open systems. When the zones of two reactions coupled as a result of the transfer through the catalyst of the substance evolved in one reaction and consumed in the other is separated by a membrane catalyst, not only is the mixing of the reactants of the two reactions prevented but it is also possible to obtain more complete data for the elementary stages of these reactions, which is very important in view of the decisive role of the coupling of the stages in catalysis.

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The Reactions of Certain Aromatic Cations

S.V.Krivun, O.F.Alfërova, and S.V.Sayapina

The review gives a systematic account of the most characteristic reactions of heteroaromatic cations and also tropylium and cyclopropenylium salts. The properties of these cations are compared and classified in accordance with three types: 1. reactions involving recyclisation; 2. reactions of substituents in aromatic cations; 3. reactions with retention of the ring. Attention has been concentrated on the recyclisation reactions and studies which have not been described in previous reviews. The bibliography includes 220 references.

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I. INTRODUCTION

There has been a considerable growth of interest recently in cyclic aromatic cations. Most attention has been devoted to pyrylium salts owing to their unique capacity to be converted into a wide variety of benzenoid, non-benzenoid aromatic, and heterocyclic compounds. Such reactions are not characteristic of thia- and selenapyrylium, flavylium, and xanthylium salts, their reactions proceeding mainly with retention of the initial ring. Tropylium and cyclopropenylium cations—the most typical representatives of charged non-benzenoid aromatic systems—have also attracted much attention. The purely theoretical interest in these compounds has been combined with a search for their direct practical applications, which has led to important results. Thus certain derivatives of pyrylium salts enter into valuable light-sensitive compositions for electronic engineering (see, for example, Refs. 1 and 2). Extensive experimental data on the reactions of aromatic cations have now accumulated. On the other hand, many of the available reviews are devoted mainly to the synthesis of these compounds (see, for example, Refs. 3–10) and no systematic account has been given of the reactions of the cations. Dimroth's review of the reactions of pyrylium salts and aromatic compounds[4] is an exception. Ring expansion reactions of cyclopropenylium cations, ring contraction reactions of tropylium cations, a number of new examples of the recyclisation of pyrylium salts, and also numerous reactions of heteroaromatic cations with retention of the ring were discovered in recent years. Therefore the present review is restricted to a brief consideration of the transformations of pyrylium salts into aromatic systems, attention being concentrated on studies of the reactions of aromatic cations which have not been described in the reviews published previously.

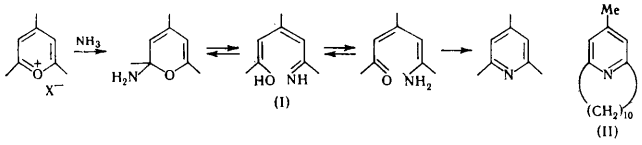
All the reactions of aromatic cations can be divided into three main types: 1. reactions of aromatic cations involving recyclisation; 2. reactions of substituents in aromatic cations; 3. reactions with retention of the ring.

II. REACTIONS OF AROMATIC CATIONS INVOLVING RECYCLISATION

When nucleophilic agents add to aromatic cyclic cations, their aromaticity is destroyed which frequently leads to ring opening. If there is a possibility of the formation of a new aromatic system, the open-chain form cyclises.

1. Pyridines and Pyridinium Salts. *N*-Oxides

The most typical example of the reactions of pyrylium salts is their interaction with ammonia and its derivatives leading to the formation of pyridine and other heterocyclic nitrogen-containing bases. In an early study Baeyer[11] established that pyrylium salts are readily converted into pyridine derivatives on heating with an aqueous ammonium carbonate solution. After Baeyer and Piccard[12], Dilthey[13], Gastaldi[14], and Balaban and Nenitzescu[15] synthesised a series of substituted pyridines from the corresponding pyrylium salts. The reaction almost always proceeds readily and with a quantitative yield. It is convenient to employ aqueous and alcoholic ammonia solutions[11,13] or ammonium acetate in acetic acid[16]. The reaction mechanism consists of nucleophilic attack by ammonia on the α-position of the pyrylium ring, the opening of this ring, and subsequent closure of the pyridine ring[17]:

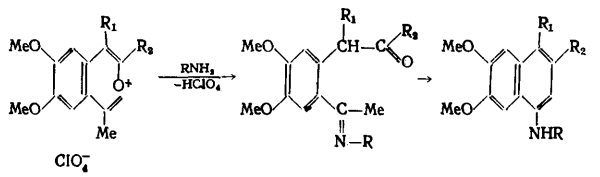


Balaban and Toma succeeded in isolating the intermediate iminoenols[17]. The conversion of the pyrylium salt into a pyridine derivative does not occur when the oxygen atom of the pyrylium salt heteroring is provided by the phenolic component, i.e. neither chromylium nor xanthylium salts can be converted into quinolines or acridines[18,19]. However, Dimroth[19] found that naphthopyrylium salts nevertheless react with ammonia to form benzoquinoline derivatives.

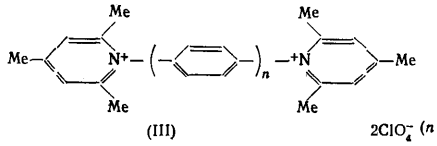
5,6,7,8-Tetrahydrochromylium[20–26] and 2-benzopyrylium[24–26] salts as well as a number of salts condensed with pyrrole, thiophen, indole, and selenophen rings[23,24,26–30] or steroid moieties[31,32] are also capable of being converted into the corresponding pyridine derivatives. Balaban et al. used this reaction to synthesise compound(II)—an analogue of natural muscopyridine[33].

Like ammonia, primary aliphatic and aromatic amines interact with 2,4,6-trisubstituted pyrylium salts, forming *N*-alkyl- and *N*-aryl-pyridinium salts[11,17,34]. A number of investigators[11,12,15,17,34] used this method to prepare pyridinium compounds which are otherwise difficult to obtain.

A non-trivial reaction of primary amines with 2-benzopyrylium salts, leading to naphthylamines, has been described[35]:

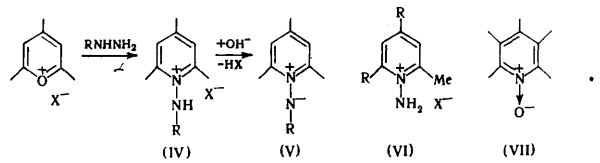


2,4,6-Trimethylpyrylium perchlorate reacts with aromatic diamines to form bispyridinium salts (III):[36]



(III) $2ClO_4^-$ ($n = 1, 2$)

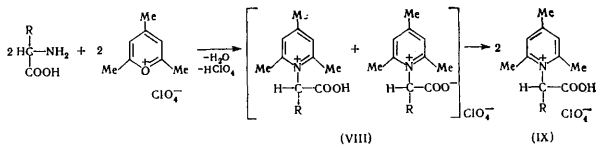
Phenylhydrazine, α-methylphenylhydrazine[4,37,38], and semicarbazide[15] behave similarly, the products being aminopyridinium salts of type (IV). In the presence of bases the salts (IV) are converted into coloured pyridine-betaines (V):[39,40]



(IV) (V) (VI) (VII)

Hydrazine hydrate leads to 1-aminopyridinium salts (VI).[41] A similar reaction has been described for *sym*-octahydroxanthylium[42]. Pyrylium salts react with hydroxylamine form the *N*-oxides of substituted pyridines (VII).[15,43] *p*-Hydroxyphenylpyridinium salts (obtained from pyrylium salts and aminophenols), which are converted by bases into pyridinia-*N*-phenol-betaines[44,45], are interesting.

Certain aminoacids, aminoacid esters, and peptides react with pyrylium salts via the amino-group to form quaternary pyridinium derivatives of aminoacids, peptides, and pyrimidines[34,46-48]. It is suggested that the interaction of aminoacids and peptides with 2,4,6-trimethylpyrylium proceeds via the formation of the betaines (VIII), which are then converted into the pyridinium salts (IX):

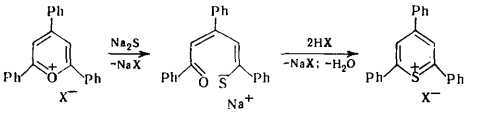


(VIII) (IX)

It has also been suggested that pyrylium salts can block the primary amino-groups in biological systems without involving other functional groups. This can occur in reactions with aminoacids and proteins but not with aminopurines, aminopyrimidines, nucleotides, and nucleic acids[47,48].

2. Thiapyrylium Cations

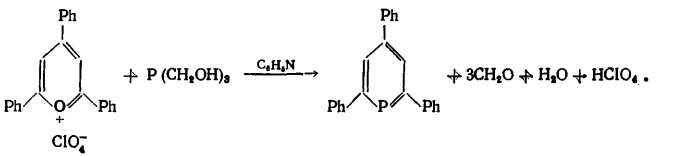
The addition of sodium sulphide to pyrylium salts leads to the opening of the pyran ring. After the addition of an inorganic acid, the resulting open-chain species undergoes ring closure at the sulphur atom. The reaction usually proceeds in acetone, the products being thiapyrylium salts[49]. Wizinger and Ulrich[49,50] proposed the following reaction mechanism:



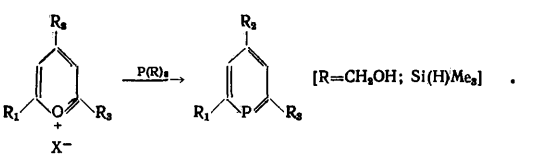
The reaction of chromylium and isochromylium salts with sodium sulphide in aqueous acetone solution does not result in the formation of the corresponding benzothiapyrylium salts[19].

3. Phosphabenzene Derivatives

The attempts to synthesise phosphorin—a representative of a new class of heterocyclic compounds—were undertaken a long time ago[51]. Success was achieved for the first time by Märkl[52], who obtained 2,4,6-triphenylphosphabenzene from 2,4,6-triphenylpyrylium perchlorate and tri(hydroxymethyl)phosphine by the reaction



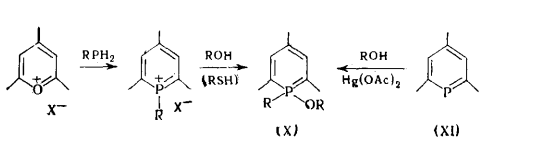
Subsequently Tolmachev and Kozlov extended this method to various pyrylium salts[53] and Zhungietu et al.[54] extended it to indolyl- and pyrrolyl-pyrylium salts[54]. Three main methods for the synthesis of phosphabenzene derivatives from pyrylium salts are now known: 1. from tri(hydroxymethyl)phosphine in pyridine[52]; 2. from tris-(trimethylsilyl)phosphine in acetonitrile[55]; 3. from phosphine in butyl alcohol under pressure[56]:



We may note that the third method is the most general and is suitable for the synthesis of any alkyl- or aryl-phosphabenzene.

Benzophosphorins cannot be obtained from chromylium salts. Nor is oxygen replaced by phosphorus in isochromylium salts[55,57]. The recyclisation (carried out by Dimroth[19]) of naphthopyrylium salts into naphthophosphorins is therefore particularly interesting.

The syntheses of the various *P*-substituted phosphorins (X) (1-aryl-, 1-alkyl-, 1-alkoxy-, or 1-mercapto-phosphabenzene) are possible[58,59] both directly from pyrylium salts and primary phosphines and via compounds (XI) by the reaction



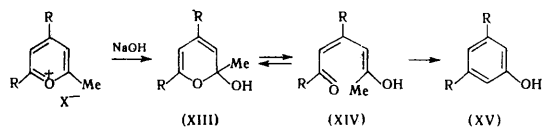
(X) (XI)

Dimroth described the conversion of 2,4,6-triphenylphosphabenzene into the corresponding anion[57], radical, radical-anion[57], and dianion, and also its oxidation to the

radical-cation[60]. Phosphabenzenes constitute a unique heterocyclic system the formation of which involves the *d*-orbitals of phosphorus. A number of studies have been made on the physical and chemical properties of phosphorins[55-62].

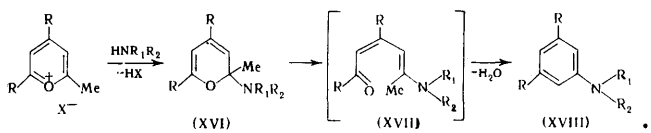
4. Aromatic Hydrocarbons and Their Functional Derivatives

Trisubstituted pyrylium salts containing an α-methyl group in the ring are converted into substituted phenols on refluxing with a 10% solution of alkali[11,14,15]. This reaction, which has been discovered by Baeyer and Piccard[12], proceeds via the intermediate formation of the pseudobase (XIII), which is converted into compound (XV) via the tautomeric ketone (XIV):



(XIII) (XIV) (XV)

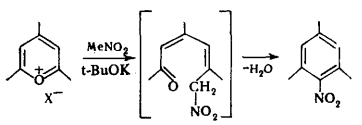
Deuterated alkylphenols have been obtained in this way[63]. Dulenko and coworkers used this reaction to synthesise thionaphthene and selenonaphthene systems[64]. The addition product (XVI) undergoes ring opening when acted upon by both secondary amines and alkali. The intermediate (XVII) subsequently condenses to *NN*-disubstituted amines (XVIII)[65]:



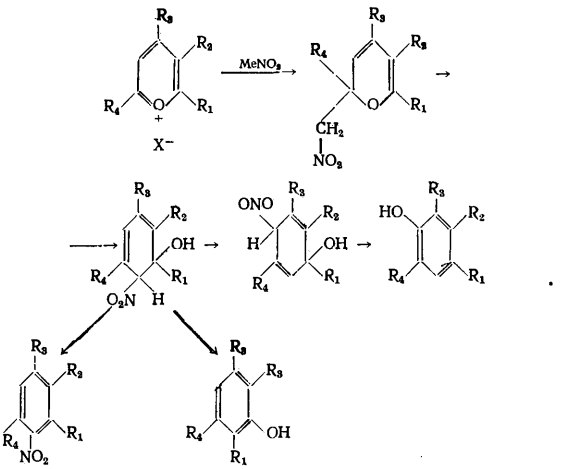
(XVI) (XVII) (XVIII)

The reaction is of interest for the synthesis of certain tertiary aromatic amines which are otherwise difficult to obtain, for example aminostilbenes[66]. *N*-Arylindolines have been obtained in this way from indoline[67].

Dimroth and coworkers[68-70] discovered a novel method for the preparation of alkyl- and aryl-substituted nitrobenzenes by the reaction of pyrylium salts with nitromethane in the presence of potassium t-butoxide. The reaction proceeds as follows:

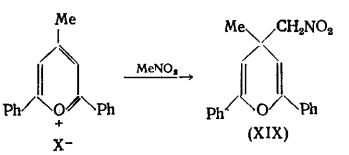


Phenylenebispyrylium salts yield the corresponding terphenyls[71]. When this reaction is carried out in the presence of one mole of base (potassium t-butoxide) in chlorobenzene, dichloroethane or ethyl alcohol, substituted phenols are obtained[72]:



Chromylium salts do not react with nitromethane and isochromylium salts are also not converted into 2-nitronaphthalene derivatives (according to Dimroth's data[70]). 2,4-Diphenyl-5,6,7,8-tetrahydrochromylium fluoroborate can be successfully converted into the corresponding 1-nitro-2,4-diphenyltetrahydronaphthalene[4].

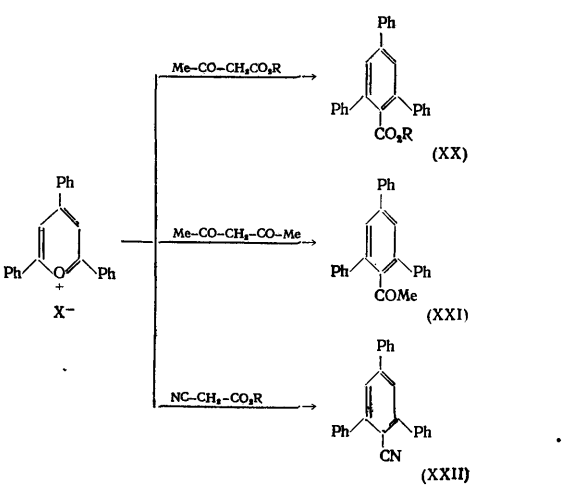
If the 4-position is free or contains the methyl group, the addition of CH_3NO_2 with formation of the stable pyran (XIX) is sterically more favourable[4]:



(XIX)

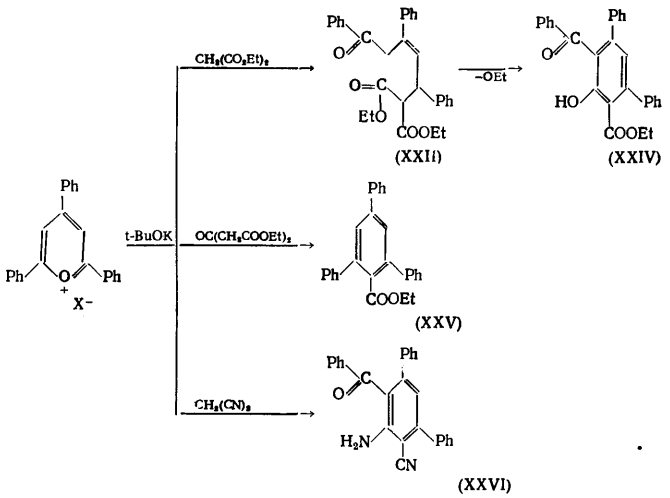
Trisubstituted pyrylium salts react with phenylnitromethane to form tetrasubstituted nitrobenzenes[73].

Compounds containing an active methylene group also react to form benzene derivatives. Their reaction with 2,4,6-triphenylpyrylium in the presence of two moles of potassium t-butoxide leads to the elimination of the acetyl or ethoxycarbonyl group with subsequent formation of the benzene derivatives (XX), (XXI), and (XXII)[74]:



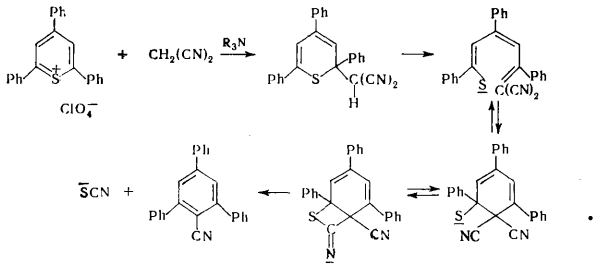
(XX) (XXI) (XXII)

The interaction of triarylpyrylium cations with malonic ester leads to the ring-opening product (XXIII), which recyclises without the elimination of the ethoxycarbonyl group to the benzene derivative (XXIV). The reaction with the diester of acetonedicarboxylic acid leads similarly to the formation of the benzoate ester (XXV) and the reaction with malonodinitrile results in the formation of the aminonitrile (XXVI) [75]:

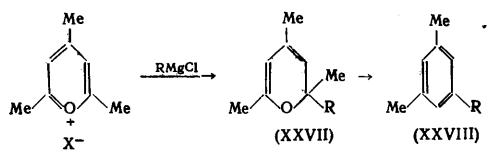


(XXII) (XXIV) (XXV) (XXVI)

In the series of heteroaromatic cations reactions involving recyclisation to benzene derivatives are characteristic only of pyrylium salts. The single instance of the conversion of 2,4,6-triarylthiapyrylium into a substituted benzonitrile has been described [76]. This reaction is believed to proceed via the mechanism:

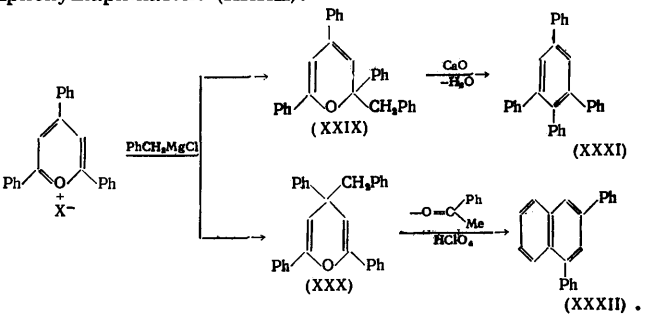


When 2,4,6-trisubstituted pyrylium salts are acted upon by a Grignard reagent, the nucleophilic addition of the organomagnesium compound takes place preferentially in the α-position of the pyran ring. If this position of the pyran (XXVII) contains a methyl or methylene group, recyclisation to the substituted benzene (XXVIII) takes place [71,73]:



(XXVII) (XXVIII)

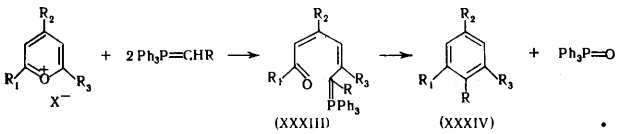
Benzyl-lithium or benzylmagnesium chloride acts similarly on 2,4,6-triphenylpyrylium. On heating with CaO, the product (XXIX) is converted into tetraphenylbenzene (XXXI), while the product (XXX) gives rise to diphenylnaphthalene (XXXII): [68,75,77]



(XXIX) (XXXI) (XXX) (XXXII)

Phenanthrene and benzothiophen derivatives were obtained in the same way [75,77].

Thus there are two methods for the recyclisation of pyrylium salts into benzene derivatives: (1) by using the α-methyl group of the pyrylium ring and (2) by the introduction into the ring of a carbon atom of the nucleophilic component. Preference must be given to the second method, since it is more universal and leads to a wide range of aromatic compounds. A novel instance of the conversion of triarylpyrylium salts into benzene derivatives by an intramolecular Wittig reaction has been described by Märkl [78]:

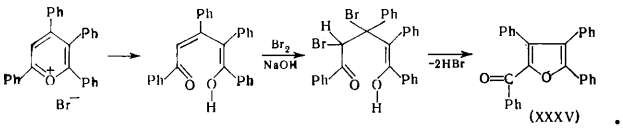


(XXXIII) (XXXIV)

The intermediate phosphoranes (XXXIII) can be isolated or converted immediately into hydrocarbons of type (XXXIV).

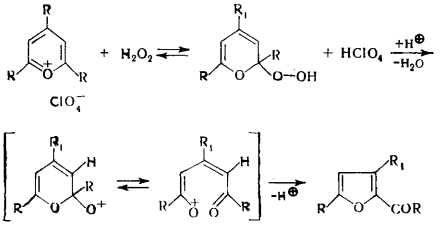
5. Ring Contraction Reactions

An important feature of certain aromatic cations is their ability to undergo ring contraction reactions under the influence of inorganic nucleophiles. This is most typical for pyrylium salts. Thus in an early investigation Dilthey [79,80] found that 2,3,4,6-tetraphenylpyrylium bromide is converted into the furan (XXXV) by the reaction

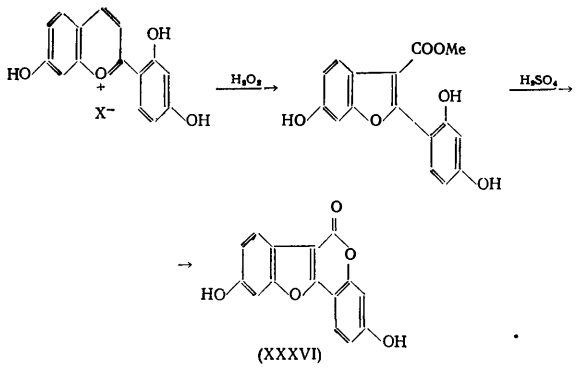


(XXXV)

Balaban and Nenitzescu [63,81] achieved the recyclisation of trialkylpyrylium salts into furans with the aid of hydrogen peroxide and proposed the following reaction mechanism:

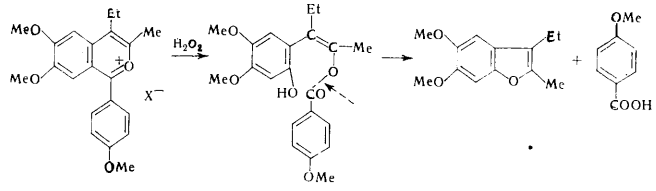


Benzopyrylium salts react with hydrogen peroxide to form benzofuran derivatives. Coumoestrol (XXXVI), an oestrogenic plant preparation, was synthesised in this way [82]:

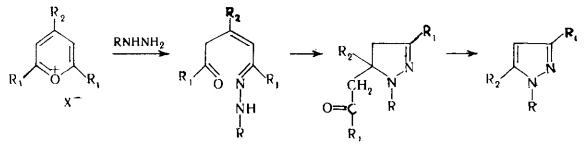


(XXXVI)

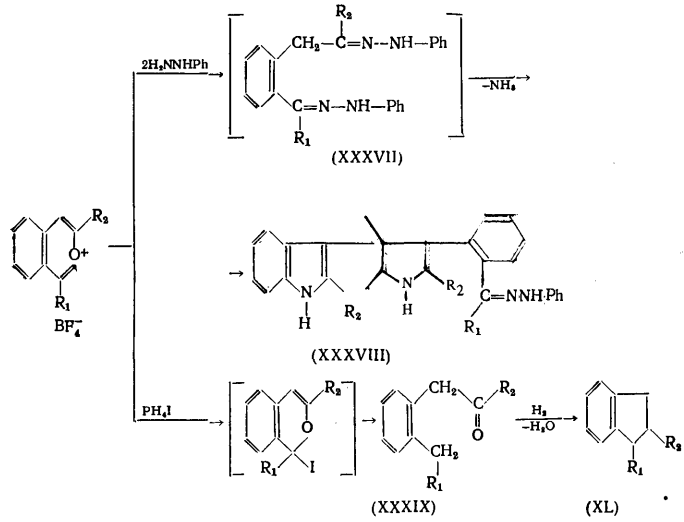
Benzofuran derivatives are also formed when 2-benzopyrylium salts are oxidised by hydrogen peroxide [83]:



When 2,4,6-trisubstituted pyrylium salts are acted upon by two-centre nucleophiles, the reaction probably involves the α- and γ-positions of the pyran ring, which ultimately leads to recyclisation with formation of a five-membered ring containing two heteroatoms. Thus, on reaction with a twofold excess of hydrazine or phenylhydrazine, pyrylium salts are converted into pyrazoles [42,46,84]:

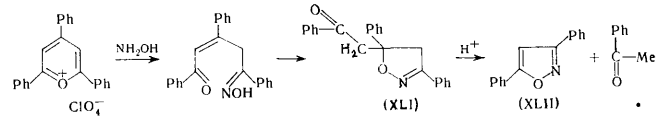


The reaction of chromylium salts with hydrazine and phenylhydrazine also proceeds with ring contraction [85]. When an isochromylium salt reacts with phenylhydrazine, the product is an indole (XXXVIII) formed via the bisphenylhydrazone (XXXVII). [19] The reaction of an isochromylium salt with phosphonium iodide (PH_4I) in glacial acetic acid results in the formation of an indan (XL) via the intermediate ketone (XXXIX) [19] in accordance with the following scheme:



(XXXVII) (XXXVIII) (XXXIX) (XL)

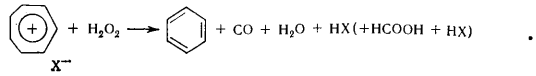
Like hydrazine and phenylhydrazine, hydroxylamine (another two-centre nucleophile) leads to isoxazolines (XLI), which can be readily converted further into isoxazoles (XLII): [84,86]



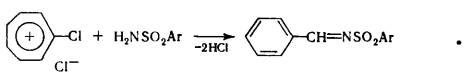
(XLI) (XLII)

Zhungietu and coworkers [87,88] applied this reaction to 4-indolylpyrylium salts and obtained indole derivatives containing isoxazole and isoxazolium rings.

The seven-membered ring of the tropylium cation has been found to contract to a six-membered ring on treatment with hydrogen peroxide. Vol'pin and coworkers [7] showed that, when the tropylium ion is treated with dilute hydrogen peroxide, the products are benzene, carbon monoxide, and formic acid:



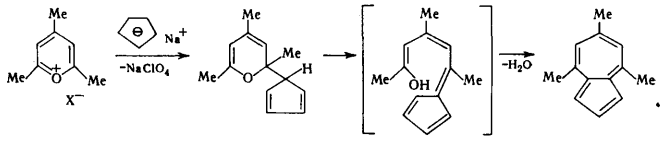
When a chlorine-substituted tropylium cation reacts with sulphonamides in the presence of dimethylamine, a rearrangement with ring contraction also takes place [89]:



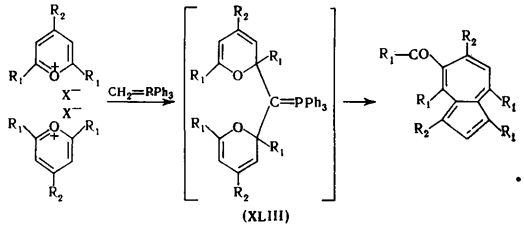
6. The Expansion of the Rings of Aromatic Cations

Formally the reaction of pyrylium salts involving the expansion of the six-membered ring to a seven-membered ring can be represented as the interaction of both α-positions of the pyran ring with a two-centre nucleophilic agent (organic or inorganic). Historically the first

instance of such a reaction was the synthesis of 4,6,8-trimethylazulene by the interaction of 2,4,6-trimethylpyrylium perchlorate with cyclopentadienylsodium in tetrahydrofuran (THF), developed by Hafner and Kaiser [90]:



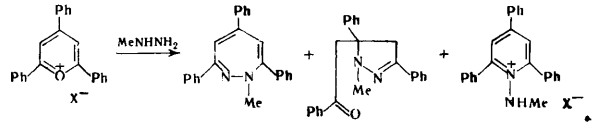
This type of synthesis was extended to other pyrylium salts [91]. When 1,3-dimethyl-5,6,7,8-tetrahydro-2-benzopyrylium perchlorate was allowed to react with cyclopentadienylsodium, 4,10-dimethyl-5,6,7,8-tetrahydrobenzazulene was obtained [92]. The synthesis of azulenes from pyrylium salts by the Wittig reaction proceeds in a somewhat different way [78,93]. Thus methylenetriphenylphosphorane reacts with two molecules of a pyrylium salt as follows:



(XLIII)

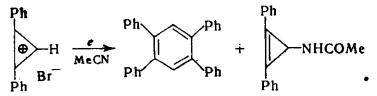
The reaction probably takes place via the intermediate (XLIII).

Pyrylium salts react with alkylhydrazines and hydrazines to form 1,2-diazepines, albeit in low yields [94], the main product being *N*-aminopyridinium salts:

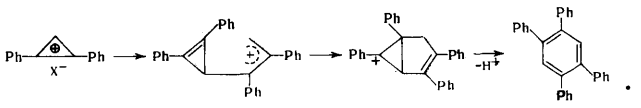


1-Aminopyridinium derivatives, formed from alkylpyrylium salts and hydrazine, can be converted subsequently into diazepines [95]. Zhungietu [88,96] obtained diazepines from indolylpyrylium salts. When 2,4,6-triphenylthiapyrylium tetrafluoroborate was treated with hydrazine, 3,5,7-triphenyl-4*H*-1,2-diazepine was isolated [94]; Balaban confirmed its structure [84,97].

The addition of nucleophilic agents to the cyclopropenylium cation frequently leads to ring opening and the formation of less strained four-, five-, or six-membered cyclic systems. Thus 1,2,4,5-tetraphenylbenzene was isolated on reduction of the 1,2-diphenylcyclopropenylium cation in acetonitrile [98,99]:

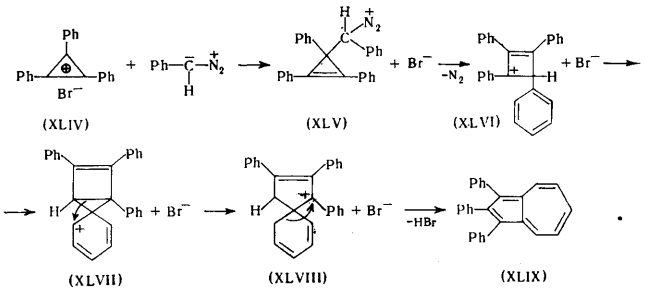


The following mechanism has been proposed on the basis of the structure of the final product for the reaction of the 1,2-diphenylcyclopropenylium cation with cyclopropene leading to tetraphenylbenzene [98]:



The analogous reaction of triphenylcyclopropenylium bromide with 1,2,3-triphenylcyclopropene leads to hexaphenylbenzene. Its yield is small, the main product being 2,3-diphenylindan.

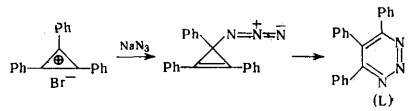
Yet another method for the synthesis, from cyclopropenylium salts, of azulenes which are otherwise difficult to obtain is based on the scheme



(XLIV) (XLV) (XLVI)

(XLVII) (XLVIII) (XLIX)

The addition of phenyldiazomethane to the cation (XLIV) results in the formation of the diazonium salt (XLV), which reacts further in a series of consecutive steps [(XLVI) → (XLVII) → (XLVIII) → (XLIX)]. [99] On reaction with sodium azide, compound (XLIV) is converted into 4,5,6-triphenyltriazine (L): [100,101]

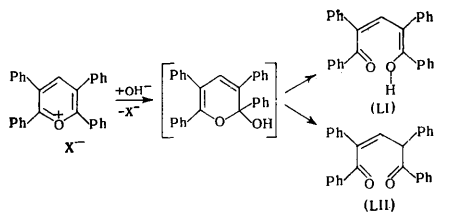


(L)

This reaction, involving the formation of a stable unstrained ring, is typical for many cyclopropene derivatives.

7. Ring Opening

The opening of the rings of cyclic cations whose recyclisation to a new aromatic system is impossible may be regarded as the simplest reaction of aromatic cations with nucleophilic agents. The products of the addition of hydroxide ions [102,103], cyanide ions [104], and phenylhydrazines [105] have been investigated in fair detail. The hydrolysis of 2,3,5,6-tetraphenylpyrylium salts yields two isomers—the enolketone (LI) and a *cis*-diketone (LII):

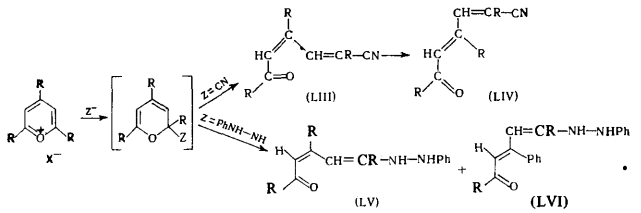


(LI)

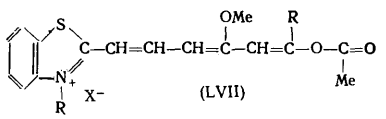
(LII)

Balaban and Nenitzescu [104] established that the cyanide ion reacts with a pyrylium salt to form a cyano-*cis*-alkadienone (LIII), which is converted in an acid medium

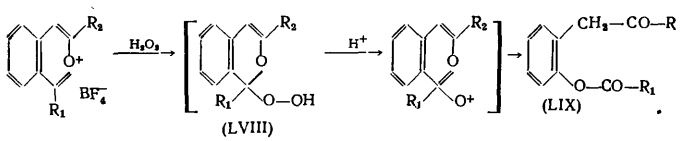
into the *trans*-isomer (LIV). The reaction of arylpyrylium salts with phenylhydrazine gives rise to two isomers and only α-phenylhydrazides (LV) are converted into pyridinium salts[37], while β-phenylhydrazides (LVI) remain in the open-chain form[105]:



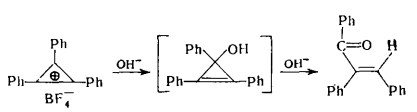
Tolmachev[106,107] studied the interaction of alkoxypyrylium and benzopyrylium salts with quaternary salts of nitrogen-containing heterocycles containing active methyl or methylene groups. The products are cyanines: in certain cases the pyrylium ring is opened and cyanine dyes of type (LVII) are formed:



When isochromylium salts are acted upon by hydrogen peroxide, the oxidation product (LVIII) is formed and then the phenyl ester (LIX). The phenyl ester was also obtained previously by Dilthey[108] from a chromylium salt on treatment with hydrogen peroxide:



Triphenylcyclopropenylium salts readily undergo ring opening merely on treatment with aqueous alkali[109,110]:



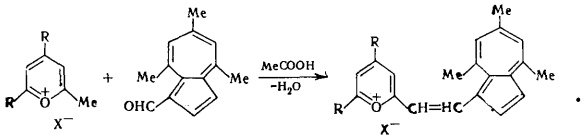
III. REACTIONS OF THE SUBSTITUENTS IN AROMATIC CATIONS

The substituents in aromatic cations alter significantly the course of certain reactions involving the retention of the pyrylium ring. Thus, when pyrylium salts containing methyl substituents are dissolved in heavy water or in deuterated acetic acid, the hydrogen atoms of the methyl groups are replaced by deuterium[63,111,112]. Deuterated or partly deuterated 2,4,6-trimethylpyrylium salts serve as the starting materials for the synthesis of aromatic or heterocyclic compounds with deuterated side chains[113].

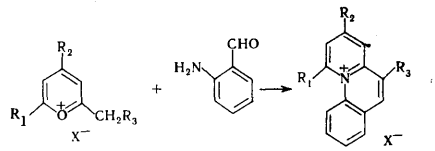
The nitration of 2,4,6-triphenylpyrylium perchlorate involves all three benzene rings, the α-phenyl groups being nitrated in the *meta*-position and the γ-phenyl group in the *para*-position[114-116]. Less active electrophilic agents (acyl and alkyl cations) do not react with phenylpyrylium salts.

1. Condensation via the α- or γ-Methyl Group

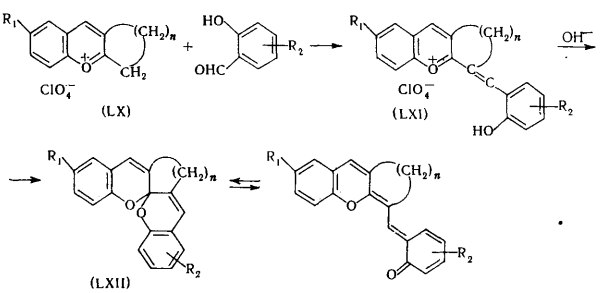
The condensation of α- or γ-methylpyrylium salts with aromatic aldehydes has been examined[117-126]. On reaction with azulenealdehydes, α-methylpyrylium salts give rise to pyrylium derivatives of azulene[127]:



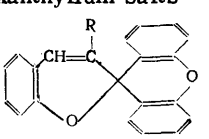
On the basis of the ability of methylpyrylium salts to react with aldehyde and amino-groups, Dimroth[128] proposed a simple method for the synthesis of benzo[*c*]-quinolizinium salts from 2,4,6-trisubstituted pyrylium salts with an α-CH_2R group and 2-aminobenzaldehyde:



The condensation of 3-formylflavene with the methyl groups of various pyrylium salts has been studied[129]. When 1-methyl-3-phenyl-5,6,7,8-tetrahydro-2-benzopyrylium perchlorate was condensed with aliphatic, aromatic, and heterocyclic aldehydes, 1-styryl derivatives were obtained[130,131]. Styryl derivatives of type (LXI), which on treatment with bases are converted into the spiropyrans (LXII), were synthesised from 2,3-cycloalkenobenzopyrylium salts (LX) and *o*-hydroxybenzaldehydes[132]:

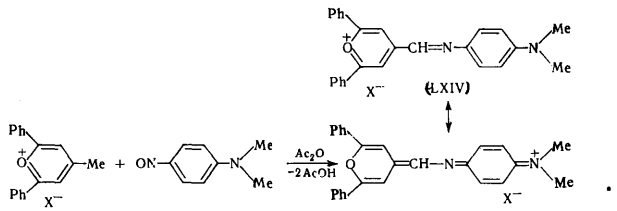


The conversion of styryl derivatives into spiropyrans is possible only for benzopyrylium salts. In the styryl derivatives obtained on the basis of pyrylium salts, the pyrylium ring is opened[132]. The alkyl group in the 9-position of xanthylium salts also condenses with the carbonyl group of aromatic aldehydes[133], forming intensely coloured styrylxanthylium salts[134]:

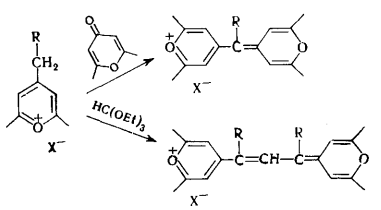


The products of the condensation of alkylxanthylium salts with *o*-hydroxybenzaldehydes are converted into spiropyrans of type (LXIII)[135]. Methyl-, ethyl-, and benzyltropylium salts react similarly with aromatic aldehydes[136], forming styryltropylium salts. Although *NN*-dimethyl-*p*-nitrosoaniline is much less reactive, nevertheless it condenses under severe conditions with α- and γ-methyl or methylene groups to form mesomeric *NN*-dimethylaminophenyliminomethylpyrylium perchlorates [Schiff

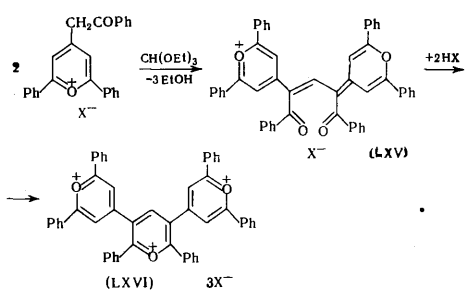
bases of type (XLIV)]. Acid hydrolysis of the resulting ketoimines leads to the corresponding ketones, while aldimines remain unchanged[137]. The following condensation mechanism has been proposed:



The condensation with pyrones takes place under analogous conditions. A number of investigations[138-141] led to the development of a method for the synthesis for pyrylocyanines which are important in practice. Pyrylocyanines are obtained also by the condensation of methyl or methylene derivatives of pyrylium salts with orthoformic ester[142]:

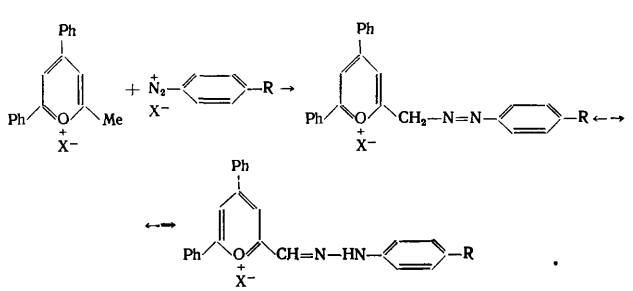


The pyrylocyanine (LXV), obtained from 2,6-diphenyl-4-phenylacylpyrylium and orthoformic ester, cyclises on protonation to the trispyrylium cation (LXVI):[143]



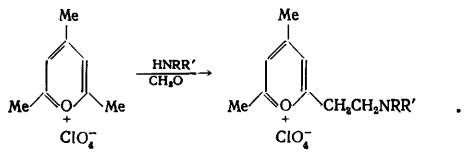
The interaction of pyrones of various pyrylium salts in acetic anhydride has been investigated[139-144]. The products are coloured symmetrical and asymmetric pyrylocyanines.

It was shown[145,146] that, in the presence of hydrogen chloride, 6-methyl-2,4-diphenylpyrylium chloride undergoes azo-coupling with diazonium salts in alcoholic solution:



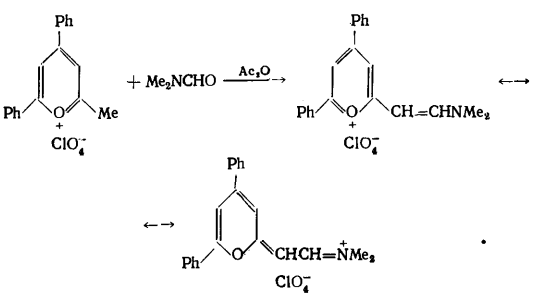
The methyl group in the 9-position of xanthylium also condenses with diazonium salts, forming azo-compounds[147].

Owing to the high reactivity of the hydrogen atoms of the α-methyl groups, it was possible to introduce pyrylium salts into the Mannich reaction with formaldehyde and various amines to form aminopyrylium salts[148]:

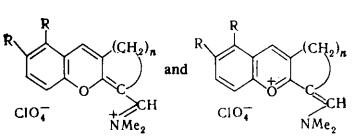


The Mannich reaction has been carried out also with certain natural amines[148].

The reaction of α-methylpyrylium salts with *NN*-dimethylformamide in acetic anhydride yields monoiminium salts, while the reaction with the Vilsmeier complex gives rise to di-iminium salts[149]:



Monoiminium salts can be obtained from alkylpyrylium salts and *NN*-dimethylthioacetamide in acetic anhydride or on the basis of other *NN*-dialkylamides in the presence of phosphoryl chloride. On hydrolysis, the iminium salts give rise to aldehydes or ketones[149]. 2,3-Cycloalkenobenzopyrylium has been formulated and vinylformylated[150]. The compounds obtained can be represented by two formulae:

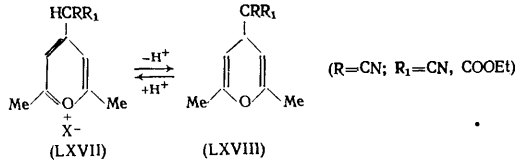


2. Nucleophilic Substitution of the Alkoxy-Groups of Cyclic Cations

The alkoxy-groups in the 4-position of pyrylium salts very readily undergo nucleophilic substitution even by weak nucleophilic agents. Thus, when 4-methoxy-2,6-dimethylpyrylium perchlorate is recrystallised from ethanol, the methoxy-group is substituted by the ethoxy-group, while recrystallisation of the ethoxypyrylium salt from methanol reconverts it into 4-methoxy-2,6-dimethylpyrylium[151]. In water alkoxy-groups are substituted by hydroxy-groups, alkoxypyrylium salts being hydrolysed to pyrones[11]. Thiols (such as phenylmethanethiol) and secondary amines (such as piperidine or morpholine) behave similarly[151,152].

On reaction with 4-alkoxypyrylium salts, sulphides (H_2S, NaHS, and Na_2S) replace alkoxy-groups by mercapto-groups[153]. Compounds containing active methylene groups

displace the methoxy-groups in the pyrylium salts with formation of compounds of type (LXVII), which can be converted into the methylenepyran derivatives (LXVIII)[154]:

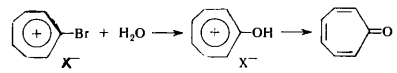


(LXVII) (LXVIII)

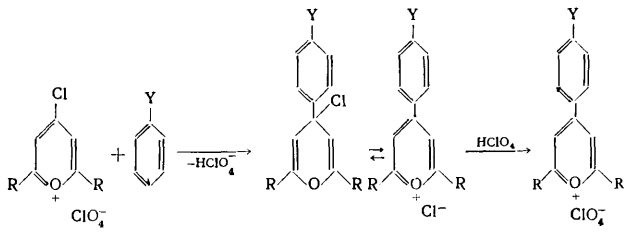
The reaction of methoxytropylium salts with secondary amines in acetonitrile give rise similarly to dialkylaminotropylium derivatives[155]. The reactions of alkoxytropylium and cyclopropenylium cations with various nucleophilic agents have been described[156].

3. Reactions of Halogenopyrylium and Halogenotropylium Salts

The reaction of bromotropylium salts with water results in the formation of tropones[157]:

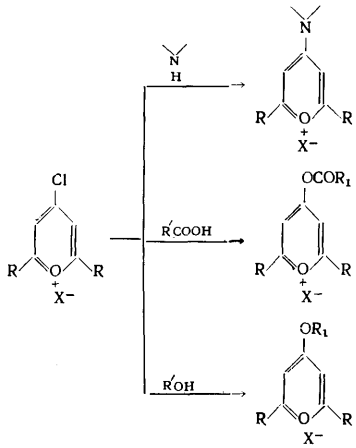


It was shown recently[158,159] that halogenopyrylium salts can react with organic nucleophilic agents to form pyrylium salts with substituents corresponding to the nucleophilic agent employed [salts of type LXIX]:



(LXIX)

The above reaction was also applied to thiapyrylium, benzopyrylium, and xanthylium salts[159]. 4-Halogenopyrylium salts react with secondary cyclic and acyclic amines[160] and also with hydroxy-compounds (alcohols, acids, and phenols)[161] to form amino-, alkoxy-, acyloxy-, and phenoxy-pyrylium salt derivatives respectively (the *N*- and *O*-pyrylation reactions):



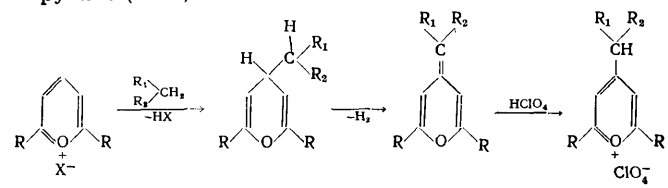
In the reaction of the chlorotropylium cation with alcohols, mercaptans, and alkylarylamines nucleophilic substitution analogous to *N*- and *O*-pyrylation takes place[89,162].

IV. REACTIONS WITH RETENTION OF THE RING

Numerous reactions of aromatic cations with nucleophilic agents take place preferentially with retention of the ring. Monocyclic 2,4,6-trisubstituted pyrylium salts constitute an exception. However, if the γ-position in the pyrylium ring is not substituted, there is a possibility of nucleophilic attack on this free position with formation of the relatively stable 4*H*-pyran.

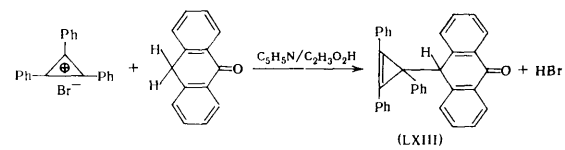
1. Interaction with Compounds Containing Active Methylene Groups and with Organometallic Compounds

2,6-Disubstituted pyrylium cations react with compounds containing active methylene groups in the presence of potassium t-butoxide to form the corresponding 4*H*-pyrans (LXX):[163,164]



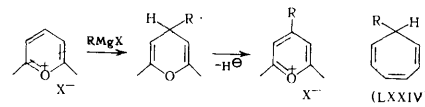
(LXX) (LXXI) (LXXII)

The pyrans (LXX) react with acids to reform the initial salts and only by mild oxidation to (LXXI) or by reaction with triphenylphenoxy-radicals and subsequent treatment with perchloric acid is it possible to convert the system into a new pyrylium salt (LXXII). Wizinger and coworkers condensed pyrylium and thiapyrylium salts with compounds containing active methylene groups in the presence of sodium acetate[165,166]. Similar reactions are also known in the flavylium series[164,167]. Tropylium salts form substituted tropilidenes in reactions of this kind[168,169]. The reactions of tropylium salts with aliphatic aldehydes[170,171], aliphatic and aliphatic-aromatic ketones[169], and compounds containing activated double bonds proceed similarly. In the series of cyclopropenylium cations these reactions have been little investigated. Triphenylcyclopropenylium bromide is known to react with anthrone in the presence of pyridine and acetic acid to form compound (LXXIII):[172]



(LXIII)

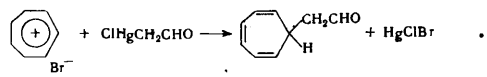
Aromatic cations readily react with organometallic compounds. In an ethereal solution of a Grignard reagent, pyrylium salts are converted into 4*H*-pyrans, which can split off a hydride ion with formation of 2,4,6-trisubstituted pyrylium salts[163]. Thus 2,6-diphenylpyrylium perchlorate can be converted into 4-alkyl-2,6-diphenyl- or 4-aryl-2,6-diphenyl-pyrylium salts[163]:



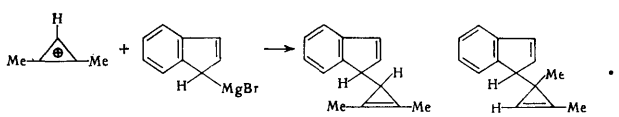
(LXXIV)

When acted upon by organometallic compounds, tropylium bromide is converted into tropylidenes (LXXIV)[156,173]. The reaction of the cyclopropenylium ion with organomagnesium and organolithium compounds proceeds

similarly [174,175]. The reaction of tropylium salts with certain organomercury compounds is interesting [170,171]:

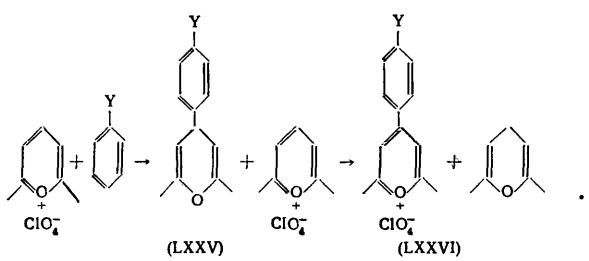


Tropylium cations react with cyclopentadienylsodium or cyclopentadienyllithium to form cyclopentadienylcycloheptatriene [156,171]. The dimethylcyclopropenylium cation reacts with indenylmagnesium bromide to form a mixture of two isomeric dimethylindenylcyclopropenes. The formation of the mixture shows that the charge of the cyclopropenylium cation is distributed among the three ring carbon atoms and is not fixed at any one of them [176]:



2. The Pyrylation Reaction

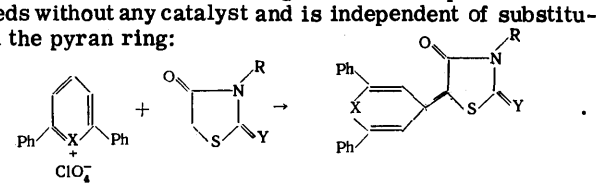
Pyrylium salts without substituents in at least one of the α- and γ-positions should presumably interact with reactive compounds to form new 2*H*- or 4*H*-pyrans [for example (LXXV)]. However, it was found [177-179] that the intermediate pyran (LXXV) splits off a hydride ion in the presence of 2,6-diphenylpyrylium perchlorate and is converted into the pyrylium cation (LXXVI) via the mechanism



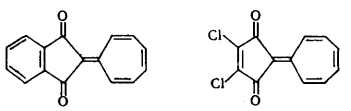
(LXXV) (LXXVI)

The elimination of a hydride ion by the pyrylium cation is possible only when there is a fairly high electron density in the γ-position of the pyran (LXXV) (higher than in the pyran whose γ-position is free). The pyrylation reaction has been extended to nucleophilic agents and heteroaromatic cations [179].

Earlier Wizinger and coworkers [165,166] carried out the condensation of thiapyrylium and flavylium salts with dimethylaniline in acetic acid in the presence of sodium acetate and Krönke and Dickore carried out the reaction in acetic anhydride [164], but these reactions have not become commonly used in the synthesis of pyrylium salts. The reaction of various 4-azolidinones with unsubstituted pyrylium salts has been investigated [180]. The process proceeds without any catalyst and is independent of substitution in the pyran ring:

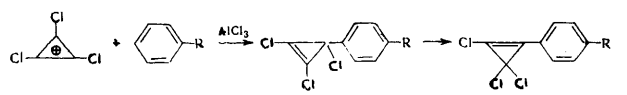


The substitution of a mobile hydrogen atom in the series of tropylium salts by the cycloheptatrienyl residue has been used extensively in the synthesis of cycloheptatriene derivatives [181]. Thus it proved possible to introduce the seven-membered ring into the molecules of various cyclic compounds [182,183]. Hafner et al. [184] and Anderson and Reploge [185] introduced the tropylium group into azulene and Kitahara et al. obtained the quinones (LXXVII) and (LXVIII) of the sesquifulvalene series with the aid of the tropylation reaction [186]:

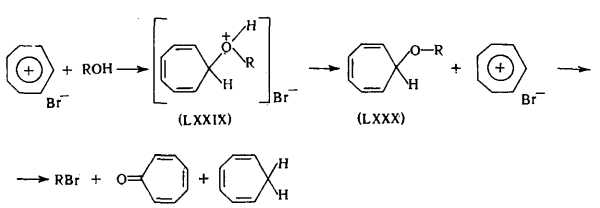


(LXXVII) (LXXVIII)

The trichlorocyclopropenylium cations enters into reactions involving electrophilic substitution of the aromatic ring (with benzene, toluene, chlorobenzene, and fluorobenzene) [187,188] of the Friedel–Crafts type:

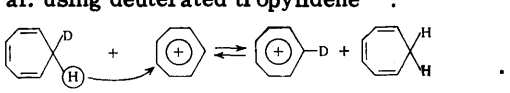


The reaction can be carried out with subsequent substitution of the three positions. Tropylium and cyclopenylium cations react with alcohols (primary, secondary, and tertiary) to form alkoxy-derivatives of tropylidene and cyclopropene [189,190]. It is believed that the first step in the reaction of the tropylium cation with alcohols is the formation of an oxonium compound (LXXIX), which readily loses a proton and is converted into an alkyl tropyl ether (LXXX). The latter interacts with a second molecule of the tropylium salt to form cycloheptatriene, tropene, and an alkyl halide [190]:

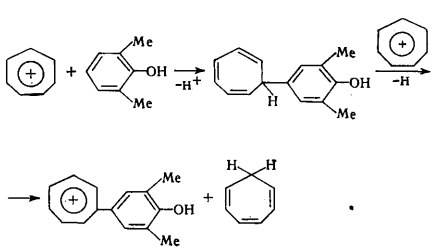


(LXXIX) (LXXX)

Kursanov et al. [191] studied the reaction of the tropylium ion with ethers. The hydride shifts in the tropylium–cycloheptatriene system have been examined in detail by Vol'pin et al. using deuterated tropylidene [192]:



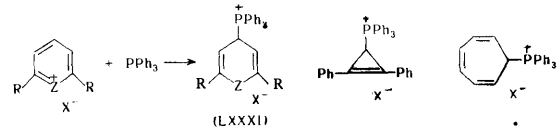
Repeated hydride shifts in this system lead to a redistribution of deuterium between tropylium and cycloheptatriene. Numerous reactions of the tropylium ion with reactive organic compounds take place with hydride ion transfer. Thus, according to van Helden et al. [193], the reaction with 2,6-dimethylphenol proceeds via the mechanism



Numerous hydride shift reactions involving the tropylium ion have been examined in detail in a monograph [194].

3. Organophosphorus Derivatives of Aromatic Cations

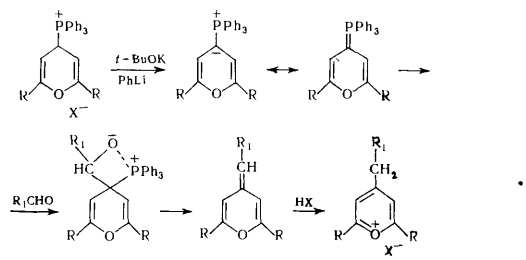
Heteroaromatic cations with a free α- or γ-position react readily and almost quantitatively with triphenylphosphine to form phosphonium salts (LXXXI).[195,196] It was found that this reaction is applicable also to tropylium and cyclopropenylium ions[197]:



(LXXXI)

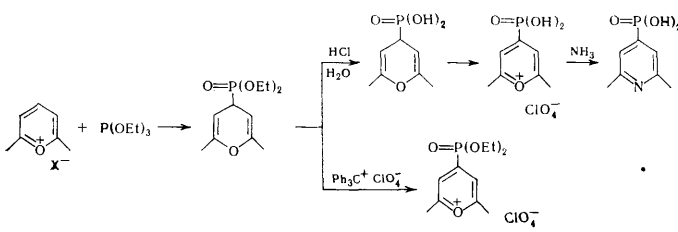
(X = ClO_4, BF_4, Br. Z = O, S, Se)

When bases are allowed to act on a suspension of these salts in ether, with cooling (to −30°C and below), phosphoranes are formed (for example, from phosphonium salts and phenyl-lithium or potassium t-butoxide); these normally react with carbonyl compounds[195]:



The synthesis of phosphonium salts and phosphoranes and the reactions of the latter with carbonyl compounds have been studied in very great detail[198]. The reaction is general and permits the variation of the carbonyl components within wide limits[199].

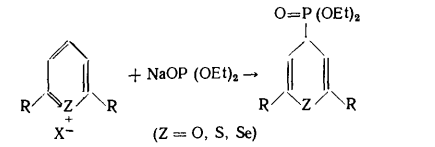
The reaction of the halides of the aromatic cations considered with triethyl phosphite, which is of the type of the Arbuzov rearrangement, has been investigated in detail[200–202]. The resulting phosphonates undergo various further reactions. For example, pyranylphosphonates (obtained from various pyrylium salts and triethyl phosphite) have been converted by acid hydrolysis into pyranylphosphonic acids and the latter have been converted by the elimination of a hydride ion into the corresponding pyrylium salts with a phosphonic acid residue. The recyclisation of these salts led to pyridylphosphonic acids:



On the other hand, pyranylphosphonate is readily converted into pyrylylphosphonate. The reaction is applicable to any charged aromatic systems but cyclopropenyl- and cycloheptatrienyl-phosphonic acids and their esters could not be converted into the corresponding salts.

The Arbuzov rearrangement in the series of aromatic cations is carried out under fairly severe conditions, which gives rise to side reactions. This rearrangement is applicable only to the corresponding chloride, bromide, and iodide salts. However, the latter are difficult to obtain, hygroscopic, and frequently unstable on storage.

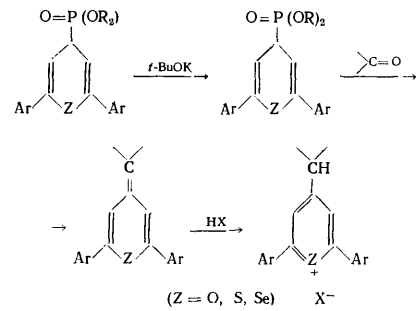
These advantages can be avoided by carrying out the Michaelis–Becker reaction of the above compounds with the sodium salt of diethyl phosphite[203]:



(Z = O, S, Se)

The resulting phosphonates are converted into phosphonic acids and into pyrylium salts with phosphorus containing substituents[204], as described above.

Phosphonates derived from various aromatic cations and obtained by the Michaelis–Becker reaction interact with potassium t-butoxide to form coloured reactive carbanions. The latter readily react *in situ* with various carbonyl compounds to form ultimately arylidene or alkylidene derivatives of pyrans and similar compounds[204,205]. The following reaction mechanism has been proposed:

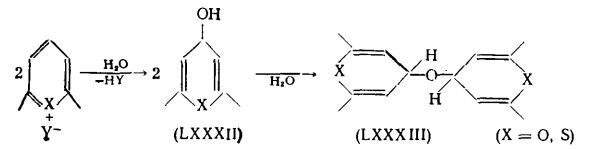


(Z = O, S, Se) X^-

This is probably the simplest and most convenient method for the introduction of an exocyclic double bond into pyran, thiapyran, selenapyran, and other cyclic systems based on pyrylium, flavylium, xanthylium, tropylium, cyclopropenylium, and other salts.

4. Interaction with Certain Inorganic Nucleophilic Agents

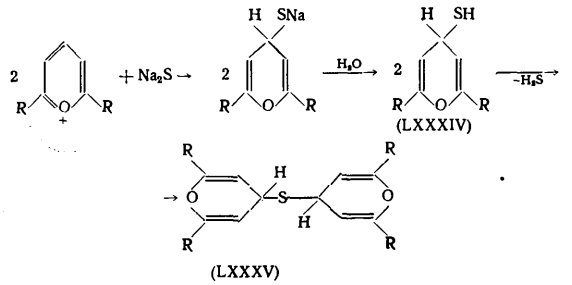
Pyrylium and thiapyrylium salts with a free γ-position are converted in the presence of organic bases (pyridine, hexamethylenetetramine) into di-($\alpha\alpha'$-diphenyl-γ-pyranyl) or di-($\alpha\alpha'$-diphenyl-γ-thiapyranyl) ether (LXXXIII).[206] The reaction most probably proceeds via the intermediate formation of 4-hydroxy-2,6-diphenylpyran (LXXXII):



(LXXXII) (LXXXIII) (X = O, S)

Organic bases can be replaced by aqueous sodium bicarbonate. This method for the conversion of pyrylium salts into dipyranyl ethers is similar to the formation of ditropyl[173], dicyclopropenyl[10], and dixanthyl[207] ethers from the corresponding salts. It is interesting that the reaction of 2,6-diphenylpyrylium perchlorate with sodium sulphide in an aqueous ethereal medium does not result in the formation of the corresponding dipyranyl sulphide analogous to diparanyl ether[206] and ditropyl sulphide[173].

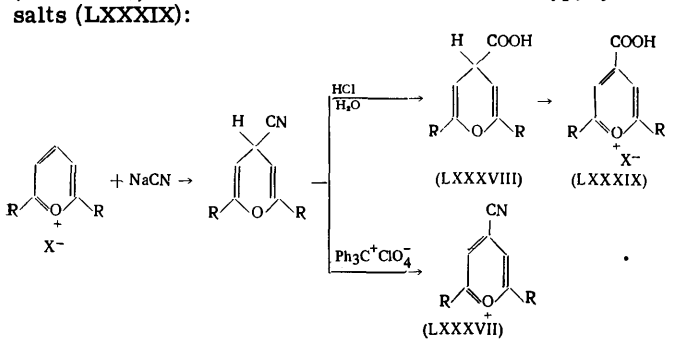
It was found that the mercaptopyran (LXXXIV) is formed under these conditions and only on heating in inert solvents does it split off hydrogen sulphide and is converted into dipyranyl sulphide (LXXXV):[208]



(LXXXIV)

(LXXXV)

The reaction of γ-unsubstituted pyrylium salts with potassium cyanide in an aqueous ethereal medium leads to the corresponding γ-cyanopyrans (LXXXVI). On being refluxed with triphenylmethyl perchlorate the latter split off a hydride ion and are converted into γ-cyanopyrylium salts (LXXXVII).[208] On the other hand, hydrolysis of pyrans by dilute hydrochloric acid yields carboxypyrans (LXXXVIII), which can be converted into carboxypyrylium salts (LXXXIX):

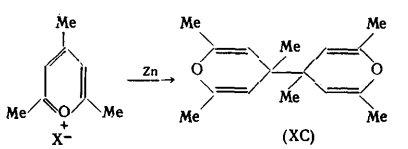


(LXXXVIII) (LXXXIX)

(LXXXVII)

The interaction of KCN with 2,4,6-trisubstituted pyrylium ions has been studied in a series of pyrylium salts[104], but the possibility of the conversion of the cyanopyrans formed initially into carboxypyrans or especially into cyano- and carboxy-pyrylium salts is ruled out in this case. The reaction of tropylium and diphenylcyclopropenylium salts with potassium cyanide leads to the formation of 7-cyanocycloheptatriene[7,156] and 3-cyano-1,2-diphenylcyclopropene respectively[8,175]. The reaction of tropylium salts with ammonia has been studied in detail. Depending on the component ratio and the reaction conditions, mono-, di-, and tri-tropylamines or their mixtures can be formed[156]. It was expected that γ-unsubstituted pyrylium salts would react similarly. However, pyridine was obtained unexpectedly[208]. Aminopyran could not be obtained either by reaction with sodamide or with potassium phthalimide. In the latter case a phthalimide derivative of pyran is readily obtained but Gabriel hydrolysis (and hydrazinolysis) leads to appreciable charring[208].

Balaban et al.[209] showed that, when metallic zinc is allowed to react with 2,4,6-trimethylpyrylium perchlorate, the salt undergoes one-electron reduction with formation of 2,2',4,4', 6,6'-hexamethyl-4,4'-bispyran (XC):

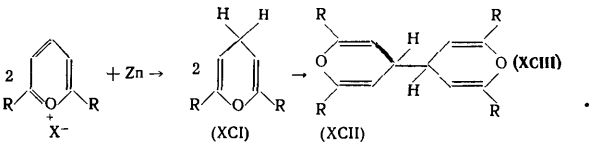


(XC)

The same product was obtained by the reaction of the disodium salt of the cyclooctatetraene dianion with trimethylpyrylium perchlorate[210].

On heating with metal powders (magnesium, copper, zinc, and aluminium) in organic solvents (alcohol and acetonitrile), triarylpyrylium salts are reduced with formation of intensely coloured species—stable free radicals[211].

When this reaction is carried out with γ-unsubstituted pyrylium salts in a polar solvent, the radicals (XCI) formed recombine and the bipyranyls (XCII) are obtained[212]:

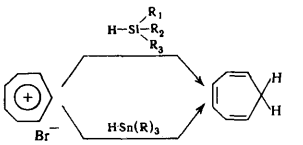


(XCI) (XCII) (XCIII)

The corresponding dimers have been synthesised from flavylium salts and their 3-alkyl- or 3-aryl-derivatives by the reaction with zinc dust in acetonitrile[213]. When xanthylium salts react with dispersed silver, stable radicals are also formed[214]. The synthesis of bitropyl (XCIII) using zinc dust and other metal powders has been described for the series of tropylium salts[173]. The tropylium ion can be reduced to bitropyl by transition metal complexes[171]. The analogy between pyrylium salts and non-benzenoid aromatic cations in the formation and recombination of radicals is completed by the cyclopropenylium ion[215].

The reduction of pyrylium salts by sodium tetrahydroborate leads to the formation of mixtures of substituted 4*H*-pyrans and pentadienones[216,217]. On reduction with sodium tetrahydroborate in alcohol, flavylium perchlorate is also converted into dimers[218].

When tropylium bromide is acted upon by lithium tetrahydroaluminate or sodium tetrahydroborate (as hydride ion donors), cycloheptatriene is formed. This property of tropylium as a hydride ion acceptor has been used to investigate hydride shifts[219]. It was found that Si-H and Sn-H bonds can also be broken heterolytically under the influence of tropylium bromide[220]:



The cyclopropenylium cation is reduced by lithium tetrahydroaluminate to cyclopropene[174].

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Diene Synthesis with 2-Pyrones and 2-Pyridones

N.P.Shusherina

The principal aspects of Diels-Alder synthesis with six membered heterocyclic dienes (2-pyrones and 2-pyridones) as well as the latest data on the *endo-exo* selectivity of this reaction are considered.
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I. INTRODUCTION

The diene synthesis reaction discovered more than 40 years ago constitutes at present a universal method for the preparation of a wide variety of cyclic systems. The employment in the Diels–Alder reaction of heterocyclic compounds with a conjugated system of C=C double bonds, among which furan, oxazole, 2-pyrone, and 2-pyridone derivatives react via the normal (4+2)-cycloaddition mechanism (with yields of adducts on a preparative scale), is of particular interest.

The practical and theoretical problems of diene synthesis with furans and oxazoles have been discussed in a number of papers and monographs [1,2], while the behaviour of 2-pyrones and 2-pyridones in this reaction has been scarcely considered in the review literature [3].

The studies published in the last decade, in which the interaction of 2-pyrones and dienophiles was used to obtain barrelene, colchicine analogues, compounds of the cyclohexatriene series and various aromatic and bridged polycyclic compounds which are difficult to obtain otherwise, demonstrate the wide synthetic possibilities of the use of 2-pyrones in the Diels–Alder reaction.

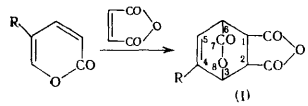
The reactions of 2-pyridones with dienophiles lead to the formation of bicyclic systems with an endazocarbonyl bridge. Extremely interesting theoretical data have been obtained in a study of the stereochemistry of diene synthesis with 2-pyrones and 2-pyridones.

The present review gives a systematic account of the literature on diene synthesis with the above six-membered heterocycles.

II. MONOADDUCTS OF 2-PYRONES {DERIVATIVES OF 8-OXABICYCLO[2,2,2]OCT-4-EN-7-ONE}

1. Synthesis

The ability of 2-pyrones to eneter into diene synthesis was first observed by Diels and Alder in the reactions of 2-pyrone and 5-methoxycarbonyl-2-pyrone (methyl coumalate) with maleic anhydride. The authors [4] showed that the monoadducts (I) {derivatives of 8-oxabicyclo-[2,2,2]oct-4-en-7-one} are formed on refluxing equimolar amounts of the initial reactant in toluene at 110°C:



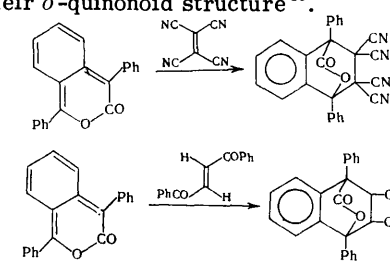
(R = H, COOMe) (I)

However, owing to their thermal instability the monoadducts of 2-pyrones are difficult to obtain. They can be synthesised only from 2-pyrones and dienophiles which enter into diene synthesis at temperatures below the decomposition temperatures of the monoadducts. It has been established that alkyl and particularly aryl groups in the 6-position of the initial 2-pyrone reduce the stability and hinder (frequently altogether preclude) the formation of the monoadducts [5,6] (cf. the part of subsection 2 dealing with thermolysis).

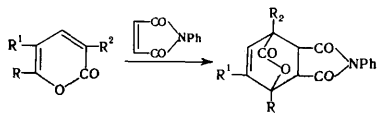
According to Alder's rule [1], electron-accepting substituents in the molecules of the initial pyrone reduce the yield of monoadducts (see Table).

An idea concerning the relative reactivities of dienophiles in reactions with 2-pyrones can be gained from a study [14] where it was shown that the yield of the monoadducts of the *o*-quinonoid 2-benzopyrone fell and the duration of the reaction increased in the series of the following dienophiles: *N*-phenylmaleimide (yield up to 85%, 25 min), dimethyl maleate (32%, 1.5 h), dimethyl fumarate (12%, 3 h).

The successive employment of tetracyanoethylene and benzoylethylene as dienophiles in reactions with 6-methyl- and 3,6-diphenyl-4,5-benzo-2-pyrones has been described. The unusual ease of this reaction is related to the enhanced diene reactivity of the above pyrones in consequence of their *o*-quinonoid structure [15].

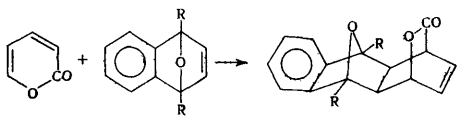


Among the dienophiles enumerated above, only *N*-phenylmaleimide [16] has been studied in reactions with the usual 2-pyrones, monoadducts being formed at 110°C:



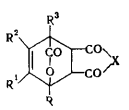
(R = R¹ = R² = H; R = R¹ = Me; R₂ = H; R¹ = R = H; R² = Br)

The ease of the reaction of 1,4-endoxy-1,4-dihydronaphthalene with 2-pyrone is due to the strain of the double bond in the dienophile [17]. The authors attributed the *exo*-configuration to the adduct without proof [17].



(R = H, Me)

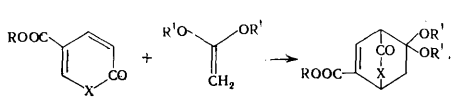
The monoadducts of 2-pyrones with maleic anhydride and *N*-phenylmaleimide.



No.	Initial 2-pyrone	R	R¹	R²	R³	X	Yield, %	Reaction conds. temp., °C	Reaction conds. time, h	Refs.
1	2-pyrone	H	H	H	H	O	50	110	10	4,7
2	ditto	H	H	H	H	NPh	80	110	1	16
3	3-bromo-2-pyrone	H	H	H	Br	O	20	110*	19	6
4	ditto	H	H	H	Br	NPh	25	110	1.5	16
5	5-methyl-2-pyrone	H	Me	H	H	O	—	110	1	9
6	5-isopropyl-2-pyrone	H	Et	H	H	O	—	110	12	10
7	5-methoxycarbonyl-2-pyrone	H	COOMe	H	H	O	30	110	3	4
8	5,6-dimethyl-2-pyrone	Me	Me	H	H	O	55	80	1	5
9	ditto	Me	Me	H	H	NPh	48	80	3	16
10	5-cyclohexyl-2-pyrone	H	C_6H_{11}	H	H	O	—	110	14	8
11	5,6-tetramethylene-2-pyrone	$(CH_2)_4$	$(CH_2)_4$	H	H	O	8—10	80*	10*	5
12	6-acetoxymethyl-5-methyl-2-pyrone	CH_3OCOMe	Me	H	H	O	72	110	3	13
13	ditto	CH_3OCOMe	Me	H	H	NPh	60	110	3	16
14	6-bromomethyl-5-methyl-2-pyrone	CH_2Br	Me	H	H	O	40	110	2	5
15	6-methyl-5-phenyl-2-pyrone	Me	Ph	H	H	O	13	110*	1*	6
16	6-methyl-4,5-benzo-2-pyrone	Me	R¹+R²-ato-benzene		H	NPh	81	140	1.5	14
17	3,6-diphenyl-4,5-benzo-2-pyrone	Ph	R¹+R²-ato-benzene		Ph	NPh	—	20	264	15

*An increase of the reaction temperature and of the duration of heating lead to a sharp lowering of the yields of the monoadducts owing to their conversion into bisanhydrides and bisimides (see Section III, 1). [5,6,11,12]

Keten diacetals, whose interaction with 5-alkoxycarbonyl-2-pyrones and their sulphur analogues gave monoadducts with yields on a preparative scale, proved to be extremely reactive dienophiles [18]:

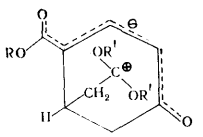


(X = O, S; R and R¹ = Me, Et)

This reaction involving 2-pyrones illustrates the possibilities of diene synthesis with "inverse electron demand", since here the electron donor is a dienophile (keten diacetal) whose double bond exhibits enhanced nucleophilic properties and the acceptor is the diene system of the 2-pyrone.

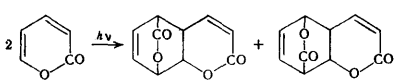
The present authors achieved the interaction with keten acetals via the inverse mechanism only for 2-pyrones with electron-accepting groups: the unsubstituted 2-pyrone does not enter into this reaction [18].

It might have been expected that two structural isomers would be obtained in the reaction of asymmetric diene synthesis addends—5-alkoxycarbonyl-2-pyrones and keten diacetals. However, in the instances investigated only the isomer with the *para*-disposition of the substituent was obtained, which the authors explain by the greater stabilisation of the transition state (A) of this isomer compared with the possible transition state for the *meta*-isomer [18].



(A)

On the other hand, the dimerisation of 2-pyrone (on ultraviolet irradiation) via a process of the diene synthesis type, in which the asymmetric 2-pyrone molecule behaves both as the diene and the dienophile, leads to a mixture of both possible structural isomers [19]:

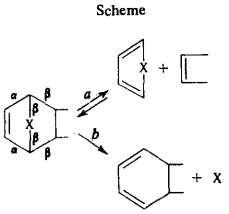


2. The Properties of Monoadducts

Thermolysis. A characteristic property of bridged 1,4-cycloadducts is their ability to dissociate on thermolysis the bond in the β-position relative to the double bond and to undergo retrodiene decomposition (reversible reaction *a*) and retrodiene elimination of the bridge (irreversible reaction *b*, see Scheme). Both modes of cleavage of the cycloadducts predicted by the Schmidt rule [20,21] are associated with a weakening of the above σ-bonds in ethylene compounds owing to the additional stabilisation of the intermediate species arising in the decomposition of these bonds, as happened, for example, with allyl cations.

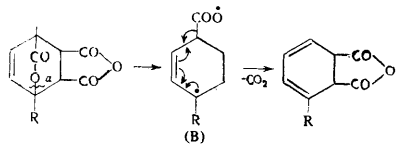
Among the known bicyclic adducts with various *endo*-bridges [X = CH_2, O, CO, $(CH)_2$], [1] the monoadducts of 2-pyrones (X = CO_2, see Scheme) are the least stable on heating, whereupon CO_2 is usually eliminated (retrodiene elimination of the bridge, reaction *b*). Certain adducts decompose at a temperature as low as 60°C and only in rare instances (in the absence of substituents at the head of the bridge) can they withstand heating above 130—140°C.

Scheme



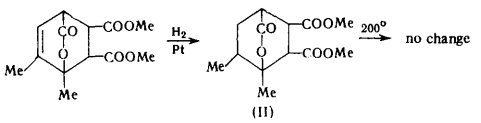
X = CH_2, $(CH_2)_2$, O, CO, CO_2

On the basis of the primary isotope effects of carbon and oxygen found for the monoadducts of 2-pyrone with maleic anhydride, Goldstein and Thayer [7] concluded that the elimination of CO_2 is a two-stage process, which begins with the dissociation of bond *a*. The resulting biradical (B) is converted further into the more stable cyclohexadiene system:

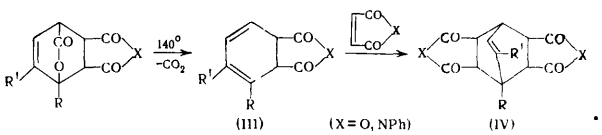


This hypothesis concerning the course of the thermolysis explains the instability of monoadducts with substituents at the bridgehead (R = alkyl or aryl) by the stabilisation of the biradical (B) owing to the $+I$ and $+M$ effects of the substituents. On the other hand, even weak electron-accepting groups in this position (for example CH_2Br and CH_2OCOMe, see Nos. 12–14 in Table) appreciably increase the stability of the monoadducts.

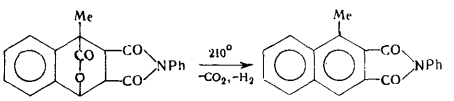
The lability of the bridge due to the influence of the double bond disappears in the hydrogenated adducts—8-oxabicyclo[2,2,2]octan-7-ones (II), which withstand heating above 200°C: [22]



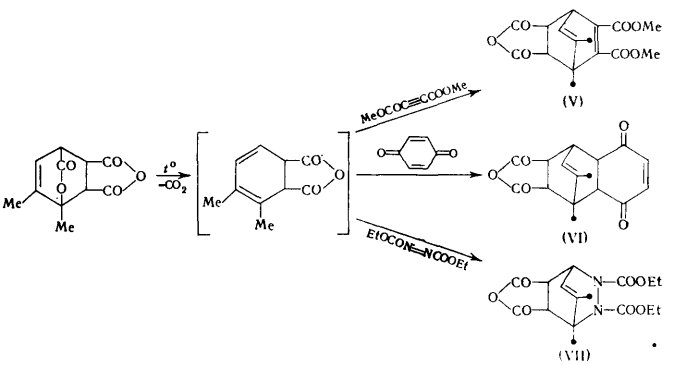
The products of the elimination of CO_2 from the adducts of 2-pyrones with maleic anhydride and *N*-phenylmaleimide, the corresponding derivatives of cyclohexadienecarboxylic acids (III), were characterised as bisanhydrides [5] and bisimides [6] (IV):



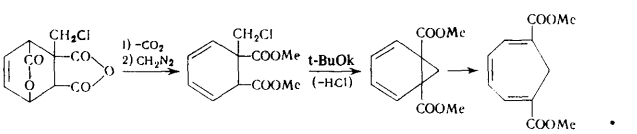
On heating above 200°C in nitrobenzene, the adducts are aromatised [14]:



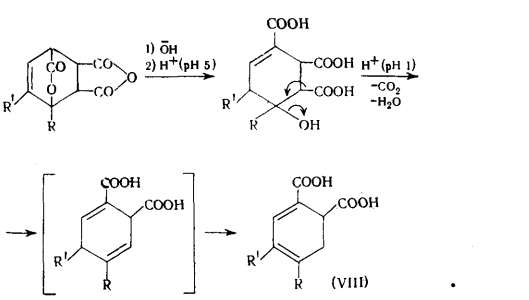
The thermolysis of the adducts with maleic anhydride in the presence of other dienophiles (acetylenedicarboxylic acid ester, benzoquinone, azodicarboxylic acid ester) made it possible to obtain mixed adducts with two dienophiles of different chemical types—compounds of the bicyclo[2,2,2]-octadiene (V) and bicyclo[2,2,2]octene (VI) series and a heterocyclic analogue (VII) of the latter with two nitrogen atoms in the ring [23]:



The cyclohexadiene systems formed on thermolysis of the monoadducts have been used also for other synthetic purposes, for example, for the formation of the cycloheptatriene ring [24,25]:

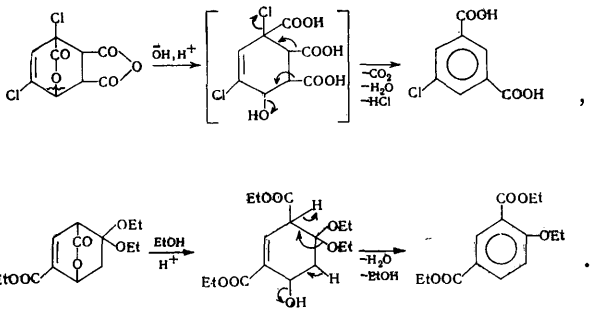


The opening of the lactone bridge under the influence of nucleophilic agents takes place with different degrees of difficulty depending on the substitution of the 6-position. Levina, Shusherina and coworkers, established that the hydrolysis of the bridge in the adducts of 5,6-disubstituted 2-pyrones with maleic anhydride (by treatment with aqueous solutions of alkali at 20–60°C) leads to the formation of the corresponding hydroxytricarboxylic acids which undergoes synchronous dehydration and decarboxylation at pH 1 (at 20°C), being converted into cyclohexadienedicarboxylic acids (VIII); the latter are readily aromatised on heating [13].

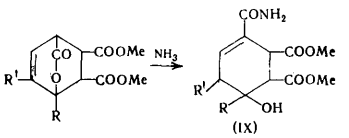


An example of the direct conversion of the adducts of 2-pyrones into aromatic compounds under the influence of nucleophilic agents is provided by the synthesis of 5-chloroisophthalic acid (in the alkaline hydrolysis of the adduct of 3,5-dichloro-2-pyrone with maleic anhydride [26])

and diethyl 4-ethoxyisophthalate (in the acid ethanolysis of the adduct of 5-ethoxycarbonyl-2-pyrone with the diethyl acetal of keten [18]):



In the ammonolysis of the esters obtained from the adducts of 2-pyrones with maleic anhydride it was possible to isolate the primary bridge-opening products—the amides of the corresponding hydroxyacids (IX): [27]

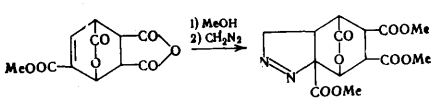


(IX)

It has been shown by ^{1}H NMR that the hydrolysis and ammonolysis of the monoadducts are accompanied by the migration of the double bond to the position conjugated with the carboxy- or carboxamido-groups arising in these processes [13,27].

Electrophilic addition to the double bond of the monoadducts of 2-pyrones (halogenation and oxidation) has been investigated to establish their configuration (see Section V).

1,3-Cycloaddition to the double bond of 8-oxabicyclo[2,2,2]oct-4-en-7-ones has been studied for adducts of alkyl coumalates with keten acetal [18], maleic anhydride, and *N*-phenylmaleimide [28]. The activated (by conjugation with the carboxy-group) double bonds of these compounds combine very readily with diazomethane, forming tricyclic Δ′-pyrazolines (X) with an endoxycarbonyl bridge:



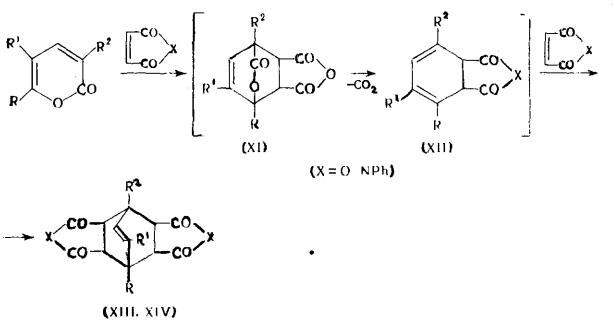
(X)

Similarly the adducts of alkyl coumalates with keten acetal combine with phenyl azide via the double bond [18]. However, the adducts of 2-pyrones with maleic anhydride without electron-accepting substituents at the double bond react neither with diazomethane nor with phenyl azide [28], which indicates an extremely weak strain of the double bond in 8-oxabicyclo[2,2,2]oct-4-en-7-ones whose geometry is close to that of the unstrained bicyclo[2,2,2]oct-4-enes [29].

III. DIENE SYNTHESIS WITH 2-PYRONES ACCOMPANIED BY THE ELIMINATION OR RUPTURE OF THE LACTONE IN THE MONOADDUCTS

1. Double Diene Synthesis (the Formation of Bridged Polycyclic Systems)

As a rule the interaction of 2-pyrones with dienophiles above 140°C is accompanied by the elimination of CO_2 from the monoadducts (XI) and the addition of a second dienophile molecule to the cyclohexadiene systems (XII) formed [3]†. Therefore, the reactions of 2-pyrones with maleic anhydride [4,11,12] and *N*-phenylmaleimide [16] under these conditions lead immediately to the bisanhydrides (XIII) and bisimides (XIV) respectively. The mechanism of the formation of (XIII) and (XIV) was confirmed by synthesis [the interaction of authentic *cis*-1,2-dihydrophthalic anhydride (XII, X = O) with maleic anhydride [4]] and also by the isolation of cyclohexadiene compounds (XII) in the thermolysis of the monoadducts (XI) (see above [16,17]):



(XI) (XII) (X = O, NPh)

(XIII, XIV)

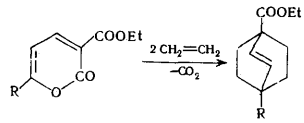
While the monoadducts can be obtained only from a few 2-pyrones substituted in specific positions (cf. the reaction described above), the products of double diene synthesis—bisanhydrides (XIII) and bisimides (XIV)—have been obtained from pyrones with different structures and a wide range of dienophiles. Thus bisanhydrides (XIII) are obtained in high yields from 6-aryl-2-pyrones [31], 5,6-dialkyl-2-pyrones [11,12], coumalic acid esters [32], tetrachloro-2-pyrones [26], 3-benzyl-2-pyrones [33], and other 2-pyrones [34-36] by the reaction with maleic anhydrides at 140°C.

High-melting crystalline bisanhydrides or the tetracarboxylic acid esters obtained from them are derivatives of 2-pyrones and are used to demonstrate the presence of the α-pyrone ring in the molecule [11,32-33,37].

Bisanhydrides are readily formed from 2-pyrones with weak electron-accepting groups (Br, CH_2Cl, CH_2OCOMe, NHCOMe) in the 3-position [38,39] (at 140°C) and also in the 3- and 5-positions [34,35]. However, 3-nitro- and 3-sulpho-2-pyrones [40,41] as well as 3,4,5-trichloro-6-phenyl-2-pyrone [26] do not react with maleic anhydride. A number of other dienophiles (benzoquinones and anthraquinones [32], acrylonitrile [42], phenyltriazoline-3-dione [43], and ethyl vinyl ether [18]) react with 2-pyrones only via the double diene synthesis mechanism (the elimination of CO_2 from

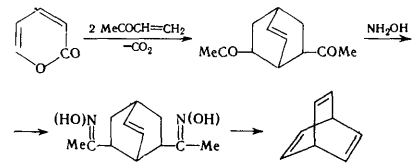
† Double diene synthesis occurs also with other cyclic dienes whose adducts readily eliminate the *endo*-bridge (for example with cyclone adducts [30]).

the monoadduct and the addition of a second dienophile molecule). 2-Pyrones react via this mechanism with ethylene, which is a weak dienophile (120–165°C, 1000 atm):[44]

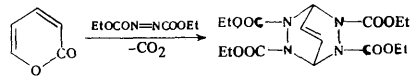


(R = Me, Et)

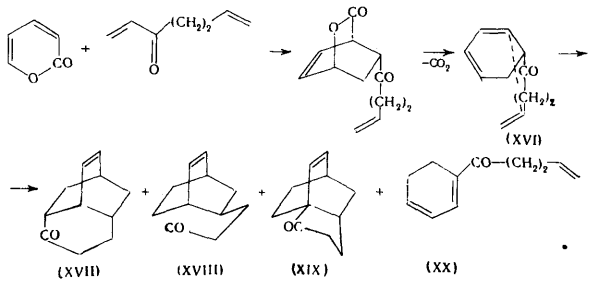
A classical example of the employment of double diene synthesis with pyrones is provided by the synthesis of barrelene {bicyclo[2,2,2]octa-1,4,7-triene} by the reaction of the unsubstituted 2-pyrone with methyl vinyl ketone[45,46] according to the following Scheme:



The employment of azodicarboxylic acid ester in diene synthesis with 2-pyrone made it possible to obtain a new heterocyclic system of the tetrazabicyclo[2,2,2]oct-2-ene series (XV):[47]

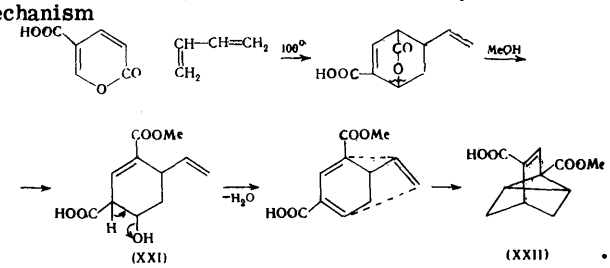


The recently investigated interaction of 2-pyrones with certain diene systems, which provide in succession both double bonds as dienophilic moieties, constitutes an unusual variant of double diene synthesis. Cyclohepta-1,6-diene-2-one reacts in this way with 2-pyrones. After the elimination of a CO_2 molecule from the monoadduct, the intramolecular interaction of the cyclohexadiene system of compound (XVI) with the double bond of the dienone fragment leads to the formation of a mixture of three isomeric tricyclic ketones (XVII), (XVIII), and (XIX) and the cyclohexadiene ketone (XX):[48]



(XVII) (XVIII) (XIX) (XX)

The double Diels–Alder reaction between coumalic acid and butadiene[49] served as a convenient method for the synthesis of tricyclene derivatives (XXII). When the process is carried out under pressure in methanol solution, the bridge in the monoadduct undergoes methanolysis, which is followed by intramolecular diene synthesis via the mechanism

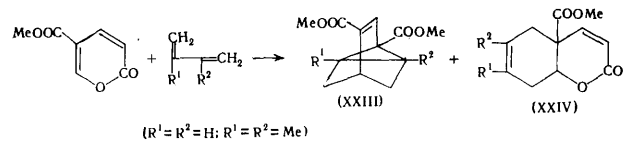


(XXI) (XXII)

Thus, in contrast to the examples described above, in this case the cyclohexadiene system does not arise in consequence of the elimination of the bridge but as a result of its rupture under the influence of methanol with subsequent dehydration of the hydroxyacid (XXI).

The interaction of coumalic acid with isoprene and dimethylbutadiene takes place similarly[49]. The unusual behaviour of typical dienes functioning as dienophiles in the reaction with coumalic acid can be explained by the occurrence of diene synthesis with "inverse electron demand" (cf. Section II, 1).

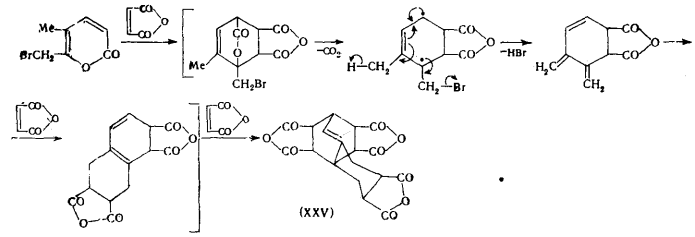
Methyl coumalate reacts with dienes in two ways—with formation of substituted tricyclo-octenes (XXIII) (as described above) and lactones (XXIV), which are obtained when methyl coumalate plays the role of the dienophile[50]:



(XXIII) (XXIV)

($R^1 = R^2 = H$; $R^1 = R^2 = Me$)

The only example of triple diene synthesis described in the literature is the synthesis of the tricyclic trisanhydride (XXV) by the reaction of 6-bromomethyl-5-methyl-2-pyrone‡ with an excess of maleic anhydride at 140°C according to the following Scheme[51]:

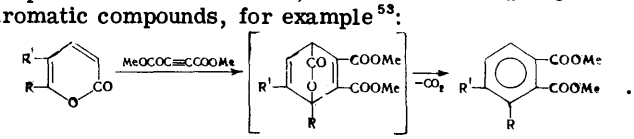


(XXV)

The above data illustrate the scope of diene synthesis with pyrones in the formation of polycyclic and "skeletal" systems.

2. Synthesis of Aromatic and Heterocyclic Compounds

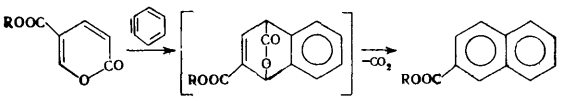
The formation of aromatic compounds by the reaction of 2-pyrones with acetylenic dienophiles was observed for the first time by Alder and Ricert[52]. The 1,4-cycloadducts produced initially in these reactions were not isolated, since they immediately split off the endoxycarbonyl bridge (because it is in the β-position with respect to two double bonds) and are converted into aromatic compounds, for example[53]:



The reaction of 2-pyrones with acetylenedicarboxylic acid ester resulted in the formation of satisfactory yields of hydroxy-,[52] dialkyl-,[53,54] and aryl-substituted[55] phthalic acids and hemimellitic acid[56] which are otherwise difficult to obtain. The reaction of diethylacetylene with 2-pyrone[57] to form *o*-diethylbenzene (yield 12%) proceeds with much more difficulty.

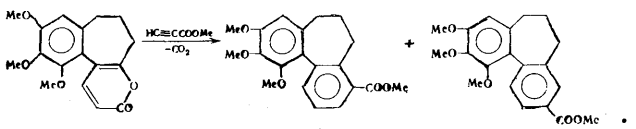
‡ The monoadduct was obtained from this pyrone at a temperature below 140°C.[5]

Derivatives of the naphthalene series have been obtained by the reaction of dehydrobenzene with alkyl coumalates [32]:

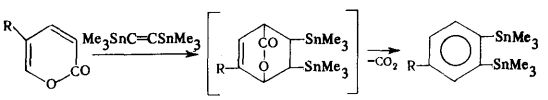


(R = Me, Et)

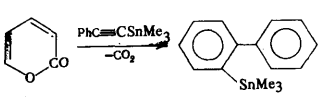
When asymmetric acetylenic dienophiles are used in reactions with 2-pyrones, the formation of a particular structural isomer is determined by polar and steric factors [58]. Thus the mode of addition of phenylacetylene to 2-pyrones is determined by the polar factor, since it proceeds in accordance with the charges of the initial reactants calculated by the Hückel method [58]. However, this rule breaks down when the dienophile employed is propiolic acid ester, which reacts with 2-pyrones to form both possible structural isomers [25,58], for example [25]:



New possibilities in the employment of diene synthesis with 2-pyrones have been discovered by Evnin and Seyferth [59]. To synthesis aromatic organotin compounds, they carried out the reaction of 2-pyrones with bis(trimethylstannyl)acetylene and trimethylphenylethynyltin:

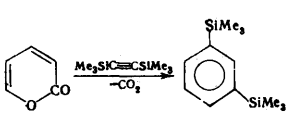


(R = H, Me, COOMe)



The study of the competing reactions of bis(trimethylstannyl)acetylene with 2-pyrone and 5-methoxycarbonyl-2-pyrone showed that only the less nucleophilic 5-methoxycarbonyl-2-pyrone reacts with the dienophile. This finding suggests that the interaction of 2-pyrones with bis(trimethylstannyl)acetylene proceeds via the inverse mechanism (cf. Section II, 1 and 2). [59]

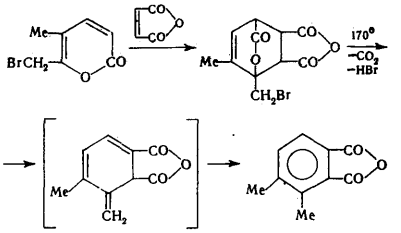
The use of bis(trimethylsilyl)acetylene in the reaction with 2-pyrone led unexpectedly to the formation of *m*-bis(trimethylsilyl)benzene as the main reaction product (53%) and only traces of the *o*- and *p*-isomers, which indicates the occurrence of a rearrangement [59]:



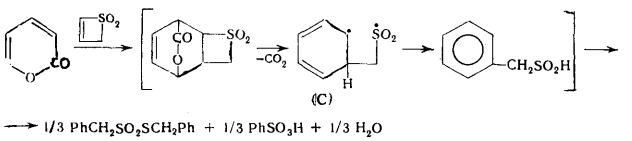
A special study [60] showed that the reason for the rearrangement is the acid-catalysed conversion of the *o*-isomer into the *m*-isomer. When acetylenic compounds of other Groups IV elements (tin and germanium) are used, such isomerisation does not take place, since the possible acid impurities are decomposed by these organometallic compounds as a result of the dissociation of the $M^{IV}-C$ bond, in agreement with the activity series of these metals (Sn ≥ Ge > Si) in protolytic reactions.

The authors admitted that the earlier explanation [59] of the above isomerisation as a result of the intermediate formation of non-Kekulé structures (prismane and benzvalene) is incorrect.

The formation of aromatic compounds in diene synthesis with 2-pyrones is possible for not only when acetylenic but also when ethylenic dienophiles are used, provided that together with the elimination of the bridge (CO_2) from the monoadduct, another simple molecule is also split off (hydrogen [32], hydrogen bromide [5], or an amine [18]), for example [5]:



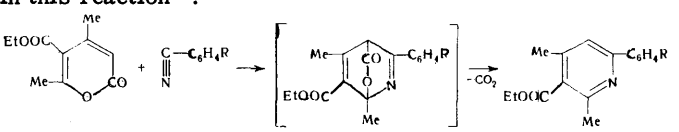
In the reaction of 2-pyrone with the sulphone derived from butadiene the resulting adduct also undergoes aromatisation in consequence of the elimination of CO_2 and the isomerisation of the biradical (C) to phenylmethanesulphinic acid, which disproportionates further according to the following mechanism [61]:



(C)

⟶ 1/3 $PhCH_2SO_2SCH_2Ph$ + 1/3 $PhSO_3H$ + 1/3 H_2O

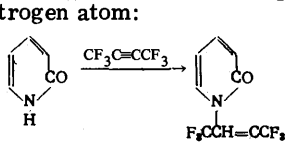
The interaction of 2-pyrones with nitriles via the mechanism of diene synthesis, accompanied by the elimination of CO_2 and the formation of substituted pyridines in a yield of about 20%, was described recently [62]. It is interesting that cyclones react similarly to nitriles, with the only difference that carbon monoxide is split off in this reaction [30]:



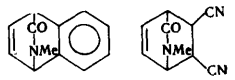
(R = H, Cl)

IV. DIENE SYNTHESIS WITH 2-PYRIDONES

The attempts to introduce 2-pyridones, nitrogen-containing analogues of 2-pyrones, into diene synthesis were unsuccessful for a long time. Pyridones unsubstituted at the nitrogen atom added to the double bonds of dienophiles (for example acrylonitrile [63], hexafluorobutyne [64], and acetylenedicarboxylic acid ester [65]) with formation of 2-pyridone derivatives alkylated or correspondingly vinylated at the nitrogen atom:



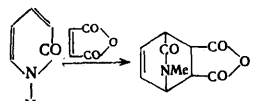
Among *N*-substituted 2-pyridones, only 1-methyl-2-pyridone could be made to undergo the diene synthesis reaction, giving rise to the adducts (XXVI) and (XXVII) respectively with dehydrobenzene [66,67] and fumarodinitrile [68] (yield 1–10%).



(XXVI) (XXVII)

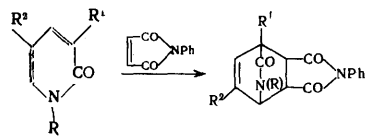
Owing to the low yields, the above reactions of 1-methyl-2-pyridone are of no preparative value. The 1,4-cycloadduct of this pyridone with tetracyanoethylene could not be obtained either [69].

In 1969 Japanese chemists obtained the adduct of 1-methyl-2-pyridone with maleic anhydride (XXVIII), in a yield of 42% (after heating for 72 h in toluene)§ [71,72], whose structure they demonstrated in detail both chemically and spectroscopically [72,73] (cf. the end of Section V).



(XXVIII)

Shusherina and coworkers succeeded in demonstrating that diene synthesis with 2-pyridones is a general reaction by employing *N*-phenylmaleimide and maleimide as dienophiles. It was found that not only do different *N*-substituted 2-pyridones form 1,4-cycloadducts (XXIX)—(XXXI) with these dienophiles in high yields [74,75], but also, and this is particularly interesting, even 2-pyridones unsubstituted at the nitrogen atom, whose interaction with other dienophiles gives rise to substitutional addition products only [63-65] (cf. the beginning of this Section) undergo this reaction to form Diels–Alder adducts (XXXII) and (XXXIII) in yields of about 50%: [76]



(XXIX–XXXIII)

(XXIX, R = Me, Pr, Bu, *i*-C_5H_{11}, H; R^1=R^2=H)
(XXX, R = Me, R^1 = H, R^2 = Me)
(XXXI, R = Me, R^1 = Me, R^2 = H)
(XXXII, XXXIII, R = R^1 = R^2 = H)

In contrast to the 2-pyrone adducts, the 1,4-cycloadducts of 2-pyridones {derivatives of 7-oxo-8-azabicyclo-[2,2,2]oct-4-ene-1,2-dicarboxylic acid} do not split off the bridge on thermolysis, but undergo retrodiene decomposition [75].

§ The cycloadduct could not be obtained by heating these reactants in benzene [70].

The results described indicate a lower diene reactivity of 2-pyridones compared with 2-pyrones. However, it is already evident that, by choosing a suitable dienophile, the Diels–Alder reaction can be widely employed in the series of 2-pyridones.

V. THE STEREOCHEMISTRY OF DIENE SYNTHESIS WITH 2-PYRONES AND 2-PYRIDONES

Like other cyclic dienes, 2-pyrones and 2-pyridones can give rise in reactions with dienophiles to monoadducts¶ with *endo*- and *exo*-configurations. The study of the *endo*–*exo* selectivity of diene synthesis, which was begun by Alder, has continued vigorously for more than 30 years. The interest in this subject is due to the employment of stereochemical data in the consideration of reaction mechanisms and transition state structures [1,77-80].

On the basis of experimental data obtained mainly in a study of diene synthesis with cyclopentadiene and its derivatives, Alder and Stein [81] concluded that the diene synthesis reactions are *endo*-stereoselective and formulated the so called Alder "*endo*-rule", which they accounted for by the possibility of the "maximum accumulation of unsaturation" only for the *endo*-orientation of the components. Further investigation of the stereochemistry of reactions between cyclic dienes and dienophiles with different structures revealed many exceptions to this rule. Thus doubt was cast on the *endo*-selectivity of diene synthesis discovered by Alder [82].

Different types of non-bonding (non-valence) or secondary-bonding interaction were considered as the main factors stabilising the *endo*- and *exo*-transition states [78-83]. The role of these forces in Diels–Alder reactions is much greater than in other processes owing to the "close packing" of the transition states, which promotes a greater proximity of the individual structural elements of the diene and dienophile [77].

Different versions of the concept, proposed at an early stage by Alder, of the overlapping of the π-orbitals of the multiple bonds of the diene and dienophile as the *endo*-orienting factor have been most widely discussed [78-81]. These ideas have now been confirmed theoretically by molecular orbital calculations and are used in the form of the Woodward–Hoffmann rule, correlating the secondary π-orbital interaction with orbital symmetry, to predict the steric course of cycloaddition reactions, including diene synthesis [84,85].

The important role of π-orbital interaction was demonstrated convincingly recently by the conversion of non-stereoselective Diels–Alder processes into *endo*-selective reactions by the introduction into the dienophile of a second and third double bond. Thus the reactions of 2,5-dimethyl-3,4-diphenylcyclopentadienone with non-conjugated mono-olefins (cyclopentene [86], *cis*-3,4-dichlorocyclobutene [87], and cycloheptene [88]), for which secondary π-orbital interaction is impossible, took place non-stereoselectively with formation of mixtures of *endo*- and *exo*-isomers, while the reactions with dienophiles having several multiple bonds (cyclopentadiene [86], tropone [86,89]

¶ The configurations of the bisanhydrides and bisimides, formed in diene synthesis, which were described above is not considered in this section since it is determined by the stereochemistry of the diene synthesis with cyclohexadiene systems and not by the nature of the 2-pyrones (see Section III, 1).

and cycloheptatriene [86]) gave only the *endo*-isomers. Thus the *endo*-rule received new experimental confirmation in these investigations†.

However, the secondary π-orbital interaction can influence stereochemistry only in kinetically controlled reactions. In those cases where *endo*–*exo* isomerisation of the adducts is possible and the stereochemical result is not determined by kinetics but by the thermodynamic stability of the stereoisomers, the more stable *exo*-isomers are frequently formed (particularly at relatively high temperatures), for example in the reactions of furan and its derivatives with maleic anhydride [21,92–94]. Furthermore, in order to be able to play a decisive role in the orientation of the components, π-orbital interaction must be sufficiently strong, as in the reactions of cyclic dienes with cyclic dienophiles containing several unsaturated groups (for example, with maleic acid derivatives and quinones) [1]. On the other hand, reactions with dienophiles whose double bond is activated by only one unsaturated group can occur non-stereoselectively (for example, the interaction of cyclopentadiene with acrylonitrile) [95].

One should also bear in mind that, when the diene molecule contains two unsaturation centres (for example, in fulvenes) the π-orbital interaction promotes both possible orientations of the reactants [1,78].

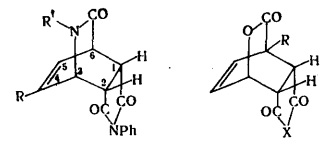
Together with π-orbital interaction, which occurs in the presence of additional unsaturated groups in the dienophiles, the stereochemistry of the reaction can be affected by saturated substituents of the diene and dienophile favouring the *endo*- or *exo*-approach of the reactants by the operation of electrostatic forces (attractive dispersion forces, repulsive van der Waals forces, and dipole–dipole interaction), which arise between the saturated diene and dienophiles substituents themselves and between the latter and the sp^2-carbon atoms of the diene [84,86]. The study of this factor, which can also be observed only under the conditions of kinetically controlled reactions, is made difficult by the fact that it may be determined by different types of interaction of the substituents some of which favour *endo*-selectivity and others favour *exo*-selectivity.

Studies on the effect of structural factors on the stereochemistry of diene synthesis have been made only recently [96–102]. For example, it has been established that the preferential formation of the *exo*-isomers in the reactions of cyclopentadiene with methacrylic acid and its derivatives is determined by the presence of the methyl group in the α-position of the dienophile [103–107]. It is at present difficult to decide [91] whether this is a consequence of the operation of repulsive forces between the hydrogen atoms of the methylene group of cyclopentadiene and the methyl group of the dienophile [101,107] or of attractive dispersion forces between the α-methyl group of the dienophile and the sp^2-carbon atoms of the diene [104,105].

The *endo*-selectivity of the reactions of cyclopentadiene with certain mono-olefins (cyclopropene, norbornene, allyl alcohol, and allyl bromide [108]) has been explained by the operation [86] of van der Waals forces.

It is evident from the data quoted that the problem of the *endo*–*exo*-selectivity of diene synthesis continues to remain controversial. More comprehensive investigation of various factors, particularly those determined by the structure of the dienophile, is necessary for its solution. In this sense the study of the stereochemistry of diene synthesis with 2-pyrones and 2-pyridones is of great interest.

The investigation by the present author (together with Levina, Stepanyants, and coworkers) of the configuration of the adducts of 2-pyrones with maleic anhydride and *N*-phenylmaleimide (by ^{1}H NMR‡ [6,16,109] and chemically [109,110], see below) and also of the adducts of *N*-alkylpyridones with *N*-phenylmaleimide by ^{1}H NMR‡ [74,75] showed that, in the absence of methyl groups at the ends of the conjugated system of multiple bonds of these heterocycles, the interaction with dienophiles proceeds *endo*-selectively with formation of the adducts (XXIX), (XXX), and (XXXIV)–(XXXVI).

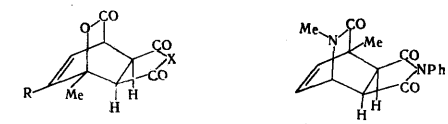


(XXIX, R = H, R' = Alk (Me, Pr, Bu, C_5H_{11})
(XXX, R = R' = Me)

(XXXIV, R = H, X = O)
(XXXV, R = Br, X = O)
(XXXVI, R = H, X = NPh

The interaction of the unsubstituted 2-pyrone with fulvene, discovered by Houk in 1973, also took place *endo*-stereoselectively [111].

On the other hand, 5,6-dimethyl-2-pyrone and 6-methyl-5-phenyl-2-pyrone form only *exo*-adducts with maleic anhydride and *N*-phenylmaleimide [(XXXVII)–(XXXIX)]. [6,16,109] A similar *exo*-influence of the methyl group in the 3α-position of the pyridone rings occurred in the interaction of 1,3-dimethyl-2-pyridone with *N*-phenylmaleimide, which led to the formation of the *exo*-adduct (XXXI) alone [75]:



(XXXVII, R = Me, X = O)
(XXXVIII, R = Ph, X = O)
(XXXIX, R = Me, X = NPh)

(XXXI)

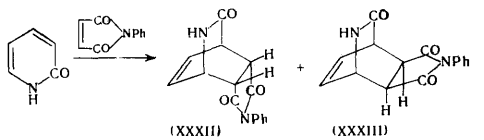
The observed breakdown of the Alder *endo*-rule for 5,6-disubstituted 2-pyrones and 1,3-dimethyl-2-pyridone cannot be due to thermal isomerisation, because the *exo*-adducts were obtained at the same (or lower) temperatures as the *endo*-adducts [16,109]. The effect of the secondary

† A fundamentally new explanation of the Alder *endo*-rule, based on the concept of the preferred geometry of the *endo*-overlapping of the π-orbitals of the carbon atoms of the diene and the dienophile directly involved in the formation of new bonds, was given by Herndon and Hall [90,91].

‡ The determination of the configuration of the adducts of 2-pyrones and 2-pyridones with maleic anhydride and *N*-methylmaleimide [(XXIX)–(XXXI) and (XXXIV)–(XXXIX)] by ^{1}H NMR [6,16,74–76,109] is based on the difference between the coupling constants of the protons at the bridgehead ($C_{(3)}H$ and $C_{(6)}H$) with the adjacent protons ($C_{(6)}H$ and $C_{(2)}H$) for the *endo*- and *exo*-isomers and also on the change in the chemical shifts of the $C_{(1)}H$, $C_{(2)}H$, and $C_{(6)}H$ protons for which the $C_{(1)}H$ and $C_{(2)}H$ signals of the *exo*-forms are in a higher field and those of the methine protons at the bridgehead ($C_{(6)}H$) are in a lower field compared with the signals of the corresponding protons in the spectra of the *endo*-forms.

π-orbital interaction, which determines the stereochemistry of the above Diels–Alder reactions with 2-pyrones [6,16,109] and *N*-alkyl-2-pyridones [74,75] unsubstituted at the ends of the conjugated system of multiple bonds, is probably suppressed in these heterocyclic dienes with 3- and 6-methyl [6,16,76,109] (or aryl [112,113]) groups, which favour the formation of *exo*-adducts.

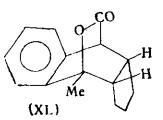
It is interesting that 2-pyridones unsubstituted at the nitrogen atom react with maleimide and *N*-phenylmaleimide via the Diels–Alder mechanism (cf. Section IV) non-stereoselectively with formation of a mixture of the *endo*-isomer (XXXII) and the *exo*-isomer (XXXIII).[76]



(XXXII) (XXXIII)

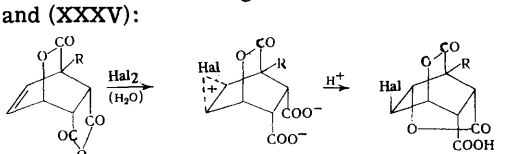
Thus the study of the stereochemistry of diene synthesis with 2-pyrones and 2-pyridones revealed for the first time the *exo*-orienting effect of the methyl and phenyl groups at the ends of the conjugated system of the heterocyclic diene in their interaction with maleic anhydride and *N*-phenylmaleimide.

However, in the reactions of 6-methyl-4,5-benzo-2-pyrone with nonconjugated dienophiles (cyclopentene, cycloheptene) the above influence of the methyl group was not observed: the reactions took place mainly with formation of the *endo*-adducts (XL), which the authors explained by the attraction of the methylene groups of the dienophile to the double bonds of the diene [114], as described above [104,105].



(XL)

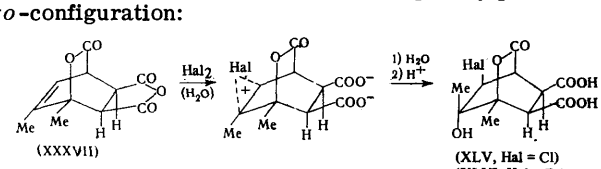
The use of chemical methods for the determination of the configuration of the adducts of 2-pyrones with maleic anhydride is based on the formation of different compounds from the *endo*- and *exo*-isomers on electrophilic addition to the double bond in the manner described for the adducts of other cyclic dienes with maleic anhydride [115–117]. Thus halogenation of the adducts (XXXIV) and (XXXV) in an aqueous medium yielded the halogenolactones (XLI)–(XLIV), formed as a result of the intramolecular stabilisation of the halogenonium ions produced initially [110,118], which confirms the *endo*-configuration of the adduct (XXXIV) and (XXXV):



(XXXIV, R = H)
(XXXV, R = Br)

(XLI, R = Br, Hal = Br)
(XLII, R = H, Hal = Cl)
(XLIII, R = H, Hal = Br)
(XLIV, R = H, Hal = I)

The formation of the halogenohydrins (XLV) and (XLVI) from the adduct (XXXVII) [110,118] demonstrates the impossibility of such stabilisation and consequently proves its *exo*-configuration:



(XXXVII)

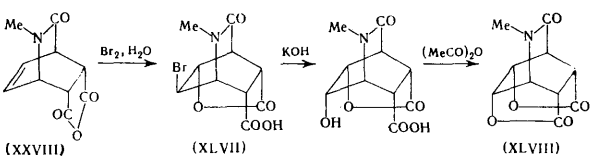
(XLV, Hal = Cl)
(XLVI, Hal = Br)

However, it is noteworthy that the halogenation of bridged bicyclic systems is accompanied by the Wagner–Meerwein rearrangement [92,119]. The formation of the isomeric halogenolactones from the *endo*- and *exo*-forms in such cases can lead to an incorrect interpretation of the stereochemistry of the reaction [92,120].

Since conclusions concerning the configuration of the adducts (XXXIV), (XXXV), and (XXXVII) based on the above reactions are consistent with ^{1}H NMR spectroscopic data (see above), one may conclude further that in the instances described the halogenation of the 2-pyrone adducts was not accompanied by a rearrangement.

The most reliable method for the determination of the configurations of bicyclic adducts—conversion into the iodolactone in which the possibility of the Wagner–Meerwein rearrangement is ruled out [121]—is unsuitable for the adducts of 2-pyrones with maleic anhydride, since the iodination of these systems takes place non-quantitatively and is accompanied by the rupture of the endoxycarbonyl bridge [118].

The *endo*-configuration of the adduct of 1-methyl-2-pyridone with maleic anhydride (XXVIII) (see Section IV) was established recently by the following series of transformations into the bromolactone (XLVII) and the bislactone (XLVIII): [71,72]



(XXVIII) (XLVII) (XLVIII)

The absence of the Wagner–Meerwein rearrangement in the bromination of the adduct (XXVIII) was demonstrated by the ^{1}H NMR spectra of the bromolactone (XLVII) and its deuteriated derivatives [73].

The data on the stereochemistry of diene synthesis with 2-pyrones and 2-pyridones described above show that the orientation of the components in these reactions is not determined solely by the secondary π-orbital interaction. Examples of the breakdown of the Alder rule when substituents are introduced in specific positions in the 2-pyrone [6,16,111] and 2-pyridone [75] rings and also the non-stereoselective course of the reactions with 2-pyridones unsubstituted at the nitrogen atom [76] are evidence for the important role of other factors, the nature of which will have to be elucidated in future investigations.

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Photoconductance of Organic Polymers

V.S.Myl'nikov

Photoelectric phenomena in organic polymers are analysed, attention being paid mainly to experimental and theoretical information on the mechanism of photoconduction. Macroscopic photoelectric properties are shown to have common features in polymers, inorganic semiconductors, and organic semiconductors of low molecular weight. A list of 218 references is included.

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I. INTRODUCTION

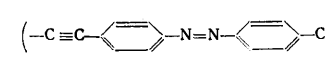
Isolated observations of an internal photoeffect in organic polymers at the beginning of the 1960s have now been replaced by regular and systematic investigations. Nevertheless, the short chapters in several monographs on organic semiconductors [1-10] and the single previous review [11] on the photoelectric properties of organic polymers have become out of date and do not give a full idea of the present-day state of this field of science. An attempt is now made to summarise information which has accumulated on the photoelectronics of organic polymers with the exception of organometallic and coordinated polymers, which have been considered in Ref. 12.

The investigation of photoelectric phenomena opens up great possibilities for studying the mechanism of the generation, drift, and recombination of current carriers, as well as for analysing the chemical and physical structure of organic polymers in the broadest sense. Use of a light beam ensures rapid transmission of information, uncoupling between individual channels of communication, high information capacity, and directional signals. In this connection organic polymers, with their specific physicochemical properties, are extremely promising materials for photosensitive cells with a wide range of uses in various technical devices. The Table sets out types of photosensitive organic polymers known at the present time.

II. POLYMERS WITH TRIPLE BONDS IN THE CONJUGATED CHAIN

Some of the first macromolecular compounds in which an internal photoeffect was detected [13] and studied systematically [11,13-28] were poly-ynes—compounds containing C≡C triple bonds in the conjugated chain—for which the main parameters determining the photoconductance and the photo-e.m.f. were examined. It was shown in particular that the dependence of the photocurrent i_{ph} on illuminance L is expressed by the formula $i_{ph} = \alpha L^n$, where $0.5 \leqslant n \leqslant 1$, [11,17-19] the photocurrent being proportional to the voltage raised to the power $1.2 < m < 1.7$. [17-19] In the large majority of poly-ynes the carriers of the photocurrent are positively charged [11,13,15-19], the kinetics of photoconduction is characterised by relaxation times from 10^{-5} s to a few minutes, and a hyperbolic law is obeyed [14].

Investigation and comparison of the photoconductance, photo-e.m.f., and absorption spectra [13,15-22] established that poly-ynes are intrinsic semiconductors, enabled the optical activation energies of photoconduction to be determined, and showed that the first stage in the generation of current carriers in polymers is the formation of excited molecular states or excitons. Preliminary exposure to ultraviolet radiation was found to activate the photoelectric sensitivity of poly-ynes [13,15]. Typical spectral curves of these compounds are shown in Fig. 1 for poly-*pp'*-diethylnylazobenzene



Optical activation energies of photoconduction determined from the photoconductance and photo-e.m.f. spectra agree with each other over the range 1.5–2.5 eV, and coincide with the edge of the fundamental absorption. This is evidence of the intrinsic character of conduction in poly-ynes. The optical activation energy of photoconduction is identical with the activation energy of electrical conduction [15], which indicates the common nature of these processes. The main photoconductivity maximum is situated, as in inorganic semiconductors, on the descending slope of the fundamental absorption, probably owing to the high rate of surface recombination.

With poly-ynes as example it was suggested that photoconduction in polymers should be regarded as a multistage process involving formation of an exciton and its subsequent dissociation on interaction with a defect or with another exciton [13,15-19]. Comparison of the absorption spectra of poly-ynes in solution and in the solid phase [16] indicates that intermolecular interaction is strengthened in the latter. The change in the photosensitivity of polymers produced by preliminary ultraviolet irradiation was explained by ionisation of the molecules followed by photopolymerisation [11,13,15] producing charged local centres, which is supported by the presence of a photoinduced electron spin resonance signal [17-20].

It is noteworthy in this connection that Wegner has obtained photoconducting polymers by exposing monomers containing conjugated triple bonds to ultraviolet radiation or high-energy electrons [28]. The photochemical modification of monomers with triple bonds and of polyacetylenes [29-31] is of interest for several recording systems. In all the cases examined the initial act of the photochemical reactions can be assumed to be the formation of free

electrons. This makes the investigation of photoelectric properties most promising for an understanding of the elementary acts in photochemical reactions. The discovery of photoconduction has enabled poly-ynes to be used for the preparation of electrophotographic layers [21,22]. Investigation of poly-ynes under electrophotographic conditions [24,25] has confirmed several effects and regularities observed under conditions of photoconduction and photo-e.m.f. (sign of carrier, spectral characteristics, activation of photosensitivity by ultraviolet radiation, etc.) and has enabled fresh information to be obtained on the properties of electrophotographic layers based on photosensitive polymers having triple bonds in the conjugated chain. It is noteworthy also that the photosensitivity of poly-ynes can be extended by dyes to longer wavelengths [18,19,34].

Photosemiconducting organic polymers.

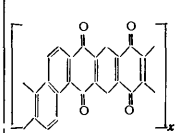
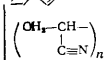
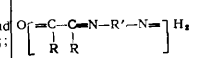
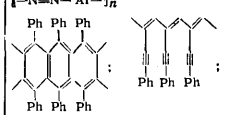
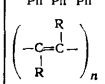
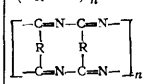
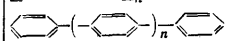
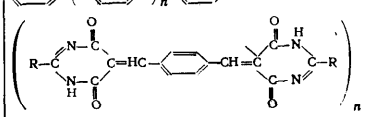
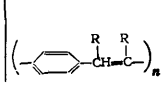
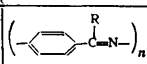
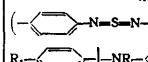
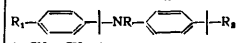
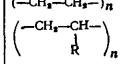
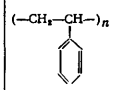
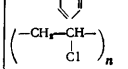
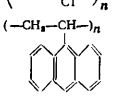
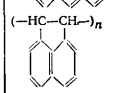
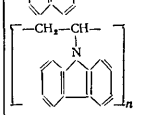
No.	Polymers	Structural formula of unit	Refs.
1	Poly-ynes (R = Alk, Ar, Hetaryl)	$R'-(-C\equiv C-R-C\equiv C-)_n-R'$ $R-(-C\equiv C-)_nR$	11; 13—28
2	Pyrolysis products from (*a*) polyacrylonitrile (*b*) regenerated cellulose (*c*) phenol-formaldehyde resin (*d*) poly(vinyl fluoride)		32, 33, 40, 41 32, 33 35, 188 34
3	Products of photochemical treatment of vinylidene-vinyl chloride copolymer		44—46
4	Acenequinone radical polymers (PAQR)		36—39
5	Polyacrylonitrile and its complexes		40—43
6	Products of radiation-thermal modification of (*a*) polyethylene (*b*) poly(vinyl acetate) (*c*) polyimidazopyrrolones		4, 52—55 53 56
7	Polymeric Schiff bases and polyazines: R = H, C_6H_5; R' = *p*-C_6H_4		57—59, 68, 69
8	Polyazopolyarenes	$[-N=N-Ar-]_n$	60
9	Products of catalytic and thermal polymerisation of polydiphenyldiacetylene		62
10	Polyvinylenes		61, 63, 65—70, 75—77, 81—84, 100 121, 134
11	Polymeric acid diamides: R = CH_2, $CH_2.CH_2$, CH:CH		64
12	Polyphenylenes		61, 65, 66, 135
13	Polystyrylpyrimides		71
14	Polymers obtained in a discharge from monomers containing S, Se, N, and various metal atoms		72—74
15	Polyxylidenes		78, 79

Table (contd.)

No.	Polymers	Structural formula of unit	Refs.
16	Polyarylenazomethines		78, 79
17	Polyarylenethiodiimides		78, 79
18	Oligoanilines		80
19	Polyethylene	$(-CH_2-CH_2-)_n$	85—93, 95—100
20	Vinyl polymers with aromatic and heterocyclic side-chains		101, 102, 107—113, 117, 135, 180, 183, 186
21	Polystyrene (*a*) complexes of polystyrene		103—110, 114—116 135, 176 123, 131—133
22	Poly(vinyl chloride)		118, 184, 185
23	Poly-9-vinylanthracene		183
24	Polyacenaphthylene		181, 182
25	Polyvinylcarbazole		134—143, 165—173 179, 212—218
	(*a*) complexes		144—151, 162—164
	(*b*) with sensitisers		21, 24, 129, 134—139, 142—145, 151—161
	(*c*) with amorphous selenium		174—176
26	Polymers with added photosemiconductors		120—130, 177
27	Biopolymers		189—204

III. PRODUCTS OF THE THERMAL AND RADIATION-THERMAL TREATMENT OF POLYMERS

In the early stages thermal and radiation-thermal treatments were among the main methods of obtaining semiconducting organic polymer systems. Probably the first publications on the photoelectronics of these systems were brief communications by Mrosowski et al. on the possibility of using polyacrylonitrile and regenerated cellulose films pyrolysed at 800 °C as infrared detectors with sensitivity extending to 5 μm. [32,33] Pyropolymers based on poly(vinyl fluoride) and on a phenol–formaldehyde resin have since been proposed for infrared detectors [34,35]. Photoconduction has been observed in conjugated polymers based on acenequinone radical systems, polyacenes, Aniline Black, etc. by Pohl and his coworkers [36-39], who found that the *n*- and *p*-type conductivities of these compounds may vary from 10^3 to 10^{-13} ohm^{-1} cm^{-1}, and the mobilities of the current carriers from 10^{-6} to 100 cm^2 V^{-1} s^{-1}.

The photoconductance of the pyrolysis products of polyacrylonitrile was investigated in detail by Rozenshtein and his coworkers [40,41] who showed that, in the initial stage of thermolysis at 200–300 °C, conjugated segments of statistically unchanged lengths are formed in the polymer by cyclisation at nitrile groups. The kinetics of the growth of photoconductance during heat-treatment is

identical with that of the increase in the number of conjugated segments. Thus at this stage the increase in photoconductance is due solely to increase in the number of absorbing centres, not to a change in the mobility of the carriers. With rise in the treatment temperature the photoconductance spectra broaden and move to longer wavelengths with simultaneous increase in the absolute magnitude of the photoconductance and decrease in its relaxation time. Estimates of the upper limit of mobility based on the band model have shown that it increases from 0.01 to 40 $cm^2 V^{-1} s^{-1}$ with rise in the temperature of thermolysis from 200° to 500°C. The main result of work on the photoconductance of polyacrylonitrile must be regarded as the establishment that conjugated bonds are sufficient for the appearance of electronic conduction. Photoconduction may be observed in polyacrylonitrile also on complex formation with solvents, donor and acceptor molecules, as well as during its exposure to infrared radiation[42,43].

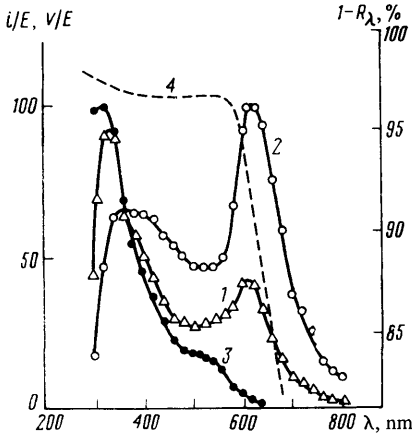


Figure 1. Spectra of poly-*pp'*-diethynylazobenzene[15,20]: 1) photoconductance; 2) as (1) after preliminary ultraviolet exposure (10 min); 3) photo-e.m.f. after preliminary ultraviolet exposure (10 min); 4) reflectance spectrum of unexposed polymer.

Exposure of a copolymer of vinylidene and vinyl chlorides to ultraviolet radiation results in the appearance of photosensitivity in the product[44-46]. The nature of the photoconductivity depends on the free radicals formed during irradiation, since conditions which induce and destroy the e.s.r. signal have similar effects on the photoconductance. Exposure to shorter wavelengths, e.g. X-rays, also produces an e.m.f. and induced conductance in polymeric materials[47-51].

Products of the radiation-thermal modification of polyethylene were investigated by Vannikov et al.[52,53]. Photocurrents of $\sim 10^{-12}$–10^{-14} amp were observed in the range 300–900 nm with light fluxes of 6 mW cm^{-2} and a multiplicity factor (ratio of photocurrent to dark current) exceeding 10. The activation energy of photoconduction ΔEph proved to be considerably smaller than the activation energy of electrical conductivity ΔEth, and decreased with increase in the photon energy on passing to more severely treated specimens. This decrease is probably due to the convergence of the conduction level of the polymer towards local levels determining the temperature dependence of the photoconductance. The photosensitivity under the same conditions of products based on poly(vinyl acetate) exceeds that of modified polyethylene some hundredfold[53].

Preliminary irradiation of high-pressure polyethylene with high-energy electrons led to a sharp increase in the photocurrent, whose principal region of sensitivity was situated in the near infrared[54,55]. Such irradiation had produced donor and acceptor traps, the formation of double bonds in the chains, and the cross-linking of separate macromolecules. A correlation probably exists between these double bonds and the traps of donor type. An energy diagram was given for the irradiated polyethylene with traps at levels 0.5, 1.1, and 1.7 eV below the conduction band. The activation energies for photoconduction and electrical conductivity are identical. The volt–ampere characteristics of the photocurrent indicate that space charges play an important part in establishing a photoresponse.

With polyimidazopyrrolones[56] at energies of ~ 15 mW cm^{-2} (polychromatic light) the observed current exceeded the dark current by a factor of 300. Maximum photosensitivity was reached after vulcanisation at 300°C for 24 h, when sensitivity was observed in the ultraviolet, visible, and near infrared regions with maxima at 610 and 550 nm. The photoconductance spectrum is displaced by about 35 nm to longer wavelengths compared with the optical absorption spectrum. Attempts to sensitise polymers by means of dyes were unsuccessful. The photocurrent obeys Ohm's law at field strengths of 10^2 to 10^5 V cm^{-1}. The observed thermal activation of the photocurrent suggests that generation of the carriers involves a complicated mechanism[56].

IV. POLYMERS WITH DOUBLE BONDS, HETEROATOMS, AND HETEROCYCLES IN THE CONJUGATED CHAIN

In this class of polymers photoconduction was first observed with certain polymeric Schiff bases and polyazines[57-59]. The lux–ampère dependence of the photocurrent was found to be below linear for all the specimens. The photocurrents increase exponentially with temperature and have activation energies of ~ 0.1–0.2 eV. The considerable polarisation phenomena made interpretation of the results difficult.

As the conjugated system in polyazopolyarenes[60] and their carbon analogues[61] becomes shorter, the photocurrent in the region of maximum absorption becomes smaller, the thermal activation energy of electrical conduction decreases, and the optical spectra undergo a hypsochromic shift. It is interesting that the activation energy of photoconduction increases with decrease in the photon energy. This has been linked with the molecular-weight distribution in the polymer, but requires detailed verification. In this case there may exist definite prospects for controlling and determining molecular-weight distributions in polymers by photoconduction methods. Variation of the activation energy of photoconduction with wavelength has been observed also in polydiphenyldiacetylenes[62], and is due to differences in the depth of the trapping levels involved in photoconduction. It has been shown for poly-ω-iodophenylacetylenes that the absorption in the range 400–1100 nm by various fractions is independent of the molecular weight of the polymer, the conjugated segments being shorter than the macromolecule[63]. The

photoconductance spectrum coincided with the form of the optical absorption spectrum. Photoelectric sensitivity was observed in a group of ladderlike polymers by Polak et al.[64] Photoconduction was suppressed by oxygen.

Photoconduction was established and studied in poly-*p*-phenylenes and several polyvinylenes by Beck[65,66]. The resistivity of specimens was $10-10^{15}$ ohm cm depending on the conditions of polymerisation and the oxygen content, and the activation energy of photoconduction varied from 0.025 to 0.96 eV. A tunnel mechanism of the passage of carriers through potential barriers was suggested for these polymers, and the mobility of the carriers was estimated as 0.6 $cm^2\ V^{-1}\ s^{-1}$.

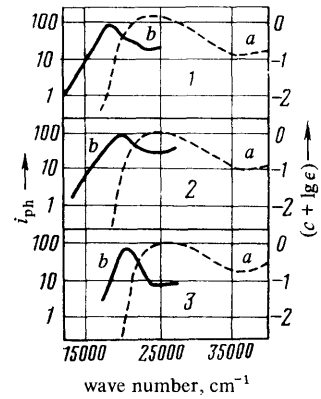
Grenishin, Cherkasov, and their coworkers[67-70] have been concerned with aspects of the relation between the structure and the photoelectric properties of polyenes (polyphenylacetylene, polydiphenylacetylene), acene structures (polydiphenylbutadiyne), structures with heteroatoms in the conjugated chain, and polymeric Schiff bases. Various methods have confirmed that the macromolecule is considerably larger than the average conjugated segment. The photosensitivity of polymeric Schiff bases[68] is independent of molecular weight over the range 200–1000, but increases tenfold on passing from amorphous to crystalline structures. Under electrophotographic conditions polymers containing carbon–nitrogen bonds exhibit photoconduction in the ultraviolet with quantum efficiencies of $(5-100)\times 10^{-6}$ el quantum^{-1},[69] which increase with the degree of delocalisation of electrons along the conjugated chain and with increased regularity of the structure. The photosensitivity of crystalline structures usually exceeds that of amorphous structures. It is generally concluded that segments of π-conjugation in polymers are no longer than those in low-molecular organic semiconductors, and hence that their electronic nature is the same. This evidently holds only for the stage of generation of photocarriers, which is regarded[70] as involving the formation and destruction of excitons as in poly-ynes.

The dependence of photoconductance on the chemical structure of the macromolecule has been studied on polystyrylpyrimidines[71]. With certain polymers and undispersed light the variation was about 10 000-fold. The photocurrent in a vacuum exceeds that in air almost hundredfold, a steady photoconductance is established within 1–2 min, and the range of photosensitivity is 400 to 900 nm. Maxima in the photoconductance spectra coincide with minima in the absorption spectra. No specific mechanism of photoconduction is suggested[71]. The variation in the absorption spectra of these compounds was ignored in the study of the effect of chemical structure on photoconductance, so that the results obtained by these workers must be approached with caution.

Photoconductance in the visible region has been observed with a multiplicity of several thousand in films obtained by the polymerisation in the glow discharge of monomers containing nitrogen, sulphur, selenium, and certain metal atoms[72,73]. A significant increase in photoconductance was observed on the addition of traces of iodine during polymerisation. The activation energy of photoconduction was 0.25 eV over the range 25–175°C, and 0.05 eV at lower temperatures. The first step in the generation of photocurrent carriers was regarded as the formation of excitons. Unfortunately, no information was given on the structure of the polymer films obtained in the discharge. They may contain several monomeric compounds which determine their properties. Photoemission data[74] indicate that films obtained in a discharge behave as large unsaturated molecules—not as polymers.

The action of dehydrogenating agents on poly(vinyl alcohol) yields a polymer having photosensitivity in the near infrared, electronic conductance with a concentration of charge carriers of 10^{16} cm^{-3}, and mobility 10^{-3} $cm^2\ V^{-1}\ s^{-1}$, both determined from the Hall constant[75]. Photosensitivity extending to 8 μm is observed in polyacetylene obtained by means of a Natta–Ziegler catalyst[76]. This polymer exhibited an identical thermal activation energy (0.27 eV) for electrical conduction and for photoconduction, which was regarded[76] as that needed for the transition of electrons from impurity levels to the conduction band. Prolonged exposure led to a decrease in photoconductance.

Indirect estimates have recently been supplemented by direct measurements of the mobilities of carriers in polymers. Thus values of $10^{-3}-10^{-5}$ $cm^2\ V^{-1}\ s^{-1}$ have been determined[77] for polydiphenylbutadiynes and poly(halogenophenylacetylenes). The results show the presence of many capture levels in these polymers.



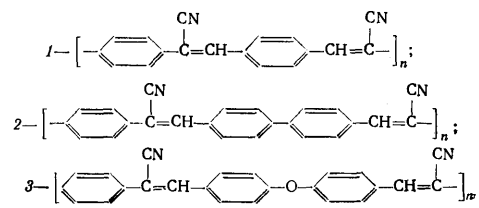


Figure 2. (*a*) Diffuse reflectance and (*b*) photoconductance spectra[79] of the polyxylidenes:

Extremely interesting work on the photoconduction of polyxylidenes[78,79] has established that the principal maxima are situated on the descending slope of the fundamental absorption, but an inverse correlation exists in the region of strong absorption (typical results are illustrated in Fig. 2). A correlation is shown between the optical activation energy of photoconduction, the activation energy of electrical conduction, and the theoretically calculated energies of $\pi-\pi^*$ transitions in isolated polymer molecules. Beyond four monomer units the optical absorption, fluorescence, and photocurrent spectra differ very little. This indicates that electron transitions in small conjugated segments are responsible for photophysical processes in polymers. Photoconduction was attributed to purely electron transitions, although a thermal activation energy of

of photoconduction was observed. Preliminary exposure to ultraviolet radiation leads to the appearance of a new maximum at longer wavelengths, which recalls the analogous phenomenon found with poly-ynes [10,13,20]. It is interesting that oxygen had opposite effects on the photoconductance at low and at high temperatures. The thermal activation energy of photoconduction lies between 0.03 and 0.2 eV depending on the surrounding atmosphere. In this work photoconduction was observed as far as the near infrared in polyarylenazomethines and polyarylenethiodiimides. All these polymers possess high resistances and may find application in electrophotography.

Photoelectric properties have been discovered and studied [80] in oligoanilines. The majority carriers in most compounds are positive holes. The optical activation energy of photoconduction is determined by shallow traps. The photoconductance spectra reproduce the absorption in the visible and the near infrared.

Finally, organic polymers containing conjugated bonds show a sharp increase in photosensitivity on reaction with electron-accepting compounds of low molecular weight [81-83]. This phenomenon is probably connected with the spectral sensitisation of low-molecular organic semiconductors by organic polymers with conjugated bonds [84].

V. POLYMERS WITH SATURATED MAIN CHAINS

Interest in photoelectric processes occurring in polymers with saturated main chains—in which conjugated bonds are either completely absent or are present in aromatic or heterocyclic side-chains—has recently increased sharply.

It has already been noted that certain types of polyethylene, after thermal treatment, develop photoelectric properties owing to the formation of segments with conjugated bonds [47,52,54,55]. Wintle et al. observed and investigated photoconduction in the untreated low-pressure polyethylene [85-88]. This work led to the most interesting conclusion, based on an examination of the absorption spectra of the polymer in solution and in the film, that the solid structure of the polymer was responsible for some absorption. The lack of correlation between photoconductance and absorption spectra indicated the impurity nature of the photoconduction. The mechanism of the production of free carriers in polyethylene was regarded as the distribution of charges in a series of irregularly connected barrier structures. It is noteworthy that van Roggen [94] detected barriers between single crystals of polyethylene that had been formed separately but were in contact. On application of an external field such structures function as current generators. Thermoluminescence data confirm the electronic–not ionic–nature of the conduction [95]. An exponential energy distribution of traps was shown [88] by the application of elementary band theory with the presence of short-range order to the charges trapped in the polymer chain. The conduction bands were very narrow, and mobility had a thermal activation energy of 0.1 eV. The photoconductance spectrum of polyethylene in the range 180–360 nm was determined by the corresponding structure in the optical absorption spectrum and the injection of electrons from the metal electrodes at their characteristic wavelength [90,91]. Photoelectric phenomena, governed mainly by contact-polarisation processes, were observed with polyethylene in the visible and in the near infrared from 0.6 to 1.7 μm. [89,91] Problems connected with the nature of photoelectric processes occurring in polyethylene and the role of the contacts have been discussed also in other papers [91-93,96,98,99]. The larger photocurrent observed with positive polarities on the leading electrode must be due to the photoinjection of holes, whose migration is determined by the Schottky type of emission [96]. The mobility of current carriers in polyethylene has been estimated as 10^{-5} cm^2 V^{-1} s^{-1} with activation energy ~0.25 eV, which is due to the thermal activation of charges out of traps or to a hopping mechanism of conduction [99]. Another study of the temperature dependence of photoconduction in polyethylene has appeared [97]. Papers on photoelectric processes in polyethylene are sometimes contradictory, especially with regard to the sign of the charge carriers, their mobility, and the interpretation of contact-polarisation phenomena.

Kryszewski et al. [100] observed photoconduction in the ultraviolet in polyethylene and several vinyl polymers; the multiplicity of the current reached hundredfold. It is significant that a larger photocurrent is observed in polymers having a higher degree of crystallinity; no clear relation was established between the photocurrent and chemical structure. The range of "saturated" polymers (i.e. containing no large conjugated fragments), in which photoelectric processes are observed has been extended considerably [101,102]. Photoelectrons emitted from the electrodes are assumed to govern conduction via traps. The current multiplicity reached 10^4 in individual commercial polymers (polyethylene, polypropylene, polystyrene, poly(ethylene terephthalate), polyvinylpyrrolidone, etc.). With several polymers (poly(vinyl fluoride), nylon-66, Viton, etc.) the density of the photocurrent attained 10^{-5} amp cm^{-2}, which is of interest for technical purposes. No special measures were undertaken to purify the commercial polymers, and most of the photoelectric processes in them are probably due to the presence of impurities and to contact phenomena.

Extremely interesting work has been done on the photoconductance of saturated organic polymers in the vacuum ultraviolet. Polystyrene shows an increase in photocurrent from 1400 to 500 Å. [103] Since the ionisation threshold of benzene molecules is 1330 Å, it may be assumed that the total ionisation energy is required to liberate an electron into the conduction band. The divergence between absorption and photoconductance spectra is interpreted here as the absence of an exciton stage in the generation of photocarriers. However, this disregards the effect of the thickness of specimens on the photoconductance spectrum. It is interesting that photocurrent and fluorescence increase simultaneously at wavelengths below 1400 Å. Detailed analyses have been made [104,105] of memory effects and of volt–ampère and lux–ampère relations in polystyrene. The volt–ampère characteristics are saturated at certain voltages, which depend on the light intensity. Oscillations of the photocurrent are observed in the same range. The mobility in amorphous polystyrene is 5×10^{-5} cm^2 V^{-1} s^{-1}; [106] the temperature dependence of charge transfer is small for jumps between molecular chains and strong for jumps between traps.

Aspects of the photoelectric properties of saturated polymers of type $[CH_2.CHR]_n$ have been dealt with in a series of papers by Grenishin, Cherkasov, et al. [107-113], who were the first to suggest using such systems to record images (electrography, photothermoplastic recording) in the spectral range 110–400 nm. Maximum photosensitivity under electrophotographic conditions was exhibited by layers of polyacrylonitrile, and minimum sensitivity by poly(vinyl chloride). In vinyl polymers the displacement (the product of the lifetime of the carriers and their

mobility) was 10^{-10} cm^2 V^{-1}, so that the carriers had a life of 10^{-7}–10^{-6} s, as mobilities in polymers of this type are 10^{-3}–10^{-4} cm^2 V^{-1} s^{-1}.[114] The quantum efficiency of the photoconductance of polystyrene in the range 110–160 nm is 2%. The optical absorption, reflectance, and photoconductance spectra indicated that the energy absorbed as exciton excitation is transmitted from "saturated" segments to aromatic side-chains, where dissociation with the formation of free carriers take place[108–112]. Analysis of the spectra of polystyrene showed that, the range up to 8 eV, absorption is determined by the properties of the monomer unit, but at higher energies by the electrons of the main chain. The absolute quantum efficiency of the photoeffect in the region of 6 eV was 10^{-4} el quantum^{-1}, which increased with the energy of the quantum to 0.4 el quantum^{-1} at 21 eV. Such high quantum efficiency may indicate the presence of a broad conduction band at a high level in the polymer. A partial criticism of the measurements on the photoconductance spectra of polystyrene suggests[115,116] that the application of a strong electric field in electrophotography may lead to distortion of the electron levels in the polymer and thereby to difficulties in distinguishing electrons involved in external and in internal photoeffects. These workers give a "band" model for polystyrene with an electron affinity of ~1.2 eV.

Vilesov et al.[117] have measured the photoelectric work functions of polyvinylcarbazole, poly(methyl methacrylate), polyvinylbutyral, and polystyrene as respectively 5.8, 5.9, 6.7, and 7.0 eV. Researches on the photoelectronics of "saturated" polymeric compounds include also investigations of pulsed photoconductance and of oscillating photocurrents in poly(vinyl chloride)[118], as well as the thermally stimulated conductance of poly(vinyl fluoride)[119].

Great interest is aroused by photosensitive systems comprising organic polymers into which have been introduced various photosensitive semiconductors such as zinc sulphide, cadmium sulphide, and zinc chloride, metal ions, dyes, and various doping agents[120–130].

Extremely promising investigations have been made during recent years on the photoelectric properties of charge-transfer complexes formed by two or more molecules. Such systems are distinguished by the appearance of a low-energy optical absorption band, by photosensitivity resulting from the transfer of charge, and by a sharp increase in conductance and photoconductance on complex formation. Papers have appeared on the photoelectronics of charge-transfer complexes of polystyrene[123,131–133]. One of the first and as yet one of the most actively investigated photosensitive polymer systems is polyvinylcarbazole[134–143] and its complexes[144–151,162–164], whose possible technical application in silverfree processes for recording images—electrophotography, photothermoplastic recording, etc.—is the primary reason for their interest[134–143]. References to the early patent literature on polyvinylcarbazole were given by Hoegl[135], together with data on the photoconductance of several polymers with heterocyclic and aromatic groups in the chain and of their complexes. The most photosensitive are probably complexes of polyvinylcarbazole with trinitrofluorene[138,145–149], electrophotographic layers of which are comparable in most of their characteristics with layers based on selenium[138]. The quantum efficiency in such layers reaches 0.15. Use of a laser source showed that, despite the extremely low mobility (5×10^{-8} cm^2 V^{-1} s^{-1}), the recombination rate constant is comparable with those for inorganic semiconductors. The nature, generation, and migration of current carriers in such systems have been discussed[148,149]. Photoconductance and a photoinduced electron spin resonance signal have been observed in complexes of polyvinylcarbazole with dinitrobenzene[150,151]. Hermann and Rembaum found that the Hall and Dember effects gave different signs for the carriers in iodine complexes of polyvinylcarbazole[162–164]. The photosensitivity spectra of such complexes cover the visible region with maxima in the ranges 400–500 and 700–800 nm. Pure polyvinylcarbazole possesses photoelectric sensitivity in the ultraviolet (Fig. 3). Sensitisation to the visible spectrum is therefore very important for technical purposes. A considerable number of papers have appeared on aspects of the spectral sensitisation of polyvinylcarbazole by dyes[129,134–139,142–145,151–159], and may form the basis of a separate review. The spectral sensitivity of polyvinylcarbazole can be extended by introducing other compounds, e.g. organocopper acetylides and poly-ynes[21,24,160,161].

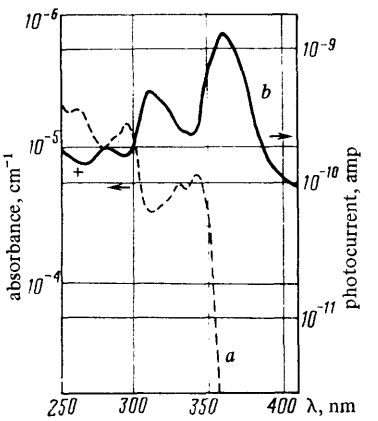


Figure 3. Spectra of polyvinylcarbazole[179]: *a*) absorption; *b*) photoconductance (with the illuminated electrode having positive polarity).

The mobility of holes in pure polyvinylcarbazole at room temperature is 0.001 cm^2 V^{-1} s^{-1} with a thermal activation energy of 0.12 eV.[165,166] The quantum efficiency of photogeneration is high (~0.1) and strongly dependent on the electric field[166,167]. The quenching of the photoluminescence of this polymer by an electric field is interesting in this connection[168]. The nature of the electrical conductivity of polyvinylcarbazole and the structure of the trapshave been examined[169,170].

Photoelectric phenomena have been studied at the contact between polyvinylcarbazole and metals[171–173]. The threshold photoemissions in the polymer were 1.28, 1.48, and 1.53 eV for gold, copper, and aluminium respectively. The ceiling of the valency band in polyvinylcarbazole is 6.1 ± 0.4 eV below the vacuum level. The development of a fine structure in the quantum efficiency spectrum is due to splitting of the electronic energy levels in the polymer by molecular vibrations. The width of the upper valency band in polyvinylcarbazole was estimated as < 0.11 eV. The generation of carriers is assumed[173] to involve intermediate formation of an exciton. Very interesting papers have appeared on the photoelectronics of polyvinylcarbazole at its interface with amorphous selenium[174–176]

and with cadmium sulphide and selenide[177]. Such heterogeneous systems may be expected to find application in several photosemiconducting devices.

A promising method for investigating the nature of photoelectric processes is the parallel study of the photoconductance and the luminescence of polymers. Examination of the latter has shown in particular that the energy absorbed by polyvinylaryls is not localised on side-chains, but is readily transmitted to neighbouring groups at distances of more than 1000 mean free paths[178,179].

Among other saturated polymers in which photoconduction has been observed and investigated are poly-1,3-diphenyl-5-*p*-vinylphenyl-2-pyrazoline[180], polyacenaphthylenes and their nitrile derivatives[181,182], poly-9-vinylanthracene[183], poly(vinyl chloride)[184,185], poly(pyrenylmethyl vinyl ether)[186], polytetrafluoroethylene exposed to X-rays[187], and an acenaphthene—formaldehyde resin[188]. All these polymers are high-resistance compounds of interest for electrophotography.

Finally, several papers have been published on the photoelectronics of biopolymers[189-024], the study of whose semiconducting properties is extremely promising for obtaining the energy parameters of these compounds and elucidating at a molecular level certain biophysical processes in living matter. The direct determination of the mobilities of charge carriers in proteins and nucleic acids gives values of 0.5–2 $cm^2 V^{-1} s^{-1}$.[197]

VI. MECHANISM OF PHOTOCONDUCTION IN ORGANIC POLYMERS

The experimental results surveyed in the preceding Sections show that the number of known photosemiconducting organic polymers is already quite large and is continuing to increase. They are of such varied types with respect to molecular (Table) and supermolecular structure that it is difficult to expect a single mechanism for the photoprocesses in all the compounds. Nevertheless, several quite general considerations will be discussed here.

The absolute photoelectric sensitivity (photoconductance, photo-e.m.f., etc.) of a polymeric compound should obviously be determined by two stages—(i) generation and recombination of free carriers and (ii) migration of the carriers through the polymer structure—a correct assessment of which would explain the following experimental principles, which have been established for most of the photoconducting polymers studied.

1. Photoelectric sensitivity is observed in polymers having conjugated bonds in the main chain in the macromolecule or in side groups.

2. The dependence of the photocurrent on the light intensity is below linear, and approaches linearity in isolated examples.

3. Ohm's law is satisfied for the photocurrent only up to field strengths of 100 V cm^{-1}.

4. Photoconduction is characterised by a wide range of relaxation times—from 10^{-5} s to several minutes.

5. The photoconductance and the electrical conductivity of polymers increase exponentially with rise in temperature, their activation energies being respectively 0.05–0.5 and 0.5–2.5 eV.

6. Mobilities of current carriers do not usually exceed 1 $cm^2 V^{-1} s^{-1}$.

7. Photoelectric effects are very sensitive to various external factors (preliminary exposure, effect of environment, illumination, etc.).

8. Photoelectric sensitivity is observed in the fundamental absorption band of the polymer, the main photoconductance maximum being located on the descending slope of the absorption spectrum.

A. Generation and Recombination of Carriers

One of the first papers on the photoconductance of organic polymers put forward the hypothesis, based on an analysis of the spectral dependence of photosensitivity in poly-ynes and on several experimental facts then known for low-molecular organic semiconductors, that the first step in the generation of current carriers in polymers is formation of an exciton, which migrates along the chain and between macromolecules[13]. The close similarity of the absorption spectra of polymers in solution and in the solid state[16,61,85] indicates that intermolecular interaction in solid polymers is quite small compared with orthodox inorganic photosemiconductors, and that the energy of the electromagnetic radiation is absorbed by individual molecules with formation of neutral excited states (excitons). The multistage generation of electron–hole pairs involving an exciton stage in the internal photoeffect in organic polymers has since received much additional confirmation[14-20,56,63,67-70,72,108-112,178,179] from data on photoconductance, luminescence, the effects of vapours and gases on photoconductance, etc. This view is now the most generally accepted. The exciton formed by the absorption of light migrates through the polymer matrix until it meets a defect or other excitons. Possible defects are disruptions in the chemical structure of the molecule, disruptions of crystallinity, cross-links between macromolecules, surfaces, etc. The number of defects in present-day polymers is so large that, in the majority of cases, these states govern the macroscopic properties. Nevertheless, direct measurement by luminescence methods of the diffusion constants of singlet and triplet excitons in polymers give extremely high values, of the order of 10^{-2}–10^{-6} $cm^2 s^{-1}$. Thus excitons are able during their existence to traverse 10–100 monomer units of the polymer. The capture of excitons by a defect or interaction with another exciton leads to its annihilation with formation of an electron–hole pair: carriers of one type remain attached to the defect, while those of the other type take part in conduction under the influence of the applied electric field, and the stage of charge transfer through the polymer structure is thus initiated.

It must be remembered that polymers have a considerable scatter of molecular weights, so that the excitons formed would also cover a certain range of energies. Such varied excitons, as well as factors influencing the drift of the carriers (barriers), may make a contribution to the usually small thermal activation energy of photoconduction (0.05–0.5 eV). This could explain in particular the wavelength dependence of this activation energy. However, there are data indicating that photoconductance is only weakly dependent on or completely independent of the molecular weight of the polymer[68,212]. However, the absence of significant bathochromic shifts in the fluorescence, absorption, and photoconductance spectra of polymers when the chain of conjugation exceeds a certain critical length[63,68,78,79,178,179] shows that the continuous chain of conjugation in organic polymers does not extend throughout the length of the macromolecule, but covers only a small number of monomer units (usually 2–7). This is supported by the observation of a hyperfine structure in the electron spin resonance spectra of certain

polyconjugated polymers[205]. It thus becomes clear why the introduction of various bridging groups which interrupt (or weaken) conjugation (those containing methylene, oxygen, nitrogen, or sulphur) does not lead to the disappearance of semiconducting properties.

Thus the optimum length of the system of conjugated bonds in polymers, that will lead to the specific photosemiconducting properties of these compounds, does not exceed a few units (usually < 10). This corresponds to the conjugated segments usually present in low-molecular compounds. Thus the first step in polymers, as in low-molecular organic semiconductors, is the formation of an exciton of a short segment of conjugated bonds. In this sense organic semiconductors of low and high molecular weights have the same electronic nature, as was to be expected. It now becomes clear why polymers with saturated main chains and aromatic side-chains can in principle be photosemiconductors, as is actually observed. The specific feature of polymeric compounds at this stage of generation of charge carriers is probably that the resulting exciton may possess a long lifetime owing to the rigidity of the polymer matrix, which ensures that excitons can migrate to great distances. The situation is analogous to the freezing of isolated molecules in solid solutions with the aim of lengthening the life of the excited state. The anisotropy of electrical properties would evidently be significant for polymers.

The concept of a "local activation effect", connecting the complex of physical (especially magnetic) and physicochemical properties of these compounds with their structural characteristics[206], may prove useful for discussing the photoconductance of polyconjugated polymeric systems obtained by thermal, radiation, etc. methods. Since photoconduction in "saturated" polymers has usually been studied on commercial specimens, it can reasonably be assumed that organic impurities having conjugated bonds were involved in the generation of current carriers. Direct ionisation of saturated bonds leading to the appearance of free carriers—and when irreversible to photodegradation of the polymer—is probably most feasible in the far and vacuum ultraviolet.

Recombination processes play a significant part in photosensitivity. They explain in particular the fact that maximum photoconductance in polymers is usually located on the descending slope of the fundamental absorption curve. Thus here, too, polymeric organic photosemiconductors behave similarly to the traditional inorganic semiconductors.

Preliminary exposure to ultraviolet radiation produces a change in photoelectric sensitivity both in organic polymeric[13–18,24,25,28,74,75] and in inorganic photosemiconductors (e.g. the formation of F-centres in crystals of alkali-metal halides, etc.[207,208]).

B. Migration of Carriers through the Polymer Matrix

Most organic polymers consist of alternating highly conducting regions (conjugated or condensed segments) and dielectric regions (disordered or amorphous structures). To effect photoconduction the electron–hole pair formed by breakdown of an exciton should drift in the applied electric field. The coincidence of the activation energy of electrical conductivity with the energy of the edge of the long-wavelength absorption and the red boundary of the photoeffect shows that the free carriers generated by the absorption of light are identical (even in the mechanism of drift) with those generated thermally.

A periodic chain of carbon atoms with the same number of hydrogen atoms attached would obviously have an electronic spectrum consisting of allowed and forbidden energy bands. Side groups replacing hydrogen atoms may act as impurities. Electropositive and electronegative substituents will correspond to acceptor and donor impurities. In contrast to covalent crystals, where impurity atoms may accept or donate one or more electrons, in the present case part of the electronic charge may be either fixed or released. Transfer of the complete charge may require several bonds acting in parallel. The numerous defects of various types present in the polymers at present available may also act as acceptor or donor impurities.

The mathematics of the band theory, which has been successfully used in studying the electronic properties of traditional inorganic semiconductors, is most fully developed at the present time. Most authors use this approach for the qualitative description of charge-transfer processes in organic polymers. When applied to macromolecular compounds, the band model supposes that current carriers move along generalised energy bands of π-electrons of the whole polymer. With decrease in the overlap of the π-electron wave functions the width of these bands diminishes, and in the limit they reduce to conduction energy levels, or to large effective masses of current carriers expressed in terms of the band model. This model implies strict periodicity in the structure of crystals and takes into account the potential for a real crystal in the effective mass of the current carriers. As already mentioned, however, most semiconducting polymers are heterogeneous or amorphous substances to a significant extent, and the application of a band model to polymers encounters certain difficulties. A possible way out may be to apply to such systems the theory of liquid and amorphous semiconductors, in which electronic properties are determined not by long-range but by short-range order[209,210]. These papers show that long-range order is sufficient but not necessary for the appearance of a band structure. Unfortunately, the main difficulties in discussing semiconducting processes in organic polymers in terms of a band model consist in the inability of this model to explain *quantitatively* several fundamental parameters observed experimentally. This applies primarily to the drift mobilities, which do not exceed a few units for most polymers, and in several cases are 10^{-6}–10^{-8} $cm^2\ V^{-1}\ s^{-1}$. The paradoxical situation arises in which the free path of the carriers becomes considerably shorter than the individual units in the molecule.

It is therefore most reasonable to adopt a hopping model of photoconduction for the majority of polymers. The free carriers formed by breakdown of an exciton probably remain localised in individual molecular segments or defects. Photoconduction is a consequence of a series of successive activated hops in the electric field. The activation energy of conductance then determines the probability of such hops[165,166]; the effective mobility or the effective concentration of current carriers should increase with rise in temperature. On theoretical grounds a hopping mechanism excludes the possibility that the Hall effect can be observed in systems where it operates. It is perhaps for this reason that attempts to observe the Hall effect on polymers have generally been unsuccessful.

The effect of light can in principle be regarded as lowering the potential barriers between separate macromolecules or regions of polyconjugation, which will increase the effective mobility of the carriers. Such a mechanism may perhaps be accepted for polymers in

which the concentrations of current carriers remain unchanged with rise in temperature. The appearance of non-equilibrium carriers exerting a polarising action may also lead to a lowering of barriers. The two processes (increase in carrier concentration and change in barrier height) may then occur simultaneously. Detailed analysis of the mechanism of conduction in semiconducting polymers is prevented by the insolubility or sparing solubility of most of the substances studied. As a consequence, comparative data are almost completely lacking on the absorption spectra of individual macromolecules (in solution) and on the absorption spectra and the photoeffect of polymers of uniform molecular weight in the condensed phase, so that no definite conclusions can be reached on collective interactions in polymeric semiconductors. It is therefore an urgent task to develop methods for synthesising soluble semiconducting polymers, which are necessary for assessing the role of intercrystalline and other defect interlayers in conduction processes, studied at present mainly on compressed pellets or powdered polymers.

A fruitful approach is to combine the concepts of hopping and band mechanisms for heterogeneous polymer structures. A band model can be applied to the motion of carriers within a conjugated segment, but transitions between such segments can be regarded as the activated surmounting of barriers. In fact, high-frequency measurements have shown that the activation energy within conjugated regions is almost zero[211]. With a large number of carriers present and sufficiently transparent barriers non-activated "percolation" of the former from one conjugated segment to another becomes possible.

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The information on the photoelectric properties of polymers which has accumulated in a comparatively short time (10–15 years) is evidence of the rapid development of this field. However, future progress in scientific research and the widespread introduction of these materials into technology will encounter several obstacles. On a scientific level this is primarily the absence of clear ideas on the structure of many of the polymers investigated, which applies especially to products of the thermal, radiation, etc. treatment of polymers. Authors generally mention that the products obtained have a heterogeneous structure with regions of polyconjugation separated by certain barriers. Ideas on the size of the conjugated segments, crystallinity, packing, etc. are extremely vague. At the same time deductions are made on the relation between the chemical structure of a single macromolecule and the electrophysical properties of the whole polymer, which in such a situation is undoubtedly little justified. Analogous attempts to link semiconducting properties with specific chemical structures in the molecules of low-molecular organic semiconductors (dyes) have encountered substantial difficulties. It has not been shown that the decisive factor in establishing specific photosemiconducting properties in low-molecular organic compounds is the supermolecular structure, whereas the structure of the molecule (the presence of π-electrons) is responsible only for the fundamental possibility of such properties. This fully applies, in the opinion of the Reviewer, to polymeric compounds.

The situation is rather better with respect to polymers obtained by direct synthesis, for in most cases the chemical structure of the macromolecules is known exactly. Here too, however, the inadequacy of information on the significance of the physical structure of the products for their semiconducting properties is clearly felt. Little is known on the influence of defects and foreign impurities on the semiconducting properties of organic polymers. Yet it became possible to obtain inorganic semiconductors with specified properties only after they had begun to be thoroughly purified and then alloyed with definite impurities. For the solution of individual problems in semiconductor electronics the total content of impurities in inorganic semiconductors should not exceed 10^{-9}–10^{-10}%. For organic polymers in the best cases this ratio should be lower by factors of 10^{8}–10^{9}.

Thus it is not only important to seek powerful new semiconducting organic polymers but also urgently necessary to make a more detailed study of their specific physical structure as solids with simultaneous development of methods for their purification and for controlling impurities. Extremely promising work involves finding methods for and investigating mechanisms of the chemical and spectral sensitisation of photosensitivity in organic polymers by introducing molecules of sensitisers and of donor or acceptor agents.

The experimental and theoretical results surveyed in this Review show that organic polymers, hitherto regarded as exclusively insulating materials, possess several interesting photoelectric properties. The macroscopic development of these properties is analogous to those of inorganic and low-molecular organic photosemiconductors, which yet again emphasises the unitary nature of electronic processes in solids.

The voluminous literature on semiconducting organic polymers that has appeared during the past decade suggests that a new branch of the physics of solids—the physics of polymers having semiconducting properties—has recently been established. As with inorganic semiconductors, the study of photoelectric phenomena should become an independent section.

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A group of Japanese workers have quite recently published a series of papers on the photoelectric properties of polyvinylcarbazole, its charge-transfer complexes, and its copolymers[213–217]. A book has appeared[218] on aspects of the application of organic polymers to electrophotography.

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Theoretical Generalisation of the Coking of Various Fuels

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The most important ideas on the coking of various types of solid and liquid fuel are examined. Theoretical results are given summarising the thermal degradation of model organic compounds and polymers. Processes involved in the coking of various petroleum products, coal tar, and their mixtures with weakly caking, low-grade coals are analysed. Data are presented on the plastic state and the caking of coals of different degrees of metamorphism. Consideration is given to the caking of lignites and to the effect of the type and origin of brown coal on the physicomechanical parameters of the coke. Formulae are set out for calculating the yield of chemical products in the coking of coals and for predicting the properties of the coke. A list of 94 references is included.

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1. INTRODUCTION

The theoretical problems associated with coking processes are usually considered in connection with either the manufacture of metallurgical coke or the production of coke from heavy petroleum fractions and resinous products of the processing of coal. The former and older scientific approach was concerned mainly with physical and colloidal processes, whereas the latter was directed solely at the chemistry of the processes.

Muck[1] considered that coking took place in several stages. Coal softens when heated and acquires plasticity, which produces various states from slight stickiness to complete fusion. He related the swelling to the extent of melting and the rate of hardening: the gases evolved distended the softened mass and, provided that the pore walls permeating it were sufficiently strong, the latter remained unbroken until solidification occurred. Weding and Rao[2] denied that coal could melt, and explained coking by thermal decomposition of hydrocarbon and resinous components of coal, with the separation of free carbon and high-melting complex carbon-rich compounds, which settle on the carbon particles and consolidate them into monolithic lumps of coke. Simmersbach[3] supported the melting hypothesis, but assumed without justification that coal contained two modifications—"caking" and "lean" coals—which under certain conditions may pass one into the other.

Very unsuccessful attempts were made to relate the coking power of coals with their elementary composition. Interesting considerations were put forward by Simmersbach[4], who regarded the hydrogen and oxygen contents as more important than the carbon content: coal does not coke if it is either very rich (brown coal) or very poor (anthracite) in these elements. It postulated the existence of upper and lower limits to the hydrogen and oxygen contents, beyond which coking was impossible.

Many papers were published during the interwar period[5-10] linking caking and coking with the presence of bitumens in the coal. Berl and Körben[11] concluded that bitumens which distilled off at higher temperatures during coking were responsible for the formation of uncaked coke. If bitumens decompose below their boiling points, they may be converted into substances which cement the remainder of the coal and form strong coke. Several investigators[12-14] were doubtful about the role and significance of bitumens and their components for elucidating coking processes. The polemics on this aspect can be explained by the varied conditions under which bitumens were extracted and the absence of a reliable and unified method for measuring the strength and structural properties of coke.

The use of modern methods yielding fresh experimental information has led during recent decades to other interpretations of caking and coking processes. Illingworth[15] and Mott[16] directed attention to the adsorption and wetting of infusible humic substances by molten bitumens and put forward the "cementation" hypothesis, which was developed by Sapozhnikov[17] as the "adhesion" hypothesis. Yakovlev[18], Onusaitis[19], Aronov[20], and Permitina[21] also discuss caking and coking in physical and physicochemical terms, linking these processes with fusion, disolution, dispersion, wetting, etc. Interesting attempts have been made by Shapiro[22], Kustov[23], and other Soviet authors to explain the formation of coke in terms of colloid chemistry.

All the above hypotheses have the common defect of underrating the role and importance of chemical processes in coking. Audibert[24] regarded the formation of coke as a complicated chemical process yielding several new high-melting compounds. As the temperature is gradually raised, coal is converted into a continuously varying system of liquid, solid, and gaseous phases, and finally passes completely into the solid state. Panchenko and Klopotov[25] consider that chemical processes are responsible for the evolution of water and carbon dioxide, with the formation of new plastic products. In the opinions of Aronov and of Nesterenko[26] caking and coking depend on the relative proportions of hydrocarbon and oxygen compounds in the plastic products and on polycondensation processes. Angelova and Lazarov[27] have established that the plastic state is characterised by an increased content of functional oxygen groups resulting from the thermal destruction of ether and other bonds.

During recent years a broad debate has been conducted in the Soviet Union on the problems of caking and coking processes[28-32]. This has clearly shown that the words of Simmersbach[33]—"The cause of the caking of coal is a problem which, in spite of all the efforts made to solve it, still awaits its final solution"—are valid even today.

2. INVESTIGATION OF COKING ON MODEL ORGANIC COMPOUNDS AND POLYMERS

In a study of the coking of individual organic compounds Tilicheev[34] found that the rate increases with the molecular mass of the aromatic ring system of unsaturated cyclic hydrocarbons. Unsubstituted aromatic hydrocarbons are most rapidly carbonised. In order to study the mechanism of coking, differential thermal and thermogravimetric investigations have been made[35] on model organic compounds, most of which are products of the processing of coal and have been isolated from coal tar (Table 1). The highest coking value was obtained in the pyrolysis of truxene and bifluorenyl, which have the highest molecular mass, melt at a high temperature, and boil above 500°C. Coke is formed comparatively rapidly from chrysene, pyrene, and brazan, whose molecules consist of fused aromatic rings (Table 1). The pyrolysis of n-docosane, naphthalene, 2,6-dimethylnaphthalene, *o*-hydroxybiphenyl, and 2-hydroxy-4-methylquinoline occurs quite differently: their coking values are exceptionally small, and the time required to form 1% of coke varies from 963 min (with naphthalene) to infinity (*o*-hydroxybiphenyl).

Table 1. Physical constants and coking power of model organic compounds.

Compound	Mol. mass	M.p., °C	B.p., °C	Coking value, %	Time for 1% coke, min.
n-Docosane	310.6	44.9	380	0.092	1177
Naphthalene	128.2	80	218	0.110	963
2,6-Dimethylnaphthalene	156.0	111	262	0.031	3419
Fluorene	166.0	116	299	0.192	552
Bifluorenyl	330.4	249	500	17.485	6
Pyrene	202.2	150	394	3.903	27.2
Chrysene	228	255	441	4.025	26.3
Truxene	342	369	550	71.063	1.5
Brazan	218.2	205	395	2.064	51.5
o-Hydroxybiphenyl	170.2	59	286	trace	∞
2-Hydroxy-3-methylquinoline	159.2	240	390	0.038	2790
Carbazole	167.2	245	353	0.985	108

An interesting conclusion can be reached from a comparison of the differential thermal and thermogravimetric curves for n-docosane and naphthalene (*a* and *b* in Fig. 1). The former curves begin with endothermic effects representing their transitions from solid to liquid state. Very characteristic of docosane is the subsequent exothermic effect with its maximum at 245°C, whereas loss in weight due to vaporisation and thermal degradation begins above 280° and is accompanied by an endothermic effect at 309°C. The sublimation of naphthalene, which begins at 150°, is especially intense between 190° and 210°C, and is responsible for an endothermic effect: the weight of a specimen decreases by approximately 90% from 195° to 210°C.

The differential thermal curve for truxene (Fig. 2*c*) exhibits an immense exothermic effect with its maximum at 188°C, whereas changes in weight begin only above 435°C, which confirms the importance in coking of exothermic polymerisation and polycondensation processes occurring between 200° and 430°C. Brazan gives two exothermic effects in the same temperature range (Fig. 2*d*).

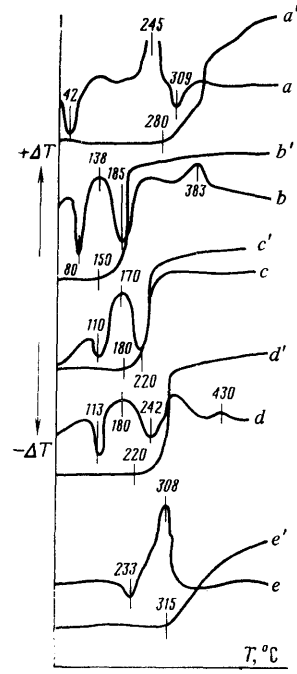


Figure 1. Differential thermal and thermogravimetric curves of: *a*,*a'*) n-docosane; *b*,*b'*) naphthalene; *c*,*c'*) 2,6-dimethylnaphthalene; *d*,*d'*) fluorene; *e*,*e'*) bifluorenyl.

It is very important to investigate the behaviour of cellulose, waxes, resins, and other coal-forming components of vegetable origin, which in more or less changed form play a considerable part in the formation of coke, in order to elucidate the processes involved in caking and coking. The heat-treatment of these coal-forming and other simply constructed natural or synthetic model substances of high molecular weight may yield very interesting information on the course of thermal degradation processes in the caking of coal and its conversion into coke. Krasyukov[36] has established that polyethylene does not form a coke residue, but polypropylene gives 16.2% of coke, which is identical with petroleum coke in texture and mechanical and electrical properties.

In investigations of the mechanism of coking, analogous experiments have been made with coumarone–indene resins, carnauba wax, technical paraffin wax, coal tar, cellulose, rosin, etc.[37,38] The results show (Fig. 3) that the characteristic endothermic effects of coumarone–indene resin and rosin (at 358° and 288°C) arise from thermal degradation associated with the evolution of volatile products. Pyrolytic processes begin in carnauba wax (*c* and *c'*) only above 370°, so that the endothermic effect is observed at 402°C.

Formation of a solid coke residue from technical paraffin wax (Fig. 3*d'*) is largely complete by 495°C. The coking value (6.516%) far exceeds that of n-docosane (0.092%). This means that the pyrolysis of a mixture of paraffin hydrocarbons creates more favourable conditions for accelerating coke formation. Coal tar gives an especially interesting differential thermal curve (*f*), characterised by an immense exothermic effect between 248° and 300°C. Heat-treatment of this mixture of many strongly aromatised compounds, of high molecular weight and high boiling point (above 400°C), leads to appreciable changes in weight only above 325°C, which is connected with the absorption of heat. Truxene and coal tar give closely similar differential thermal and thermogravimetric curves. The presence of a plateau on the differential thermal curve of the tar can be explained by the superposition of several exothermic effects similar to those of truxene with a maximum between 248° and 300°C, as can be seen from the proposed hypothetical scheme (Fig. 4).

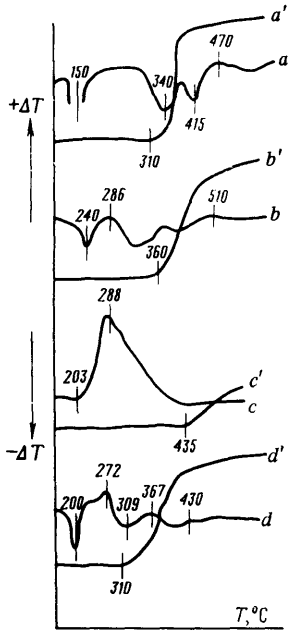


Figure 2. Differential thermal and thermogravimetric curves of: *a*,*a'*) pyrene; *b*,*b'*) chrysene; *c*,*c'*) truxene; *d*,*d'*) brazan.

Paraffin hydrocarbons, like aromatic hydrocarbons which sublime below the degradation temperature, yield a very small quantity of a coke residue consisting of highly fused aromatic compounds. Aromatic heterocyclic compounds containing oxygen and nitrogen usually undergo polymerisation—condensation processes with the formation of solid, non-volatile, strongly aromatised carbon-rich products constituting coke. Even before the start of degradation and vaporisation, the aromatic compounds of high molecular weight, which melt and boil at high temperatures, undergo intense polymerisation and polycondensation processes characterised by exothermic effects with a maximum in the range 250–310°C. They give a large quantity of a solid, non-volatile condensed residue, which forms the main mass of the coke.

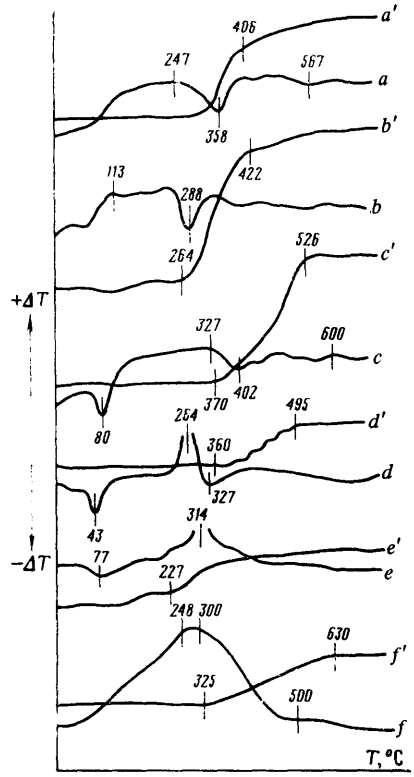


Figure 3. Differential thermal and thermogravimetric curves of: *a*,*a'*) coumarone–indene resin; *b*,*b'*) rosin; *c*,*c'*) carnauba wax; *d*,*d'*) paraffin wax; *e*,*e'*) cellulose; *f*,*f'*) coal tar.

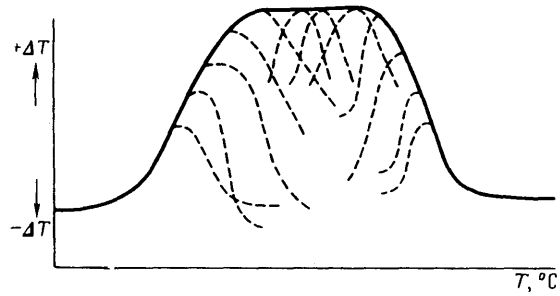


Figure 4. Aggregate differential thermal curve for a mixture of compounds.

3. MECHANISM OF THE FORMATION OF TAR COKE

Investigations of the coking of various tars, resins, and heavy hydrocarbon products and study of the properties of the resulting coke will yield additional information on

coking processes and their mechanism[39-46]. Paper chromatography indicates that silica-gel resins and asphaltenes predominate in vacuum and acid asphalt, kerogens and carbenes in mazut, and asphaltenes in coke-oven tar. Fig. 5 shows diagrammatically the yields of coke, liquid distillate, and gases obtained when these products are coked under laboratory conditions, and Table 2 lists the most important characteristics of the coke residue. Differences in hardness, porosity, and density among the cokes result from the different chemical compositions of the starting materials. Gas-works tar and stearin pitch, which are rich in paraffin hydrocarbons, yield the coke of lowest density, whereas strongly aromatised materials, e.g. coal tar and vacuum asphalt, give a resinous coke of high density. These differences have been confirmed by X-ray examination of the structure.

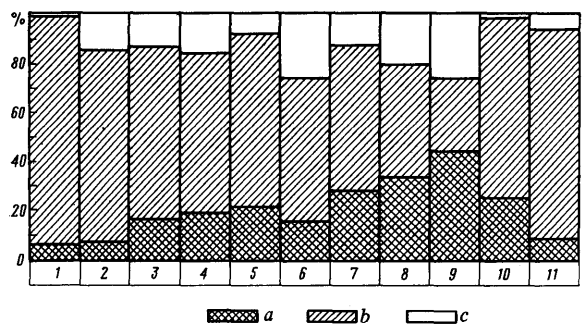


Figure 5. Material balance—(*a*) coke; (*b*) distillate; (*c*) gases—in the coking of: 1) petroleum; 2) mazut; 3) vacuum asphalt; 4) acid asphalt; 5) mazut from bituminous shales; 6) gas-works tar; 7) resin from gas-works tar; 8) coke-oven tar; 9) resin from coal tar; 10) beechwood tar; 11) stearin pitch.

Table 2. Physical constants of resinous coke.

Raw material	Density		Porosity, %	Hardness, s
	apparent	true		
Petroleum (Tyulenovskii)	0.75	1.23	39.0	180
Mazut from Tyulenovskii petroleum	0.84	1.50	44.6	190
Vacuum asphalt from Tyulenovskii petroleum	0.96	1.67	42.6	200
Acid asphalt	0.75	1.30	40.0	235
Mazut (from oil shales)	0.77	1.40	27.5	165
Gas-works tar	0.63	1.08	41.7	125
Resin from gas-works tar	1.01	1.53	33.4	300
Coal tar	0.99	1.74	43.0	170
Resin from coal tar	1.26	1.46	15.0	240
Beechwood tar	0.39	1.55	75.0	85
Stearin pitch	0.65	1.09	39.5	305

In order to elucidate the chemistry and the mechanism of the formation of coal-tar coke, systematic investigations have been made of the changes in properties and chemical composition of coal tar during its oxidative degradation and coking[47,48] (Figs. 6–8). The microstructure of the coke obtained at 450°C shows no significant changes from the initial material. A sharp change ensues at 500°C, when a bright, light-coloured coke is obtained which has strong anisotropy and a secondary structure. Such coke contains many round and oval pores. The most important physicochemical data on coal-tar coke are given in Table 3. This shows that compounds containing functional carboxyls undergo especially intense decarboxylation between 450° and 500°C, and the coal-tar coke obtained at 550°C no longer contains any carboxy-groups. The hydroxyl content increases, reaches a maximum at 500°, and falls to zero at 550°C. The hydroxy-groups are formed by the rupture of ether bonds and disappear as a result of polycondensation processes, which lead to formation of the coal-tar coke.

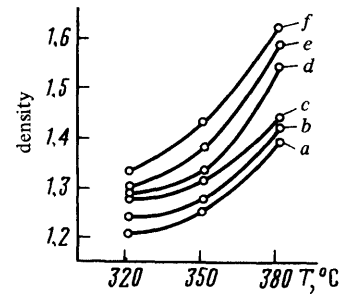


Figure 6. Temperature variation of density of pitch from (air flow, litres kg^{-1} h^{-1}/duration of heating, h): *a*) petroleum (20/3); *b*) vacuum asphalt (50/3); *c*) acid asphalt (80/3); *d*) mazut from oil shales (20/6); *e*) coke-oven tar (50/6); *f*) gas-works tar (80/6); *g*) semicoke tar.

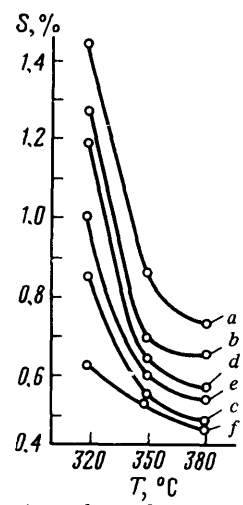


Figure 7. Temperature dependence of mean pitch content (units as in Fig. 6): *a*) 20/3; *b*) 50/3; *c*) 80/3; *d*) 20/6; *e*) 50/6; *f*) 80/6.

The course of such processes has been demonstrated by thermogravimetric examination of individual and high-molecular model compounds. The chemical structure of coal-tar coke is characterised by functional carbonyl groups, whose content steadily increases over the temperature range investigated, whereas they were not

detected at all in the original tar[48]. The infrared spectrum of the coal-tar coke obtained at 450°C shows a considerable weakening of bands in the range 770–960 cm^{-1}, and the maxima at 1450 and 1613 cm^{-1} almost disappear. This confirms that polycondensation of benzene rings has occurred.

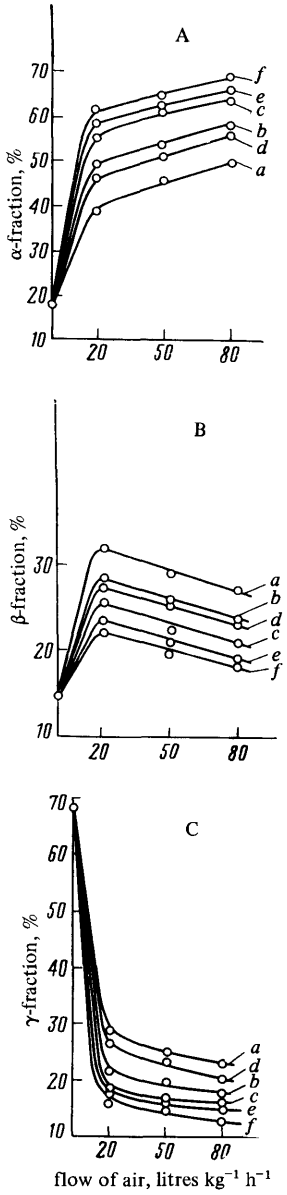


Figure 8. Effect of flow of air on contents of different fractions in the pitch for different temperatures (°C) and durations of heating (h): *a*) 320/3; *o*) 320/6; *c*) 320/9; *d*) 350/3; *e*) 350/6; *f*) 380/3.

The investigations have shown that the yield of coal-tar coke, its apparent and true densities, and its hardness increase with the molecular mass and the proportion of compounds containing a fused aromatic system (asphaltenes, carbenes, etc.) among the products undergoing coking. Pores are formed between 450° and 500°C to give a coal-tar coke varying in porosity from 15 to 75%, also depending on the chemical composition of the products. Formation of a coal-tar coke involves the decarboxylation of existing carboxy-groups with the gradual formation of new hydroxy-groups (with a maximum at 450°C) as a result of rupture of existing ether groups and the polycondensation of hydroxy-groups. Carbonyl groups, whose content increases with rise in temperature, are characteristic of the chemical structure of coal-tar coke.

Table 3. Physicochemical parameters of resinous coke obtained at various temperatures.

Analytic results	Final coking temperature, °C		
	450°	500°	550°
Yield of volatiles, %	18.30	10.40	6.35
Elementary composition, %:			
carbon	86.30	90.40	93.95
hydrogen	3.60	2.95	1.90
oxygen	6.67	2.52	0.26
sulphur	0.94	1.41	1.09
nitrogen	2.49	2.72	2.80
Functional oxygen groups, mg-equiv. g^{-1}			
hydroxy	0.12	0.23	0.00
carboxy	0.17	0.01	0.00
carbonyl	0.18	0.44	0.51

4. PLASTIC STATE, CAKING, AND DEGREE OF METAMORPHISM

Investigations of the plastic state and the caking of coals with different degrees of metamorphism[49-51] have yielded very interesting results contributing to a general theoretical explanation of the processes involved in coking. Several specimens of coal were selected from the Balkan coal-field. Pyrolysis results showed that the yield of volatile substances varied between 40.7% and 13.7% with a plastic layer varying in thickness from 23 mm to zero. Petrological analysis showed[52] that vitrinite predominated (69–76%) in the initial coals, the inertinite content varied from 8% to 12%, and very little exinite (trace to 1%) was present.

The variation in petrogaphic composition observed during the step-by-step coking of gas coal from the Lev mine showed that the vitrinite (the main mass) remained homogeneous and isotropic (up to 400–430°C). A secondary pitted structure was detected in it at 470°C, it acquired a bright greyish-white colour, and above 600°C pleochroism and anisotropy developed. The cuticles began to change even before appearance of the plastic state (400–430°C), gradually becoming thinner and difficult to detect, and they finally disappeared at 470°C. Fusain and semifusain remained unchanged even at 625°C: they played no active part in formation of the plastic phase or in caking of the coal. Between 570° and 625°C the boundaries separating these inert ingredients from the main vitrinised mass began to become obscure.

Single pores already begin to appear at 400°C, but pore formation becomes especially intense from 470° to 500°C, when the plastic phase passes into a semicoke phase.

The percentage content of pores is especially high at 570–625°C, when closely situated, large, and mostly shapeless pores are observed, probably formed by the coalescence of several smaller pores.

The coking of a fat coal releases a considerable quantity of liquid products up to 400°C, and thermal degradation is largely complete by 460°C (Fig. 9*A*). The plastic phase formed is of low viscosity and exerts a great resistance (up to 1320 mmH_2O) to gases passing through it (curve *1* in Fig. 9*A*). Pyrolysis becomes especially intense between 400° and 430°C, with maximum evolution of volatile products (curve *2*). The quantity of gases able to diffuse through the plastic phase is considerably smaller than the total quantity evolved, so that pores already begin to form at 400°C. Larger pores are produced by the union of small pores separated by thin walls of softened plastic material (Fig. 10*a*). Hardening of the plastic phase at 452°C coincides with the maximum of a large endothermic effect (Fig. 9*A*, curve *4*). It is significant that formation of a solid semicoke phase from the softened coal coincides with a maximum increase in carbonyl groups (curve *7*). It had earlier been found that these functional groups are especially characteristic also of the chemical structure of coal-tar coke. When heated above 600°C coal forms a coke possessing clearly defined anisotropic properties (Fig. 10*b*).

In the pyrolysis of a typical coking coal thermal degradation and the appearance of liquid products ensue at considerably higher temperatures, so that the initial softening is observed at 403°, and hardening of the plastic phase at 470°C (Fig. 9*B*). The maximum resistance offered by this mass to diffusing gases is considerably smaller (curve *1*). Hardening of the plastic phase is in this case accompanied by a well defined endothermic effect (curve *4*). The quantity of carbonyl groups also increases, as is indicated by the well-defined maximum (0.76 mg-equiv. g^{-1}) at 500°C, lying within the range of the newly formed solid semicoke phase (curve *7*).

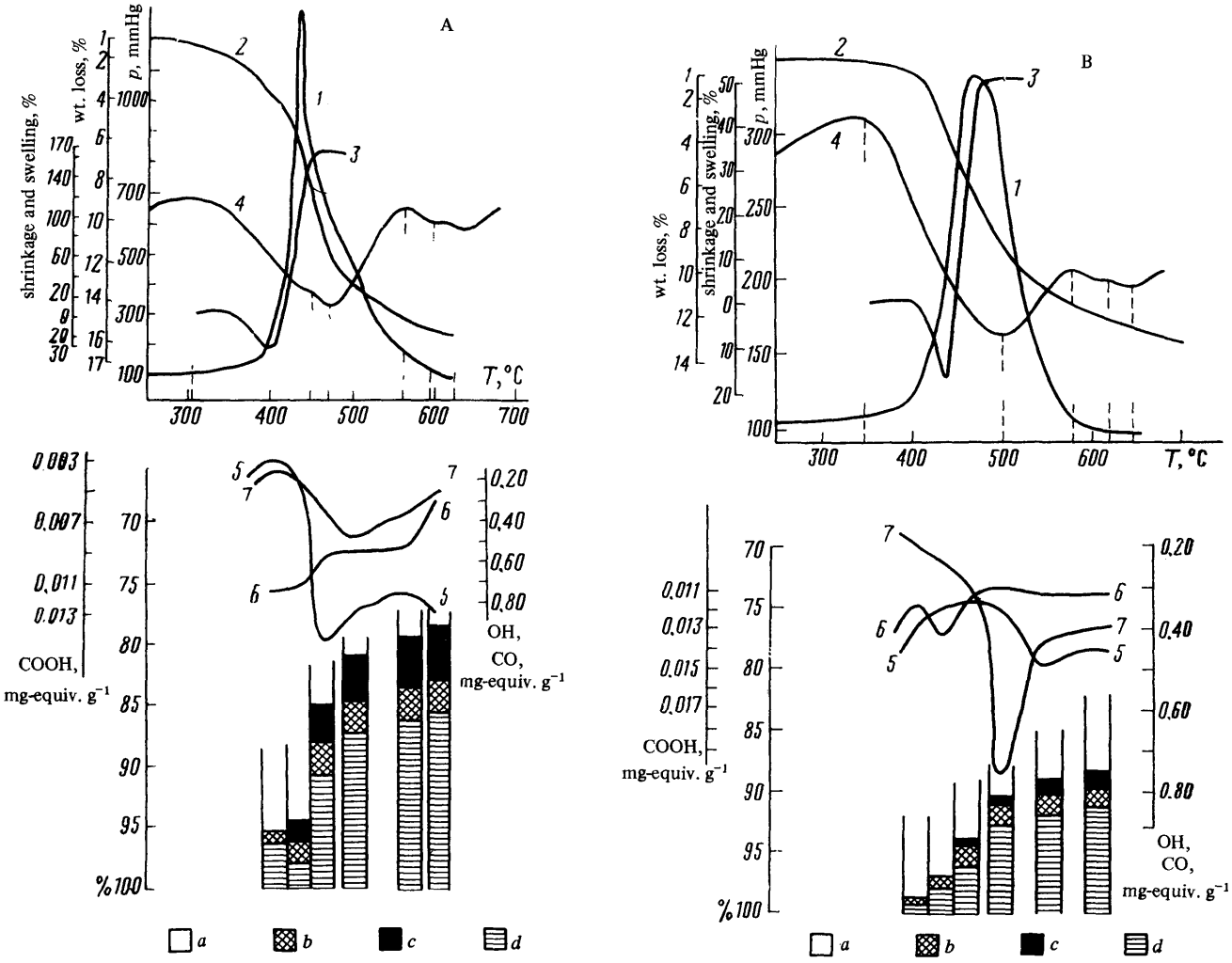


Figure 9. Investigations of plastic state of: A) fat coal from Kachulka mine; B) coking coal from Sheshkingrad mine: 1) Foxwell curve; 2) thermogravimetric curve; 3) dilatometric curve; 4) differential curve; 5) carboxy-groups; 6) hydroxy-groups; 7) carbonyl groups; *a*) semicoke; *b*) pyrogenous water; *c*) coal tar; *d*) gas.

The processes involved in the thermal degradation of, the appearance of a plastic phase in, and the caking of a fat and coking coal are clearly presented in Fig. 11. At every stage the individual phases undergo complicated pyrolytic processes associated with the formation of new products—solid (S), liquid (L), and gaseous (G)—which yield the corresponding phases of the subsequent stage. Fusain and semifusain do not pass into a plastic state, and are occluded directly into the solid coke phase. Hardening of the plastic phase is associated with the appearance of an endothermic effect, whose maximum coincides with the maximum increase in carbonyl groups. Pore formation begins approximately at 400°, and is especially intense between 470° and 500°C. Thermal degradation involves rupture of ether, ester, and other bonds, with the production of exceptionally reactive compounds of low and high molecular weight, which undergo complicated polymerisation and polycondensation processes leading to gradual formation of the continuous three-dimensional structure of high-temperature coke.

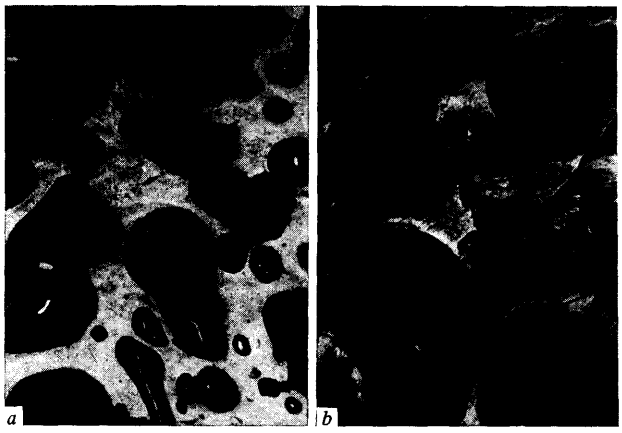
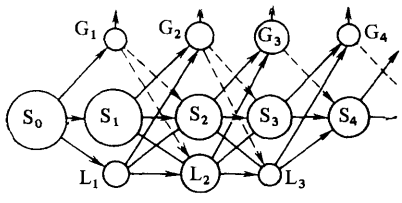


Figure 10. Photomicrographs (× 175) of structure of: *a*) semicoke obtained at 550°C; *b*) coke obtained at 750°C.



S_0	S_1	S_2	S_3	S_4
Initial coal	Start of softening, °C	Plastic state, °C	Max. plasticity, °C	Formation of solid phase, °C.
Fat	350	415	435	500
Coking	403	440	465	550

Figure 11. Thermal degradation, appearance of plastic phase, and caking.

5. COKING OF COAL–OIL MIXTURES

The value and the role of liquid products in the appearance of a plastic phase and the formation of coke were revealed by a study of the coking of mixtures of a weakly caking lean coal with various petroleum, tarry, and resinous products[53–57]. Table 4 gives some of the characteristics of the crucible coke obtained. These investigations show how great an influence the chemical composition and the quantity of liquid additives have on the appearance, density, porosity, hardness, and other properties of coke.

Table 4. Characteristics of crucible coke from weakly caking coal with various additives.

Additive	Density		Porosity, %	Hardness, s
	apparent	true		
None	0.56	1.78	68.6	27
Stearin pitch	0.55	1.66	66.8	84
Coke tar	0.32	1.77	81.9	19
Gas-works tar	0.56	1.73	67.6	45
Anthracene oil	0.52	1.71	69.6	37
Petroleum	0.55	1.93	71.5	30
Semicoke tar	0.63	1.74	63.9	35
Acid asphalt	0.51	1.77	71.2	36
Mazut	0.56	1.65	66.1	19
Coke-oven tar (8%)	0.52	1.77	70.8	27
Coke-oven tar (14%)	0.46	1.72	74.6	25
Coke-oven tar (25%)	0.40	1.69	76.4	23
Coke-oven tar (33%)	0.32	1.74	79.9	18
Coke-oven tar (40%)	0.29	1.79	83.8	10
Coke-oven tar (45%)	0.24	1.73	86.1	—

Especially interesting results were obtained in plastometric investigations of mixtures of a weakly caking coal with additions of 5%, 10%, and 15% of petroleum and tar products. Several plastometric curves are shown in Fig. 12, while Table 5 gives the plastometric parameters (x and y) and the strength of the coke obtained from these mixtures. The relation between the quantity x (%) of additives and the thickness y (mm) of the plastic layer can be represented approximately by the equation

$$y = a \cdot x^2 + b \cdot x + c .$$

Such an equation enables us to calculate the quantity of an additive necessary to convert a given weakly caking, lean coal into a coking or fat coal (Fig. 12).

The heavier is an additive and the richer in asphaltic–resinous compounds, the smaller the quantity required to obtain a plastic layer of maximum thickness. Coke-oven tar changes not only the thickness but also the temperature limits within which the plastic layer appears (Fig. 12), which occurs at considerably lower temperatures (360–460°C) on the addition of 10–15% of this material. The addition of gas-works and beechwood tars has no significant effect on the thickness of the plastic layer or on the temperature range of its formation.

Excessive increase of the additives causes intense cracking of the coke, so that its strength diminishes (Table 5). The optimum quantity of additives increases the strength of the coke by factors of 2–4. The strength is diminished by the addition of beechwood tar, which can be attributed to the large quantity of oxygen compounds present in such tar[58].

In order to establish the effect of the chemical and fractional composition of additives on the thickness of the plastic layer and the strength of the coke, coke-oven and gas-works tars were fractionally distilled, and the fractions isolated (10%) were added to a weakly caking coal (Table 6).[59] It was found that the addition of fractions rich in phenols (42–55%) and in naphthalene (80%) caused the plastic layer to break down, and an unstable coke was obtained. The thermogravimetric coking of model compounds has established[35] that naphthalene has escaped almost completely by 210°C (Fig. 1*b*), and cannot influence either formation of the plastic phase or caking. The greatest influence on the increase in the plastic phase and the strength of the coke is exerted by residues of coke-oven and gas-works tars rich in asphthaltic–resinous substances boiling above 350°C.

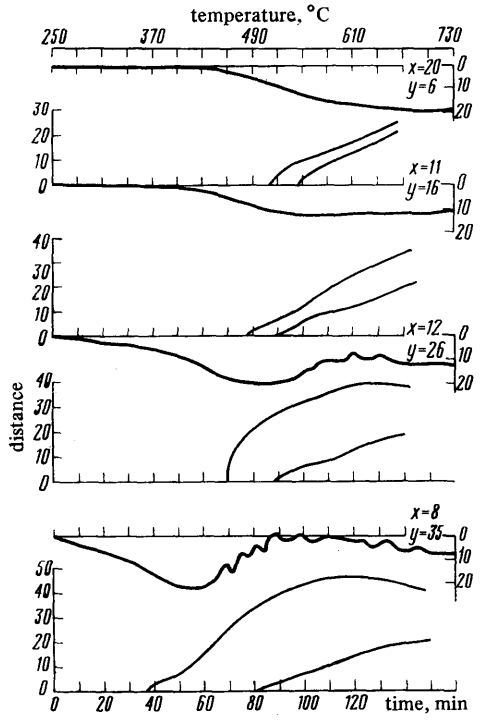


Figure 12. Plastometric curves of coal with various percentages of coke-oven tar: *a*) 0; *b*) 5; *c*) 10; *d*) 15.

Investigations of the coking of model mixtures of a weakly caking coal with various types of tar and fractions thereof revealed the mechanism of caking and coking[60,61]. On the addition of coke-oven tar and its resin the coal is readily dissolved and dispersed in silica-gel resins and asphaltenes, which leads to a great increase in the plastic layer, as a consequence of which the resulting coke is fused, light grey, and lustrous. Gas-works tar and the resin from it hardly affect the thickness of the plastic layer, since coal is insoluble in the petrolenes and kerogens that predominate in its composition. The coke obtained by cementation is grey and dull. Despite the differences in the physical processes accompanying formation of the coke, its strength is almost the same. It has thus been demonstrated that coke formation involves the dissolution and dispersion of coal and the cementation of particles of the resinous coke.

Table 5. Plastometric indices and strength of coke from coal with various additions.

Addition	Plastometric parameters, mm		Strength of coke, kg cm^{-2}	Addition	Plastometric parameters, mm		Strength of coke, kg cm^{-2}
	x	*y*			*x*	*y*	
None	20	6	39	Coke-oven tar (5%)	11	16	49
Mazut (5%)	21	10	44	Coke-oven tar (10%)	12	26	79
Mazut (10%)	19	11	64	Coke-oven tar (15%)	8	35	71
Mazut (15%)	12	12	52	Gas-works tar (5%)	22	7	25
Vacuum asphalt (5%)	20	13	48	Gas-works tar (10%)	17	8	33
Vacuum asphalt (10%)	30	13	55	Gas-works tar (15%)	18	10	35
Vacuum asphalt (15%)	12	12	50	Beechwood tar (5%)	35	5	39
Acid asphalt (5%)	21	12	55	Beechwood tar (10%)	42	7	32
Acid asphalt (10%)	21	17	80	Beechwood tar (15%)	39	7	13
Acid asphalt (15%)	18	12	44				

Table 6. Effect of tar fractions on plastometric parameters and strength of coke.

Type and fractional composition		Plastometric parameters, mm		Strength of coke, kg cm^{-2}
tar	temp. range, °C	*x*	*y*	
Coke-oven	≤180	31	10	141
Ditto	180—220	51	0	80
»	220—250	25	0	85
»	250—300	32	19	135
»	300—360	18	32	153
»	>360	17	35	203
Gas-works	≤230	29	0	disintegrates
Ditto	230—300	47	17	186
»	300—350	30	19	196
»	>350	25	20	364

6. CAKING OF LIGNITES AND COKING OF MIXTURES OF COAL AND BROWN COAL WITH OILY ADDITIVES

All brown coals are non-caking, so that they do not form a monolithic coke residue. Karavaev[62] found that Bulgarian lignites showed a slight tendency to cake, which he explained by an increased content of bitumens and sulphur. Investigation of Eastern Maritsa lignitic coal[63–68]

established that only xylite and vitrinised lignite are capable of caking, independently of the sulphur content. The differential thermal curves of these components (Fig. 13) clearly show that thermal degradation processes are closely similar in caking xylite and vitrinised lignite, but differ significantly from processes in which a caked coke residue is not formed.

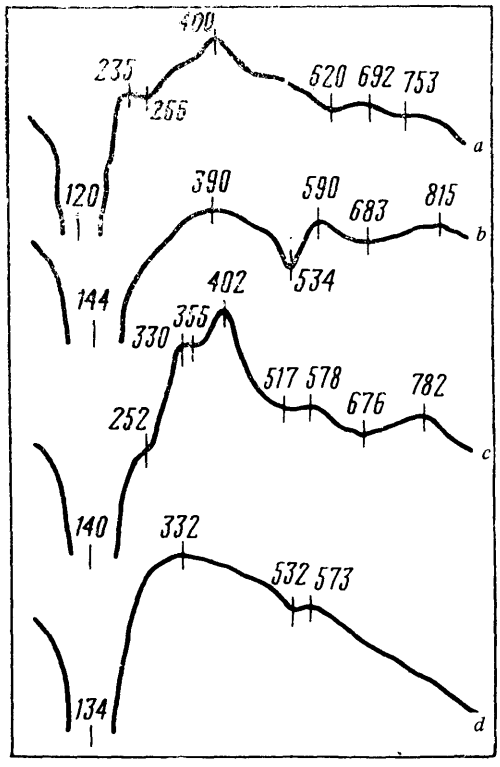


Figure 13. Differential thermal curves of: *a*) xylite; *o*) earthy mass; *c*) vitrinised lignite; *d*) fusinite.

Xylite was subjected to a combined chemical analysis[69,70] to reveal the reason for its caking. Fig. 14 gives differential thermal curves for the debituminised xylite, the residual carbon, and the humic acids liberated. The formation of a caked coke residue from the debituminised xylite (from which 16.2% of bitumens had been isolated) shows that caking is not due to the presence of bitumens. The humic acids yield a well caked crucible coke, whereas the residual coal forms an uncaked coke. This shows that the humic acids are responsible for the tendency of xylite to cake. Extraction of the humic acids leads to fundamental changes in the structure of the organic mass, involving loss of caking power, as is shown by the differential thermal results (*c* and *d* in Fig. 13).

Many investigators in various countries have worked on the use of brown coals to extend the raw-materials base of the coal-tar chemical industry. Our own researches have established the great importance of the age, origin, and previous heat-treatment of brown coals for the physicomechanical properties of the mixed coke[71-76]. A young lignitic coal, a shiny old brown coal, and a bituminous humic–sapropelic coal were used. The results show that replacing a lignitic coal by its semicoke improves the strength of the mixed coke. The best results were given by a semicoke obtained at 400°C, from which 12% of volatiles were isolated (Table 7).

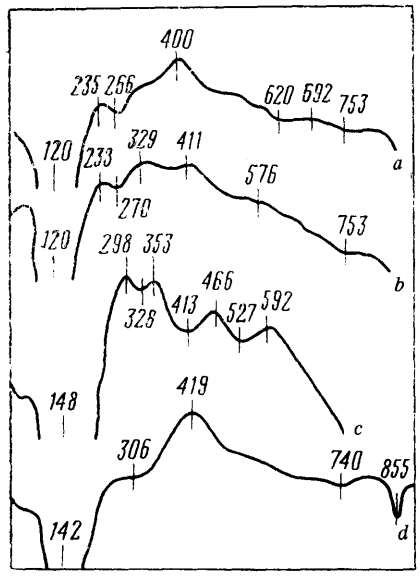


Figure 14. Differential thermal curves of: *a*) initial xylite; *b*) after evolution of bitumens; *c*) humic acids; *d*) isolated humic acids.

Table 7. Effect of semicoking temperature of lignitic coal on plastometric characteristics and strength of coke.

Mixture	Composition, %		Plastometric parameters, mm		Strength of coke, kg cm^{-2}
			x	*y*	
A	Lignites	100	54	0	—
B	Lignites	90	38	0	—
	coke-oven tar	10			
C	Coking coal	100	25	14	107
D	Coking coal	90	12	28	165
	coke-oven tar	10			
E	Coking coal	70			
	coke-oven tar	10	47	10	190
	lignites	20			
F	Coking coal	70			
	coke-oven tar	10	44	16	437
	semicoke from lignite (350°C)	20			
G	Coking coal	70			
	coke-oven tar	10	48	13	473
	semicoke from lignite (400°C)	20			
H	Coking coal	70			
	coke-oven tar	10	44	21	233
	semicoke from lignite (450°C)	20			
I	Coking coal	70			
	coke-oven tar	10			
	semicoke from lignite (510°C)	20	49	12	320

Analogous investigations with other brown coals[77,78] showed that a stronger mixed coke is formed when the older, bright brown coals are used without the addition of coke-oven tar. If the brown coals are replaced by the semicoke from them, a less stable mixed coke is formed.

When 10% of coke-oven tar is added to the charge, replacement of the coal by the semicoke almost doubles the strength of the mixed coke. A similar rule has been established also for a young lignitic coal. Replacing bituminous humous–sapropelic coals by semicoke produces no significant impairment of the strength of the mixed coke, independently of whether or not the charge contained a coke-oven tar.

Table 8. Physicomechanical characteristics of mixed coke.

Composition of mixture, %				Properties			
coking coal	brown coal	semicoke from brown coal	coke-oven tar	gas permeability Γ	total strength π	abrasion resistance π_{ab}	crushing strength π_{cr}
					kg rev. dm^{-2}		
100	—	—	—	277	19.7	114.0	22.4
young lignitic coal							
80	20	—	—	204	7.4	12.5	14.3
70	20	—	10	211	10.9	19.4	25.0
70	—	20	10	250	30.2	58.0	63.0
old bright brown coal							
80	20	—	—	229	25.9	82.5	3.8
70	20	—	10	271	6.0	197.0	6.2
70	—	20	10	263	18.7	95.0	23.3
bituminous humic-sapropelic brown coal							
80	20	—	—	225	8.3	33.4	11.0
70	20	—	10	278	11.6	58.1	1.5
70	—	20	40	234	7.7	3.8	8.1

The coking of ternary mixtures in a Nikolaev laboratory furnace showed (Table 8) that the addition of 20% of young humic lignites to a coking coal sharply impairs the characteristics of the mixed coke (gas permeability Γ = 204), which cannot be appreciably improved even after the addition of 10% of coke-oven tar (Γ = 211). If semicoke with the same content of oils in the charge is added instead of the lignitic coal, the gas permeability of the mixed coke is considerably increased, reaching 250, while other strength parameters are improved two- to three-fold. The strength characteristics Π and Π_{cr} even exceed the corresponding values for coke obtained from 100% coking coal. A test on the effect of additions of xylitic coal from the Chukurov mine[79] fully confirmed the rule.

If 20% of an older brown coal is added to a coking coal, a mixed coke of very poor physicomechanical characteristics is obtained. However, the quality of the mixed coke can be considerably improved by adding 10% of coke-oven tar, when the gas permeability is changed from 229 to 271, and both the abrasion resistance and the crushing strength are approximately doubled. Replacement of the brown coal by its semicoke leads to some decrease in gas permeability and to increases in total and crushing strengths. A sharp improvement in all the characteristics of the coke is observed if the young humic lignite is replaced by its semicoke.

The addition of 20% of a bituminous humic–sapropelic coal to a coking coal impairs all the physicomechanical characteristics of the mixed coke, and they cannot be improved by the addition even of 10% of coke-oven tar. It is interesting that replacement of this brown coal by its semicoke produces a sharp deterioration both in the gas permeability coefficient and in the strength characteristics of the mixed coke. This confirms the great value of bitumens of humic–sapropelic brown coal in caking. Coke-oven tar pitch, mazut, and vacuum and acid asphalts were also tested as additives[79]. The results showed that bitumens are as important in caking and coking as are brown coal and its semicoke.

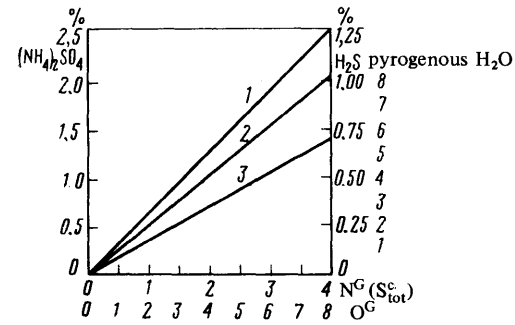


Figure 15. Graph for calculating, from the nitrogen, sulphur, and oxygen contents, the percentage yields of: 1) ammonium sulphate; 2) hydrogen sulphide; 3) "pyrogenous water".

Table 9. Physicochemical and structural properties of coke.

Property characteristic	Soviet coals		Bulgarian coals	
	gas	mixed fat	mixed coking	mixed
I. Chemical composition				
1. Moisture, %	0.30	1.75	1.09	1.70
2. Ash, %	12.90	10.29	12.05	20.45
3. Total sulphur, %	0.79	1.76	1.52	1.65
4. Volatiles, %	1.86	1.94	2.33	3.06
II. Physicomechanical				
1. Gas permeability	239	281	277	—
2. Total strength π, kg rev. dm^{-2}	11.0	10.5	14.1	1.7
3. Abrasion resistance π_{ab}	75.0	75.0	35.8	—
4. Crushing strength π_{cr}	10.8	113.0	24.7	—
5. Class > 40 mm, %				
after 150 rev.	71.0	87.3	88.0	18.0
after 300 rev.	65.0	76.1	81.8	0.0
6. Class < 10 mm, %				
after 150 rev.	9.5	12.7	12.0	80.0
after 300 rev.	11.2	10.9	18.2	100.0
7. Specific surface, m^2 g^{-1}	32	28	38	42
III. Structural				
1. Density	0.809	0.632	0.770	0.841
2. Porosity	86.6	65.5	87.4	96.6
3. Cellularity	83.4	76.0	88.6	90.6
4. Mean pore size, mm	0.258	0.378	0.141	0.074
5. Mean wall thickness, mm	0.078	0.105	0.058	0.054

7. YIELDS OF CHEMICAL PRODUCTS FROM COAL–PROPERTIES AND STRUCTURE OF COKE

The theoretical investigations of caking and coking enabled formulae to be deduced for calculating the yields of chemical products[80–83] and for predicting the qualitative indices and the physical structure of the resulting coke[84–90]. Examination of the coking of individual types of coals and their mixtures has established graphical relations (Fig. 15) and formulae for calculating the yields of ammonium sulphate, hydrogen sulphide, and pyrogenous water as functions of the contents of nitrogen, sulphur, and oxygen in the original coal[90,91]. Table 9 lists the most important physicochemical and structural indices of the coke obtained in these investigations[92].

Box coking[93,94] has been based on preliminary experiments on the use of Scheffe's simplex-grid plan for predicting the properties of coke. The scheme of experiments is shown in Fig. 16, and the results are listed in Table 10. Mathematical processing of the data on an electronic computer has given the equations below for calculating the most important chemical and structural characteristics of the coke.

1. For the ash (A^c,%)

$$Y_1 = 13.44X_1 + 20.32X_2 + 10.79X_3 + 22.8X_1X_2 + 0.86X_1X_3 + 0.22X_2X_3 + 2.4X_1X_2 \cdot (X_1 - X_2) + 4.2X_1X_3(X_1 - X_3) - 0.13X_2X_3(X_2 - X_3) - 8.8X_1X_2 \times (X_1 - X_2)^2 - 6.2X_1X_3(X_1 - X_3)^2 + 12.9X_2X_3(X_2 - X_3)^2 + 92.8X_1^2X_2X_3 + 47.1X_2X_3 - 1.7X_3X_2^2.$$

2. For the total sulphur in the coke (A^a, total %)

$$Y_2 = 1.03X_1 + 1.87X_2 + 2.16X_3 - 0.08X_1X_2 - 0.14X_1X_3 - 0.06X_2X_3 - 1.01X_1X_2(X_1 - X_2) + 0.08X_1X_3(X_1 - X_3) - 0.93X_2X_3(X_2 - X_3) + 1.49X_1X_2 \times (X_1 - X_2)^2 - 1.47X_1X_3(X_1 - X_3)^2 + 9.52X_1^2X_2X_3 + 0.88X_2X_3(X_2 - X_3)^2 - 3.92X_1X_2^2X_3 (8; 38X_1X_2X_3^2).$$

3. For M_{40} in micuum drum

$$Y_3 = 67.0X_1 + 50.0X_2 + 77.0X_3 + 8.0X_1X_2 + 12.8X_1X_3 + 48.0X_2X_3 + 34.7X_1X_2 \times (X_1 - X_2) - 12.8X_1X_3(X_1 - X_3) - 1.1X_2X_3(X_2 - X_3) + 10.7X_1X_2(X_1 - X_2)^2 - 49.1X_1X_3(X_1 - X_3)^2 - 13.9X_2X_3(X_2 - X_3)^2 - 462.5X_1^2X_2X_3 + 635X_1X_2^2X_3 + 54.8X_1X_2X_3^2.$$

4. For M_{10} in micuum drum

$$Y_4 = 8.0X_1 + 43.8X_2 + 8.3X_3 - 15.2X_1X_2 + X_1X_3 + 69.0X_2X_3 - 9.6X_1X_2 \times (X_1 - X_2) + 18.9X_1X_3(X_1 - X_3) - 16.2X_2X_3(X_2 - X_3) + 43.2X_1X_2(X_1 - X_2)^2 + 46.1X_1X_3(X_1 - X_3)^2 + 56.3X_2X_3(X_2 - X_3)^2 + 262.1X_1^2X_2X_3 - 320.1X_1X_2^2X_3 + 55.4X_1X_2X_3^2.$$

5. For the structural strength

$$Y_5 = 79.8X_1 + 68.4X_2 + 80.1X_3 + 5.4X_1X_2 - 2.4X_1X_2 + 32.2X_2X_3 + 89.6X_1X_2 \times (X_1 - X_2) - 2.9X_1X_3 - X_3 - 14.1X_2X_3(X_2 - X_3) - 258.1X_1X_2(X_1 - X_2)^2 + 4.0X_1X_3(X_1 - X_3)^2 - 96.8X_2X_3(X_2 - X_3)^2 + 354.3X_1^2X_2X_3 - 66.6X_1X_2^2X_3 - 186.3X_1X_2X_3^2.$$

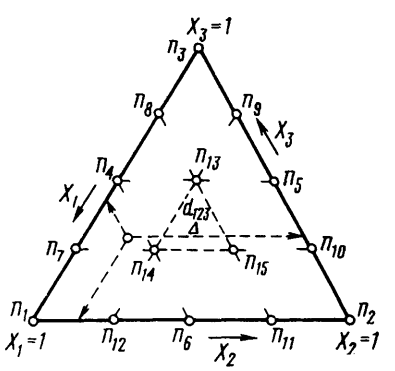


Figure 16. Plan of box experiments used to obtain a fourth-power model.

The equations were checked for five points in Fig. 16: one of the points lies at the centre of the diagram ($X_1 = X_2 = X_3 = 0.333$), while the others correspond to the compositions of the coal charges which are promising for the by-product coke plant at the Kremikovtsy mining complex. Values calculated for M_{40} by means of Eqn. Y_3 differ from the experimental values by ±1.5%, and those for M_{10} (from Eqn. Y_4) by ±1.0% (absolute). Very good agreement was obtained also for the ash, total sulphur, and structural strength.

Table 10. Results of planned experiments.

Ash A^c, %	Total sulphur S_{tot}, %	Micuum drum, %		Structural strength, %	Ash A^c, %	Total sulphur S_{tot}, %	Micuum drum, %		Structural strength, %
		M_{40}	M_{10}				M_{40}	M_{10}	
13.44	1.03	67.0	8.0	79.8	13.75	2.16	78.7	8.4	80.0
20.32	1.87	50.0	43.8	68.4	18.49	1.87	85.0	23.1	71.5
10.79	2.16	77.0	8.3	80.1	18.39	1.81	53.0	36.8	50.3
12.33	1.56	75.2	8.4	81.3	15.40	1.20	68.0	17.1	72.8
15.50	1.97	75.5	8.8	82.3	15.05	1.68	78.0	9.4	80.8
17.45	1.45	60.5	24.6	73.5	16.77	1.50	69.4	15.2	83.7
13.04	1.21	68.4	12.2	80.8	17.93	1.78	74.4	14.8	72.5
10.93	1.75	75.8	8.8	81.5					

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Advances in the Synthetic Chemistry of Aminoglycosides

S.E.Zurabyan and A.Ya.Khorlin

Data on the methods for the formation of the aminoglycosidic linkage in the synthesis of alkyl and aryl aminoglycosides and oligosaccharides containing 2-amino-2-deoxyglycosyl residues are reviewed systematically.
The bibliography includes 229 references.

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I. INTRODUCTION

Aminosugars and in the first place 2-amino-2-deoxyhexoses play a significant role in vital processes, being important structural components of polysaccharides and mixed biopolymers. The central problem of the chemistry of biopolymers containing aminosugar residues is that of the nature of the chemical bond joining the monomeric units of the macromolecules. Since the aminosugar residues in polysaccharides and other carbohydrate-containing polymers are as a rule linked by the aminoglycosidic linkage, the development of methods for its formation and the study of its properties constitute the most important problem in the chemistry of aminosugars.

The present review deals with methods of synthesis of aminoglycosides, including the formation of a new aminoglycosidic linkage, but not with the chemical reactions of glycosides and oligosaccharides without the formation of glycosidic linkages. The methods for the formation of the aminoglycosidic linkage are considered from the standpoint of the main requirements which must be met by glycoside synthesis in general, namely (1) the reaction must be structurally specific and stereospecific, (2) in view of the lability of the protecting groups for the "aglycone" component, the reaction must proceed under fairly mild conditions, and (3) the protecting groups of the glycosylating agent must be fairly stable under the conditions of the glycosylation reaction and at the same time must be removed easily and selectively from the final products without alteration of their structure.

From the chemical point of view, the synthesis of the glycosides of 2-amino-2-deoxysugars is of special interest, since it exhibits many important differences from glycoside synthesis with neutral sugars and other aminosugars. These differences are due to the location of the amino-group in the immediate vicinity to the glycosidic centre.

We have surveyed the studies in which the foundations were laid for the method of synthesising aminoglycosides, their reactions were investigated, or significant improvements were introduced into methods already known. Attention was concentrated on the synthesis of acetamidoglycosides, including oligosaccharides containing acetamidoglycoside residues, since in most cases aminosugars are encountered in nature as *N*-acetyl derivatives.

The problems of aminoglycoside synthesis were considered in previous reviews[1-3], but the intense development of this branch of carbohydrate chemistry, particularly the synthetic chemistry of aminosugar oligosaccharides, led us to write the present review, which covers the literature up to the middle of 1973.

II. THE SYNTHESIS OF ALKYL AND ARYL AMINOGLYCOSIDES

1. Alcoholysis of Monosaccharides

Fischer's method, which is widely used in the synthesis of alkyl glycosides of neutral sugars, is sometimes employed to obtain mixtures of anomeric glycosides of *N*-protected 2-amino-2-deoxysugars. Thus treatment of *N*-acetyl-*D*-glucosamine with alcohols in the presence of hydrogen chloride, toluene-*p*-sulphonic acid, ion-exchange resins in the H^+-form, or Lewis acids[4-13] leads to a mixture of alkyl 2-acetamido-2-deoxy-α-*D*-glucopyranosides and the corresponding β-*D*-glucopyranosides in which the α-anomers predominate. Glycosylation of benzyl alcohol with *N*-acetyl-*D*-glucosamine also leads to a mixture of anomeric glycosides from which benzyl 2-acetamido-2-deoxy-α-*D*-glucopyranoside, used in the synthesis of many 2-amino-2-deoxysugar derivatives, was isolated[14-16]. Treatment of *N*-acetyl-*D*-galactosamine (or its acetate) by lower alcohols gives analogous results[11,17-19]. Since, regardless of the nature of the aglycone, aminogalactosides are formed under the same conditions as aminoglucosides, special attention will not henceforth be devoted to their synthesis.

2-Amino-2-deoxysugars with a free amino-group do not form glycosides under the conditions of the Fischer synthesis in consequence of the electrostatic repulsion of cationic groups from the glycosidic centre by the NH_3^+ group[4].

2. The Helferich Synthesis of Aryl Aminoglycosides

The Helferich method (see the review of Conchie et al.[20]), which consists of fusing together peracetylated aminosugars with phenols in the presence of catalytic

amounts of toluene-*p*-sulphonic acid or zinc chloride, has been used in the synthesis of aryl aminoglycosides[20-25]. Toluene-*p*-sulphonic acid catalyses the preferential formation of 1,2-*trans*-aminoglycosides, while in the presence of zinc chloride a mixture of anomeric aryl aminoglycosides is formed. This method is relatively unsuitable for the synthesis of aminoglycosides with an aglycone having a complex structure and particularly for the glycosylation of labile compounds.

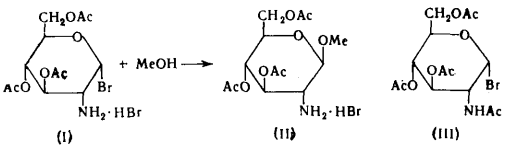
3. The Action of Alkylating Agents

N-Acetyl-D-glucosamine (or its acetate) reacts with methyl iodide in dimethylformamide (DMF) in the presence of barium oxide and hydroxide and is converted into methyl 2-acetamido-3,4,6-tri-*O*-methyl-2-deoxy-β-D-glucopyranoside[26]. When derivatives of *N*-acetyl-D-glucosamine are alkylated with dimethyl sulphate, derivatives of both α- and β-D-glycosides are formed, depending on the reaction conditions[27,28]. A very mild alkylation method was proposed by Kuhn and Baer[29], involving the treatment of *N*-acetyl-D-glycosamine and also its *N*-formyl and *N*-benzyloxycarbonyl analogues with diazomethane in aqueous methanol, which leads to methyl β-D-glycosides. The methods quoted here are specific and their preparative value is apparently small.

III. THE KOENIGS–KNORR REACTION AND ITS MODIFICATIONS IN THE SYNTHESIS OF AMINOGLYCOSIDES

1. Acylhalogeno-derivatives of Aminosugars in the Koenigs–Knorr Reaction

The Koenigs–Knorr reaction (see reviews[20,30,31]), which is based on the reaction of acylhalogenosugars with alcohols and phenols in the presence of hydrogen halide acceptors, has found extensive applications also in the synthesis of aminoglycosides. (The information about acylhalogenosugars of the 2-amino-2-deoxysugar series accumulated at the present time is summarised in Table 1.) As early as 1911, it was shown[32] that the hydrobromide of 2-amino-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl bromide (I) is converted into the glycoside hydrobromide (II) on reaction with methanol:

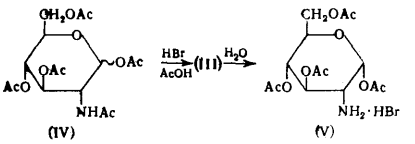


(I) (II) (III)

However, the bromides of fully acetylated 2-amino-2-deoxysugars differ significantly from the bromides of the corresponding neutral analogues[31], and for this reason the structures and properties of the acylated bromides and chlorides of 2-amino-2-deoxysugars must be specially considered.

The bromide (I) and the corresponding chloride are quite stable and resemble the acylhalogeno-derivatives of neutral hexopyranoses. Compared with tetra-*O*-acetyl-α-D-glucopyranosyl bromide, the bromide of the acetylated D-glucosamine (III) is significantly more reactive. The explanation is that in the heterolysis of the C–Br bond the acetamide group at 2-C is more involved in the formation of a stable intramolecular cyclic derivative with the 1-C atom than the acetoxy-group at 2-C in the D-glucose derivative. The reactivity can be reduced (and hence the stability and the acylhalogeno-derivatives increased) by increasing the electronegativity of the substituents in the acylamino-group.

The extreme sensitivity of the bromide (III) to moisture remained for a long time an obstacle to its isolation in a pure state. When hydrogen bromide in acetic acid was allowed to react with the acetate (IV), the expected bromide (III) was not obtained[4]; instead, as shown subsequently[33-35], the hydrobromide (V) was isolated:

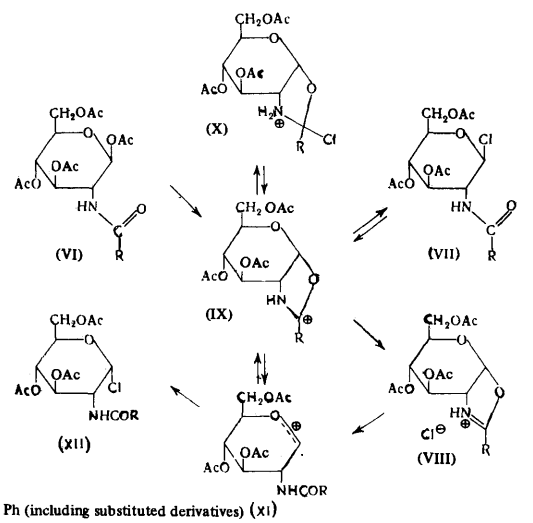


(IV) (V)

However, the bromide (III), formed in this reaction, and also the bromide of the D-galacto-series obtained under similar conditions[19], were used without purification in aminoglycoside synthesis, as will be described below. The bromide (III) was obtained much later in a pure state by treating the acetate (IV) with a limited amount of hydrogen bromide in acetic acid, taking precautions to prevent contact of the product with moisture[36] (cf. Fodor and Ötvös[37]).

Osawa[38] characterised in detail the processes occurring when hydrogen chloride, titanium tetrachloride, or aluminium chloride are allowed to act on 1,2-*trans*-acetylated derivatives of 2-amino-2-deoxysugars (VI). Initially the acetoxy-group at 1-C is eliminated rapidly with participation of the adjoining acylamino-group, which leads to the unstable β-D-glycosyl halide (VII). In this stage the *N*-aroyl derivative is rapidly stabilised as the result of the formation of a salt of the oxazoline derivative (VIII) in which the C=N bond is conjugated with the aromatic ring. If R is an alkyl group, the intermediate cation (IX) formed can react with hydrogen halide to form the oxazolidinium cation (X). Powerful electronegative acyl residues such as *p*-nitrobenzoyl or chloroacetyl favour the rapid formation of the oxonium ion (XI)—the direct precursor of the α-D-glycosyl halide (XII) (see Scheme 1). The mixture of anomeric acetates reacts with hydrogen bromide in acetic acid in a more complex manner[36].

Scheme 1



(VI) (VII) (VIII) (IX) (X) (XII)

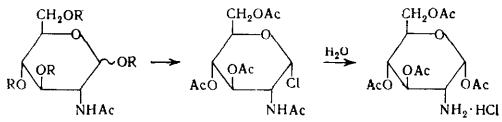
R = Me or Ph (including substituted derivatives) (XI)

The stability of the acylated bromides of 2-amino-2-deoxysugars can be enhanced not only by the introduction of electronegative substituents into the acylamino-group but also by the introduction of aryl or arylalkylidene substituents at the amino-group of the 2-amino-2-deoxysugars, since such groups at 2-C are incapable of forming the intermediate cyclic cation. *O*-Acylated α-D-glycosyl bromides were obtained in this way with the following *N*-protecting groups: benzoyl[39,40], toluene-*p*-sulphonyl[41,42], phenylmethanesulphonyl[43], 2,4-dinitrophenyl[44-46], diphenylphosphoryl[47], anisylidene[47], benzyloxycarbonyl[47], trifluoroacetyl[48,49], dichloroacetyl[50-52], and certain others[47,49,53-58]. These compounds were subsequently used in the synthesis of aminoglycosides.

The stability of acylhalogeno-derivatives of the 2-amino-2-deoxysugar series depends also on the nature of the halogen atom and increases in the sequence Br < Cl < F. Iodides are still unknown and fluorides are so inactive that they can be deacetylated in the presence of sodium methoxide with retention of the C–F linkage[42].

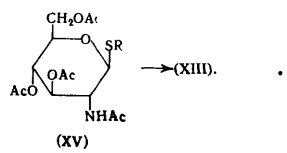
Among aminosugar chlorides, the greatest interest attaches to the peracetylated 2-amino-2-deoxy-α-D-glycosyl chlorides formed when 2-acetamido-2-deoxysugars (or their acetates) are treated with hydrogen chloride[34,54,59-62], acetyl chloride[63,64], both hydrogen chloride and acetyl chloride[65], and titanium tetrachloride[19,33,34]. The chlorides of *N*-acetylated aminosugar di- and tri-saccharides were also obtained by these methods[62,65,66].

The chloride (XIII) is fairly stable and is only slowly converted into the hydrochloride (XIV), which permits its isolation even when moist solvents are employed[33,34,38]:



R = H or Ac (XIII) (XIV)

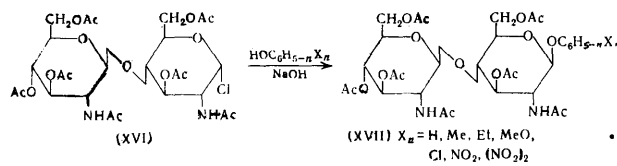
Another method for the synthesis of acetylated aminoglycosyl chlorides[67], including furanosyl chlorides[68], consists of the chlorination of *S*-substituted 1-thioanalogues (XV, R = Et, CSOEt, COMe) (cf. Bonner[69]), for example:



However, from the preparative point of view this method can hardly compete with that discussed above.

The use of the stable bromide (I) in the synthesis of aminoglycosides is restricted to the formation of glycosides from lower alcohols[32] and certain phenols[70] owing to the low solubility of (I) in solvents used in the Koenigs–Knorr reaction. When unstable bromides of acetylated aminosugars (which have as a rule not been isolated in a pure state) or stable but insufficiently reactive chlorides were used, 2-acetamido-2-deoxy-β-D-glucopyranosides and the corresponding β-D-galactopyranosides derived from lower alcohols[19,34,60,63,71,72], phenols[34,60,65,73-77], and monoterpene[78,79], steroid[80], and certain other alcohols[59,81,82] were obtained. Different monofunctional hydroxy-compounds have been glycosylated by bromides with other *N*-protecting groups[38-48,55-57,83-92]. Although the yields of the desired products increased in such cases, the employment of bromides in which the substituents at 2-C are not involved in the reaction led in a number of instances[45,89,92] to a mixture of anomeric glycosides.

The stereospecificity of the glycosylation is apparently a key problem of glycoside synthesis. The isolation of a particular anomer from the reaction mixture (which is frequently very complex, particularly in the case of glycosides with an aglycone having a complicated structure) does not alone demonstrate the stereospecificity of the reaction. Since an answer to this question can be obtained only by a detailed analysis of all the reaction products, the data on the stereospecificity of glycosylation must be treated with caution.



To obtain alkyl or aryl glycosides derived from oligosaccharides containing 2-acetamido-2-deoxy-β-D-glucopyranosyl residues at the reducing end, the Koenigs–Knorr method[62,72] or its modifications were also used. When the disaccharide chloride (XVI) was allowed to react with phenols, aryl β-chitobioside acetates (XVII) were obtained[65,66,93-98].

Scheme 2

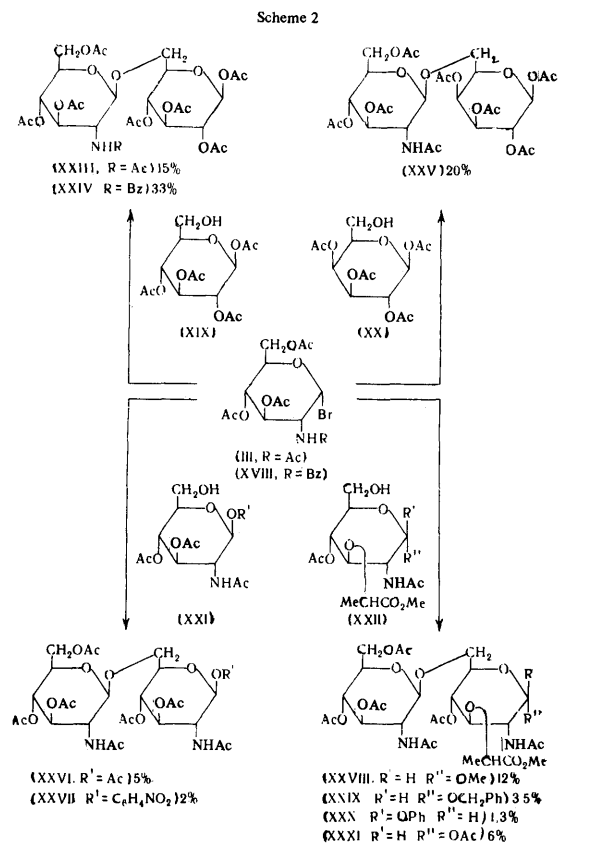


Table 1. Acylhalogeno-derivatives of 2-amino-2-deoxy-sugars.

Structure	Yield[a], %	M.p., °C	$[\alpha]_D^\beta$ and solvent[b]	Refs.
1	2	3	4	5
Glycosyl chlorides				
3,4-Di-*O*-acetyl-2-deoxy-2-nitroso-α-D--xylopyranosyl chloride, dimer	90	102–106	+164 C	171
2-Amino-2-deoxy-α-D-glucopyranosyl chloride				
[3,4,6-tri-*O*-acetyl-,				
[hydrochloride	–	161–163 d[c]	+146 C	67
[*N*-acetyl-	86	125–126 d		54
		133–134 d	+120 C	59
	69	133–134 d	+118 C	34
[β-anomer	60	syrup	+20 C	38
N-benzoyl-	53	124–127	+36 P–W	135
N-bis-(4-nitrobenzyl)phosphoryl-	80	148–149	+39 C	47
N-(3,5-dinitrobenzoyl)-	70	144	+133 C	220
N-diphenylphosphoryl-	90	125–126	+97 C	47
N-(4-methoxybenzoyl)-	11	137 d	+153 C	38
N-(4-nitrobenzoyl)-	80	129–130	+149 C	171,172
2-nitroso-analogue, dimer	64	122–124	+132 A	75
N-propionyl-	61	132–134	+21 C	38,86
NN-succinyl-, β-anomer	67	139–141	+107 C	221
N-(toluene-*p*-sulphonyl)-	80	138	+107 C	57
N-methyl-		139–140	+103 C	221
NN-phthaloyl-, β-anomer	66	149	+62 C	38,57
	86	154	+28 B	58
N-chloroacetyl-	61	143 d	+116 C	38
3,4,6-tri-*O*-benzoyl-*N*-acetyl-	45	128–130		206
2-Amino-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactopyranosyl chloride				
N-acetyl-	43	131–136 d	+134 C	19
		130	+138 C	73
2-nitroso-analogue, dimer	84	128–131	+128 C	171
2-Acetamido-3,4-di-*O*-acetyl-2,6-dideoxy-α-D-glucopyranosyl chloride	71	145 d	+153 C	222
2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride	66	208–209 d	+41 C	93
	60	202–204 d	+34 C	65
O-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 4)-*O*-(2-acetamido--3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyrano-syl)-(1 → 4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl chloride	34	169 d	+33 C	66
Glycosyl bromides				
2-Amino-2-deoxy-α-D-glucopyranosyl bromide				
3,4,6-tri-*O*-acetyl-		82–83	+75 C	37
hydrobromide	–	149–150 d	+148 A	32
	85	149–150	+151 A	47,223
N-acetyl-	10	116–118	+86 C	37
N-benzyloxycarbonyl-	30	90 d	+148 C	36
N-phenylmethanesulphonyl-	72	65–75	+89 C	43
N-diphenylphosphoryl-	91	126–127	+125 C	47
N-(4-methoxybenzylidene)-	64	112–114	+217 C	47
N-(toluene-*p*-sulphonyl)-	83	148	+64 C	41
	83	148 d	+134 C	42
N-trifluoroacetyl-	74	95–97		48
	92	96	+126C	49
N-phenylcarbamoyl-	70	105 d	+137 C	56
NN-phthaloyl-, β-anomer	48	136–137	+51 C	55,57
	50	130	+18 B	58
N-(2,4-dinitrophenyl)-				
3,4-di-*O*-acetyl-6-*O*-methyl-	78	135	+28 C	92
3,6-di-*O*-acetyl-4-*O*-methyl-	70	150–152	+68 C	92
4,6-di-*O*-acetyl-3-*O*-methyl-	–	amorph.	–5 C	92
3,4,6-tri-*O*-acetyl-	97	162–164 d	+46 C	44–46
3,4,6-tri-*O*-benzoyl-	70	150 d	+68 C	84
	94	143 d	+119 C	85
hydrobromide	81	163 d	+71 T	85
N-benzyloxycarbonyl-	47	102–104	+105 C	85
N-benzoyl-	86	126 d	+127 C	40
	88	128	+125 C	39,85
N-dichloroacetyl-	85	125–127	+89 C	51
2-Amino-2-deoxy-α-D-galactopyranosyl bromide				
3,4,6-tri-*O*-acetyl-, hydrobromide	76	144–148 d	+160 C	224
3,4,6-tri-*O*-benzoyl-*N*-dichloroacetyl-	–	amorph.		52

a The yields are quoted only for the stage where the halogen atom was introduced, disregarding the stage corresponding to the introduction of the *N*-substituent.

Table 1 Continued...

b The following abbreviations have been adopted in this and subsequent tables: A = acetone, B = benzene, W = water, D = dimethylformamide, M = methanol, N = nitromethane, P = pyridine, T = tetrahydrofuran, and C = chloroform.

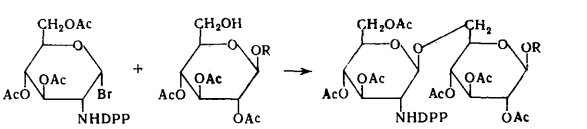
c With decomposition.

2. Synthetic Oligosaccharides†

Among the known methods for the synthesis of di- and oligo-saccharides the only ones available for oligosaccharides with 2-acetamido-2-deoxyglycopyranosyl residues remained for a long time those based on the Koenigs–Knorr reaction and its various modifications. When a freshly prepared solution of the bromide (III)[33] or its *N*-benzoyl analogue (XVIII) was allowed to react with partly substituted derivatives of D-glucose (XIX)[97,98], D-galactose (XX)[97], *N*-acetyl-D-glucosamine (XXI, R′ = acetyl or *p*-nitrophenyl)[93,99], and *N*-acetylmuramic acid (XXII)[12,100–102] under the conditions of the Koenigs–Knorr reaction, a number of disaccharide derivatives (XXIII)–(XXXI) with β-(1→6)-aminoglycosidic linkages between the monosaccharide units were synthesised. The employment of the bromide (III) resulted in a low yield also of the acetate of the non-reducing disaccharide 2,2′-diamino-2,2′-dideoxy-ββ-trehalose[33].

It is noteworthy that in all cases the yield of the desired compounds was significantly lower than in the glycosylation of the same (or similar) aglycone components of the acylhalogeno-derivatives of neutral sugars by the Koenigs–Knorr reaction.

In connection with the high lability of the bromide (III), which is the cause of the low yields of the disaccharide derivatives (XXIII)–(XXXI) (see Scheme 2), subsequently more stable glycosyl halides were used in the synthesis of disaccharides. Zervas and Konstas[47] were the first to use the stable bromide (XXXII) in the synthesis of disaccharides and, when the reaction was carried out in the presence of mercury cyanide, they obtained the protected disaccharide (XXXIV) in 60% yield. An analogous disaccharide derivative (XXXV) was synthesised subsequently[103] with the same yield by the glycosylation of (XXXIII):



(XXXII) DPP = P(O)(OPh)$_2$ (XIX, R = Ac) (XXXIII, R = CH_2Ph) (XXXIV, R = Ac) (XXXV, R = CH_2Ph)

† See Table 2, where the available information about synthetic oligosaccharides and their derivatives is summarised.

Table 2. Synthetic oligosaccharides containing 2-amino-2-deoxyglycosyl residues.

Oligosaccharides[a] and their derivatives	Method of synthesis and yield[b], %	M.p., °C	$[\alpha]_D^0$ and solvent	References
1	2	3	4	5
Glc*p*N-α-(1 → 3)-Glc				
N-acetyl-		212—215	+182→+158 W	180
1,2:5,6-di-*O*-isopropylidene-3′,4′,6′-tri-*O*-acetyl-, α-furanose	[c] 75	168—170	+32 C	180
2′-hydroxyamino-analogue	N 59	160—161	+66 C	176
Glc*p*N-β-(1 → 3)-Glc				
N-acetyl		amorph.	+59→+39 W	166
1,2:5,6-di-*O*-isopropylidene-3′,4′,6′-tri-*O*-acetyl-, α-furanose	Z 49	219—220	+68 C	166
N-phenylmethanesulphonyl-1,2:5,6-di-*O*-isopropylidene-3′,4′,6′-tri-*O*-acetyl-, α-furanose	K 6	219	−36 C	43
Glc*p*N-β(1 → 4)-Glc				
N-acetyl-		190—195	+30 W	110
hepta-*O*-acetyl-, α-anomer		148—151	+24 C	110
1,6-anhydropenta-*O*-acetyl-		194—195	−29 C	110
p-nitrophenyl β-pyranoside	E 49	256—258		186
N-dichloroacetyl-1,6-anhydro-2,3-di-*O*-acetyl-3′,4′,6′-tri-*O*-benzoyl-	K 10	112	−38 C	110
Glc*p*N-β-(1 → 6)-Glc				
hepta-*O*-acetyl-, hydrochloride		233 d.	+32 D	47
β-anomer		amorph.	+3 W	97,161
N-acetyl-		217—218	−9 C	47
hepta-*O*-acetyl-, β-anomer	K 16	218—219	−10 C	97
	Z 46	222—223	−7 C	161
benzyl β-pyranoside (monohydrate)		240—241	−50 M	103
hexa-*O*-acetyl-	Z 46	210—211	−26 C	103
N-benzoyl-		175—177	−6 W	137,226
hepta-*O*-acetyl-, β-anomer	K 33	252—253	−2 C	98
	Z 51	251—253	−2 C	137
methyl α-pyranoside		260—265 d.	+35 W	137
hexa-*O*-acetyl-	Z 55	214—216	+69 C	137
hexa-*O*-methyl-		196—198	+84 C	226
methyl β-pyranoside, hexa-*O*-methyl-		200—202	+14 C	226
N-diphenylphosphoryl-				
hepta-*O*-acetyl-, β-anomer	K 60	221—223	+3 C	47
benzyl β-pyranoside, hexa-*O*-acetyl-				
N-phenylmethanesulphonylhepta-*O*-acetyl-, β-anomer	K 61	202—203	−20 C	103
	K 34	246	−18 C	43
Glc*p*N-β-(1 → 3)-Gal				
N-acetyl-				
hepta-*O*-acetyl-, α-anomer		212—213	+80 C	51
1,6-anhydropenta-*O*-acetyl-		202—204	−78 C	51
N-dichloroacetyl-1,6-anhydro-2-*O*-acetyl-3′,4′,6′-tri-*O*-benzoyl-4-*O*-acetyl-	K 19	235—236 syrup	−41 C	51
Glc*p*N-β-(1 → 4)-Gal				
N-acetyl-		162—165	+8 W	51
hepta-*O*-acetyl-, α-anomer		178—179	+56 C	51
1,6-anhydropenta-*O*-acetyl-		238—239	−29 C	51
N-dichloroacetyl-1,6-anhydro-2-*O*-acetyl-3′,4′,6′-tri-*O*-benzoyl-	K 26	146—148	−40 C	51
3-*O*-acetyl-	K 9	235—236	−33 C	51
Glc*p*N-α-(1 → 6)-Gal				
hydrochloride (dihydrate)		50—60[d]	+112 W	106
N-acetyl-		amorph.	+126 W	180
(dihydrate)		60[d]	+126 W	106
1,2:3,4-di-*O*-isopropylidene-3′,4′,6′-tri-*O*-acetyl-	[c] 77	128—129	+23 C	180
2′-hydroxyimino-analogue	N 67	137—138	+9 C	176
N-(2,4-dinitrophenyl)-		170[d]	+103 M	106
1,2:3,4-di-*O*-isopropylidene-3′,4′,6′-tri-*O*-acetyl-	K 30	80[d] 201—202	−40 C −28 C	106 180
Glc*p*N-β-(1 → 6)-Gal				
hydrochloride		197 d.	+15 W	106
1,2:3,4-di-*O*-isopropylidene-3′,4′,6′-tri-*O*-acetyl-		245 d.	−21 M	43
N-acetyl-		amorph.	+10 W	106,161
		amorph.	+9 W	175
hepta-*O*-acetyl-	K 10	197—198	+6 C	97
β-anomer		196—197	+8 C	175
1,2:3,4-di-*O*-isopropylidene-benzyl β-pyranoside, 2,3,6-tri-*O*-benzyl-	Z 48	198 d.	+85 M	161
		213—215	+23 P	175
3′,4′,6′-tri-*O*-acetyl-	N 13	195—195.5	−28 C	175
	K 12			175
N-phenylmethanesulphonyl-1,2:3,4-di-*O*-isopropylidene-	K 50	91—100	−80 C	43
N-(2,4-dinitrophenyl)-		215—216	+33 C	106
1,2:3,4-di-*O*-isopropylidene-	K 29	198—199	−82 C	106
Glc*p*N-β-(1 → 6)-Man				
N-acetyl-		128—130 d.	−9 W	152
hepta-*O*-acetyl-, β-anomer	Z 26	187—190	−26 C	152
Glc*p*N-α-(1 → 3)-GlcN				
N-acetyl-4,6-*O*-benzylidene, benzyl α-pyranoside				
N′-dibenzylphosphoryl-		214—217	+75 P	115,117
N′-diphenylphosphoryl-3′,4′,6′-tri-*O*-acetyl-	K 5	147—149	+81 C	115,117

Table 2 continued...

1	2	3	4	5
Glc*p*N-β-(1 → 3)-GlcN				
di-*N*-acetyl-		198—199	+14 → +6 W	115,117
		180 p.	+40 → +4 W	165,166
		194—195 d.		165,166
benzyl β-pyranoside				
3′,4′,6′-tri-*O*-acetyl-		219—220	−8 AcOH	165,166
4,6-*O*-benzylidene	Z 81	297—298	−43 P	165,166
N-acetyl-		208—209 d.	+65 W	117
4,6-*O*-benzylidene		268—269 d.	+76 P	117
N′-dibenzylphosphoryl-		191—192	+72 M	117
4,6-*O*-benzylidene-		179—180	+38 C	117
N′-diphenylphosphoryl-3′,4′,6′-tri-*O*-acetyl-4,6-*O*-benzylidene-	K 26	102.5—103.5	+66 C	115,117
Glc*p*N-α-(1 → 4)-GlcN				
di-*N*-acetyl-[R]		150 d.	+96 M	115,116
5,6-*O*-isopropylidene-, diethyl acetal		syrup		116
di-*N*-acetyl-		177—179	+106 W	116
tetra-*O*-acetyl-		syrup	+62 C	116
2-*N*, 3-*O*-carbonate		100—102	+27 M	116
N′-dibenzylphosphoryl-		112—115	+18 C	115,116
N′-diphenylphosphoryl-3′,4′,6′-tri-*O*-acetyl	K 35	116—118	+30 C	115,116
Glc*p*N-β-(1 → 4)-GlcN				
di-*N*-acetyl-, *p*-nitrophenyl β-pyranoside				
5,6-*O*-isopropylidene-2-*N*,3-*O*-carbonate, diethyl acetal	E 62	253—256		187
N′-dibenzylphosphoryl-		syrup	−49 M	116
N′-diphenylphosphoryl-3′,4′,6′-tri-*O*-acetyl		173—176	−40 C	116
	K 10	93—95	−23 C	115,116
Glc*p*N-α-(1 → 6)-GlcN				
di-*N*-acetyl-	[f] 8	215	+140→+125 W	227
Glc*p*N-β-(1 → 6)-GlcN				
di-*N*-acetyl-	[f] 3,2	200 d.	+12→+6 W	227
		amorph.	+4 W	99
		199—201	+10 W	104
		200	+8 W	163
(monohydrate)		190—192	+22→−55 W	16
hexa-*O*-acetyl-, α-anomer	K 5,3	236—238	+12 C	99
p-nitrophenyl β-pyranoside		218—219	−43 W-M	162
(monohydrate)		220—221	−55 W-M	93
penta-*O*-acetyl-	Z 49	258.5—260	−27 C	162
(monohydrate)	K 2,4	257—258	−43 C	93
3,3′,4′,6′-tetra-*O*-acetyl-	Z 46	245—246	−25 M	162
benzyl α-pyranoside (monohydrate)		272—273	+97 M	16
penta-*O*-acetyl-	Z,K 50	254—255	+67 C	16
		242	+65 C	163
N-acetyl-				
N′-diphenylphosphoryl-				
hexa-*O*-acetyl-, β-anomer	K 41	206—207	−5 C	104
benzyl α-pyranoside, penta-*O*-acetyl-				
N′-dibenzylphosphoryl-, benzyl α-pyranoside	K 65	179—181	+68 C	104
		230—231	−15 M	104
N-acetyl-, *p*-nitrophenyl β-pyranoside	E 12			186
Glc*p*N-α-(1 → 6)-3-NH_2-3-deGlc				
dihydrochloride		amorph.	+76 W	107
N′-(2,4-dinitrophenyl)-3′,4′,6′-tri-*O*-acetyl-1,2-*O*-isopropylidene-, 3-azido-analogue, α-furanose	K 37	203—205	+58 C—M	107
Glc*p*N-β-(1 → 6)-3-NH_2-3-deGlc				
dihydrochloride		amorph.	+15 W	107
1,2-*O*-isopropylidene-, 3-azido-analogue, α-furanose				
N′-trifluoroacetyl-		amorph.	−16 M	107
3′,4′,6′-tri-*O*-acetyl-	K 65	syrup	−18 M	107
N′-(2,4-dinitrophenyl)-3′,4′,6′-tri-*O*-acetyl-	K 12	90—95	+15 M	107
Glc*p*N-β-(1 → 4)-MurNAc				
methyl ester				
N-acetyltetra-*O*-acetyl-, α-anomer		237—238	+38 C	113
N-diphenylphosphoryl-1,6-anhydro-3′,4′,6′-tri-*O*-acetyl	K 15	203—204	−29 C	113
Glc*p*N-β-(1 → 6)-MurNAc				
N-acetal-(monohydrate)		amorph.	+16→+14 W	228
benzyl α-pyranoside		227—228	+87 M	100
tetra-*O*-acetyl-, methyl ester	K 3,5	252—253 and 260	+58 C	100
methyl α-pyranoside, tetra-*O*-acetyl-, methyl ester	K 12	288—289	+54 C	12
phenyl β-pyranoside		235—237	−32 W	102
3′,4′,6′-tri-*O*-acetyl-, ester	K 1,3	261—262 d.	−7 C	102
penta-*O*-acetyl-, methyl ester	K 6	240—241	+40 C	101
Galp*N*-α-(1 → 3)-Glc				
N-acetyl-		212—215	+177 → +187 W	180
1,2:5,6-di-*O*-isopropylidene, α-furanose	[c] 35	223—224	+95 D	180
3′,4′,6′-tri-*O*-acetyl-, 2′-hydroxyimino-analogue	N 53	149—150	+62 C	176
Galp*N*-β-(1 → 3)-Glc				
N-acetyl-		208—210	+78 → +50 W	151
1,2:5,6-di-*O*-isopropylidene-3′,4′,6′-tri-*O*-acetyl-, α-furanose	Z 52	amorph.	−23 C	151,157

Table 2 continued...

1	2	3	4	5
Gal*p*N-β-(1 → 6)-Glc				
N-acetyl-		186—187 p.	+36 → +18 W	151
hepta-*O*-acetyl-, β-anomer	Z 74	193—194	—12 C	151, 157
Gal*p*N-β-(1 → 3)-Gal				
N-acetyl-		163—165	+56 W	118
hepta-*O*-acetyl-, α-anomer		96—97	+59 C	118
1,6-anhydropenta-*O*-acetyl-		208	—66 C	118
N-dichloroacetyl-1,6-anhydro-2-*O*-acetyl-3′,4′,6′-tri-*O*-benzoyl-	K 15	139—140	+5 C	118
Gal*p*N-β-(1 → 4)-Gal				
N-acetyl-		148—150	+56 W	118
hepta-*O*-acetyl, α-anomer		104—106	+43 C	118
1,6-anhydropenta-*O*-acetyl-		122—123	—27 C	118
N-dichloroacetyl-1,6-anhydro-2-*O*-acetyl-3′,4′,6′-tri-*O*-benzoyl-	K 30	194—195	—2 C	118
Gal*p*N-α-(1 → 6)-Gal				
N-acetyl-			+137 W	180
1,2 : 3,4-di-*O*-isopropylidene-	[c] 29	151—153	+69 D	180
3′,4′,6′-tri-*O*-acetyl-, 2′-hydroxyimino-analogue	N 80	171—172	+14 C	180
Gal*p*N-β-(1 → 6)-Gal				
N-acetyl-		204—205	+38 W	52
		182—184	+38 W	153
		204—206	+44 W	151
3′,4′,6′-tri-*O*-acetyl-				
1,2,3-tri-*O*-benzoyl-, α-anomer	Z 44	209—211	+114 C	153
1,2 : 3,4-di-*O*-isopropylidene-		142—144	—62 C	52
	Z 81	141—142	—63 C	151, 157
2′-hydroxyimino-analogue	N 9	90—92	—94 C	176
N-dichloroacetyl-				
1,2 : 3,4-di-*O*-isopropylidene-				
3′,4′,6′-tri-*O*-benzoyl-	K 90	125	—4 C	52
1,2,3,4-tetra-*O*-acetyl-3′,4′,6′-tri-*O*-benzoyl-	K 76	156—157	+4 C	52
Gal*p*N-β-(1 → 6)-GlcN				
di-*N*-acetyl-, *p*-nitrophenyl β-pyranoside		208—210	—41 P	151
penta-*O*-acetyl-	Z 71	226—227	—28 M	151, 157
Man*p*N-α-(1 → 6)-Glc				
N-acetyl-(dihydrate)	Z 55 [g]	amorph.	+36 W	161
Tal*p*N-α-(1 → 3)-Glc				
N-acetyl-		190—195	+82 → +70 W	180
1,2 : 5,6-di-*O*-isopropylidene-, α-furanose	[c] 47	163—165	+27 D	180
Tal*p*N-α-(1 → 6)-Gal				
N-acetyl-			+65 W	180
1,2 : 3,4-di-*O*-isopropylidene-	[c] 59	119—121	—10 D	180
Glc*p*N-α-(1 → 1)-α-Glc*p*	K 18 [g]	197 d.	+146 W	108
octa-acetyl-		99	+152 C	108
Glc*p*N-β-(1 → 1)-β-Glc*p*N				
octa-acetyl-	K 2,3	324—326 d.	+2 C	33
Glc*p*N-α-(1 → 1)-α-Man*f*				
2,3 : 5,6-di-*O*-isopropylidene-				
3′,4′6-tri-*O*-acetyl-, 2′-hydroxyimino-analogue	N 41	86—87	+88 C	176
Glc*p*N-β-(1 → 1)-1-*S*-β-Glc*p*N				
di-*N*-acetyl-		219—220	—37 W	61
hexa-*O*-acetyl-	K 50	314—316 d.	—146 C	61
Glc*p*N-β-(1 → 3)-Gal*p*-β-(1 → 4)-Glc				
N-acetyl-		205—209	+40 W	119
N-dichloroacetyl-, benzyl β-pyranoside		194—195	—23 M	119
2,3,6,2′, 6′-penta-*O*-acetyl-3″,4″,6″-tri-*O*-benzoyl-	K 19	125—127	—50 C	119
Glc*p*NAc-β-(1 → 4)-Glc*p*NAc-β-(1 → 6)-Glc	Z 29 [g]	amorph.	+1 W	162
Glc*p*NAc-β-(1 → 3)-Glc*p*NAc-β-(1 → 6)-GlcNAc				
p-nitrophenyl β-pyranoside		209—210	+8 W—M	166
hepta-*O*-acetyl-	Z 78	280—281	+75 C—M	166
Glc*p*NAc-β-(1 → 4)-Glc*p*NAc-β-(1 → 6)-GlcNAc				
p-nitrophenyl β-pyranoside (dihydrate)		239—241 d.	—48 W	162
hepta-*O*-acetyl-	Z 30	289—290 d.	—31 M—N	162
Glc*p*NAc-β-(1 → 6)-Glc*p*NAc-β-(1 → 4)-GlcNAc				
p-nitrophenyl β-pyranoside		257,5—259	—2 W	164
2,6,3′,3″,4″,6″-hexa-*O*-acetyl-	Z 14	273,5—275	—44 N	164
Glc*p*NAc-β-(1 → 4)-MurNAc-β-(1 → 4)-GlcNAc	E 15		—20 W	191
Glc*p*NAc-β-(1 → 4)-MurNac-β-(1 → 4) Xyl	E 9		—38 W	191
Glc*p*NAc-β-(1 → 4)-MurNAc-β-(1 → 2)-Gal	E 13		—14 W	191
Glc*p*NAc-β-(1 → 4)-Glc*p*NAc-β-(1 → 6)-Glc*p*NAc-β-(1 → 4)-GlcNAc				
p-nitrophenyl β-pyranoside	Z 13 [g]	248—249	—28 W	164

Table 2 continued...

[a] The following abbreviations not indicated in Ref. 225 were used: Xyl = D-xylose, GlcN = D-glucosamine, GlcNAc = *N*-acetyl-D-glucosamine, GalNAc = *N*-acetyl-D-galactosamine, ManN = D-mannosamine, MurNAc = *N*-acetylmuramic acid, TalN = D-talosamine, and 3-NH_2-3-deGlc = 3-amino-3-deoxy-D-glucose.

[b] E = enzymatic synthesis, K = Koenigs–Knorr reaction and its modifications, N = nitrosochloride method[174,176], and Z = oxazoline method. The yields are quoted only for the glycosylation stages.

[c] In the reduction stage of the corresponding hydroxyimino-derivative.

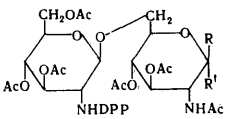
[d] Softening temperature.

[e] Solvated by ethanol.

[f] Obtained by the acid reversion of *N*-acetyl-D-glucosamine.

[g] Including the stage involving the removal of protecting groups.

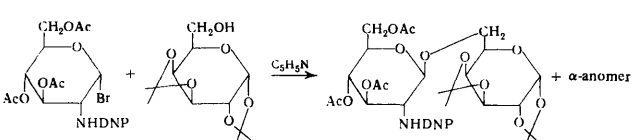
Satisfactory results in the glycosylation stage were achieved[104] when the bromide (XXXII) was allowed to react with the partly protected *N*-acetyl-D-glucosamine derivatives with a free hydroxy-group at 6-C. The yield of the glycosylation products (XXXVI) and (XXXVII) was 41–65%:



(XXXVI, R = OAc, R′ = H)
(XXXVII, R = H, R′ = OCH_2Ph)

The diphenylphosphoryl group is removed either by catalytic hydrogenation in the presence of platinum[47] or (less effectively) by alkaline hydrolysis[103].

When the bromide (XXXVIII) reacts with 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose (XXXIX), the glycosylation is non-stereospecific and depends on the nature of the solvent and the hydrogen bromide acceptor[105,106]. As in the synthesis of alkyl aminoglycosides from the bromide (XXXVIII)[89], in the presence of pyridine the α-anomer is formed preferentially (30%) and only 15% of the β-linked disaccharide (XL) is produced. When the reaction was carried out in the presence of silver carbonate, only the β-anomer (XL) was isolated in 29% yield. The dinitrophenyl group was removed by treatment with anion-exchange resins in the basic form[46]:

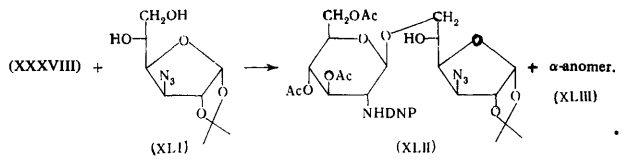


(XXXVIII) (XXXIX) (XL)

DNP = 2,4-dinitrophenyl

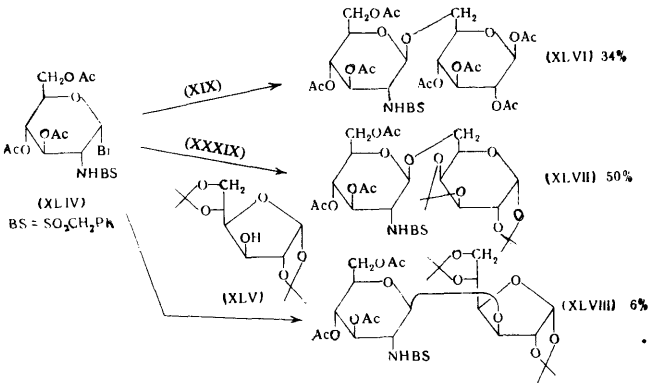
The glycosylation of compound (XLI) with the bromide (XXXVIII) in the presence of mercury salts also led[107] to a mixture of anomeric disaccharide derivatives (XLII) and (XLIII) with an overall yield of 50%, the anomers being formed in proportions of 1 : 3. On the other hand, when

compound (XLI) was glycosylated with 3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl bromide in the presence of mercury cyanide, only one disaccharide, analogous to (XLII), was isolated:



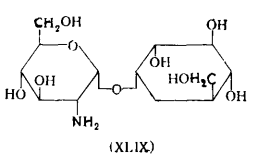
The use of the bromide (XLIV) as the glycosylating agent in the Koenigs–Knorr reaction has been described[43]. The disaccharide derivatives (XLVI)–(XLVIII), in which the phenylmethanesulphonyl group was removed by catalytic hydrogenation in the presence of Raney nickel, were obtained (Scheme 3).

Scheme 3



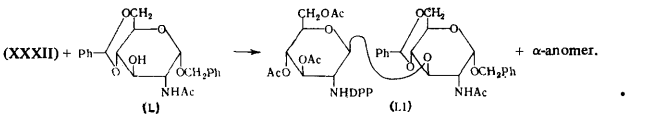
Thus the examples of the synthesis of disaccharides with the (1→6)-linkage already demonstrated the advantage of stable glycosyl bromides with electronegative and other substituents in the amino-group, which consists of a significant increase of the yield of the glycosylation products. However, the preparative value of this procedure was at the same time reduced by the large number of stages involved, particularly in the synthesis of *N*-acetylated disaccharide analogues and in many cases by the loss of stereospecificity in the glycosylation reaction.

Among the few synthetic non-reducing disaccharides containing 2-amino-2-deoxysugar moieties, mention should be made of trehalosamine (XLIX) obtained[108] by the reaction of 3,4,6-tri-*O*-acetyl-2-deoxy-2-(*p*-methoxybenzylideneamino)-α-D-glucopyranosyl bromide with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose in 18% yield after the removal of protecting groups.

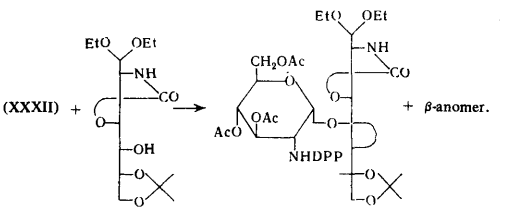


In the glycosylation of secondary hydroxy-groups of sugars difficulties arose for a long time not only because of the lack of effective glycosylating agents in the amino-sugar series but also owing to the limited choice of "aglycone" components with sufficiently reactive functionable groups capable of being glycosylated. This problem was solved, on the one hand, by employing stable bromides as the glycosylating agents. On the other hand, "aglycone" components derived from pyranose[51,109–113] and acyclic[114–116] forms of monosaccharides, in which the hydroxy-groups, particularly at 4-C, are more reactive than in the pyranose form in the 1-C conformation, were proposed recently in a number of studies.

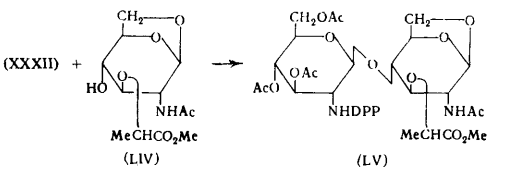
A mixture of protected disaccharides with β-(1→3)-[compound (LI)] and α-(1→3)-aminoglucosidic linkages and containing about 85% of (LI) was obtained in 31% yield by the condensation of the bromide (XXXII) with the benzylidene derivative (L)[115,117]:



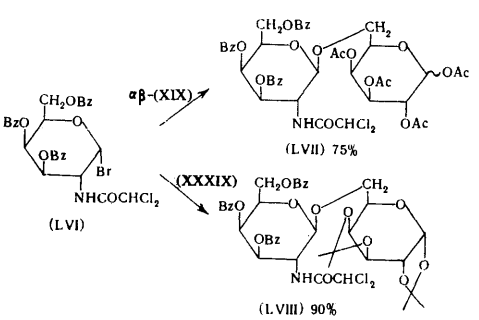
A mixture of anomers derived from disaccharides with α-(1→4)-[compound (LIII)] and β-(1→4)-glycosidic linkages was obtained similarly, in yields of 35 and 10% respectively, from the bromide (XXXII) and the acetal (LII)[115,116]:



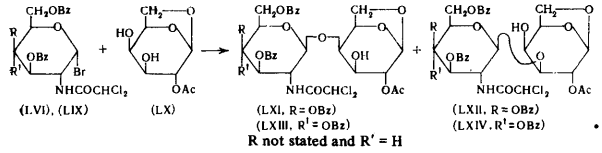
However, Merser and Sinaÿ[113] (cf. Iwamoto and Ymanaga[103] and Bundle and Shaw[104]) failed to observe the formation of a disaccharide with an α-linkage in the glycosylation of the anhydro-derivative (LIV) by the bromide (XXXII) and isolated in 15% yield the protected disaccharide (LV):



The synthesis of di- and oligo-saccharides, which form part of the carbohydrate determinants of glycoproteins and gangliosides and which contain 2-acetamido-2-deoxy-β-D-galactopyranosyl residues, was achieved recently using the reactive and relatively stable bromide (LVI)[50,52]. This version of the Koenigs–Knorr reaction leads to derivatives (LVII) and (LVIII) with a β-glycosidic linkage and with only traces of α-anomers according to infrared spectroscopic data[52]:



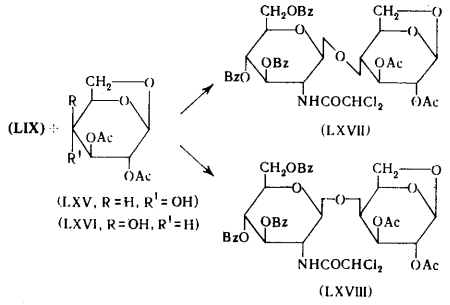
The bromide (LVI) and its D-gluco-analogue (LIX) react with the 1,6-anhydrosugar (LX) to form mixtures of isomeric disaccharide derivatives with β-(1→4)-[compounds (LXI) and (LXIII)] and β-(1→3)-glycosidic linkages [compounds (LXII) and (LXIV)] in overall yields of 45 and 47% respectively[51,118]. In both cases the isomer ratios (LXI) : (LXII) and (LXIII) : (LXIV) were close to 3 : 2. The glycosylation products (LXI) and (LXII) were separated chromatographically. In another instance the product (LXIII) was isolated from the mixture after the degradation of the (1→3)-isomer under mild alkaline conditions.



(LVI), (LIX) (LX) (LXI, R = OBz) (LXIII, R' = OBz) (LXII, R = OBz) (LXIV, R' = OBz)

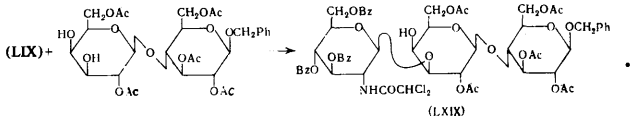
R not stated and R' = H

It is interesting to note that the glycosylation of the 2,3-di-*O*-acetates of the 1,6-anhydrosugars (LXV) and (LXVI) leads under the same conditions[51,110] to the disaccharide derivatives (LXVII) and (LXIII) in yields of only 9–10%. However, the glycosylation of the anhydride (LXV) or its analogue 1,6-anhydro-2-acetamido-3-*O*-acetyl-2-deoxy-β-D-glucopyranose with acylhalogeno-derivatives of neutral sugars is much more effective, leading to derivatives of lactose, *N*-acetyl-lactosamine, and *N*-acetylcellobiosamine in yields of 50–80%.[109,112]



(LIX) + (LXV, R = H, R' = OH) (LXVI, R = OH, R' = H) (LXVII) (LXVIII)

The same group of workers[119] achieved the synthesis of the protected trisaccharide (LXIX) in 19% yield:

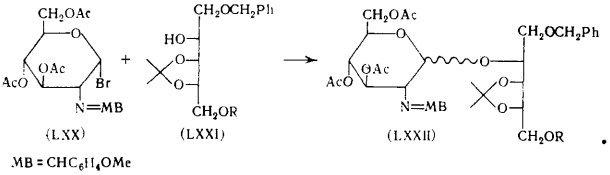


(LIX) + (LXIX)

The most convenient method for the conversion of the *N*-dichloroacetyl group into the *N*-acetyl group proved to be catalytic hydrogenation in the presence of palladium. Another procedure, involving the hydrolysis of the *N*-dichloroacetyl group to the amino-group by barium hydroxide with subsequent *N*-acetylation, is suitable only for derivatives with the β-(1→4)-aminoglycosidic linkage [for example, compounds (LXI) and (LXIII)], since the β-(1→3)-aminoglycosidic linkage in compounds (LXII) and (LXIV) is cleaved even by the action of sodium methoxide in methanol. This finding can be explained by the high electronegativity of the dichloroacetyl group, which withdraws electrons from the glycosidic centre, and this in turn facilitates the degradation of the β-(1→3)-isomer via the β-elimination mechanism.

3. Glycosylation of Polyols and Hydroxyaminoacids

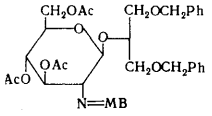
The products of the glycosylation of polyols and hydroxyaminoacids are interesting as model compounds for the investigation of the properties of glycolipids and glycoproteins. Derivatives of 2-amino-2-deoxy-D-glucopyranosyl-D-ribitol and the corresponding glycerol derivative were obtained by the Koenigs–Knorr reaction from glycosyl bromides and partly protected polyols. The glycosylation of D-ribitol derivatives (LXXI, R = CPh_3 or COPh) by the bromide (LXX) in the presence of silver carbonate led to a 15% yield of a mixture of the anomeric aminoglycosides (LXXII, R = CPh_3 or COPh), in which the α-anomers predominated[90]:



(LXX) (LXXI) (LXXII)

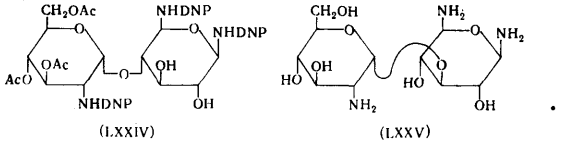
MB = CHC_6H_4OMe

The reaction of the bromide (LXX) with 1,3-di-*O*-benzylglycerol led to the formation under the same conditions[120] of the aminoglucoside (LXXIII) and its α-anomer in proportions of 1 : 0.39 and in an overall yield of 25%. In the glycosylation of 1,3-di-*O*-benzylglycerol with the bromide (XXXII) in the presence of mercury cyanide only the β-anomer, analogous to (LXXIII), was isolated in 55% yield[120].



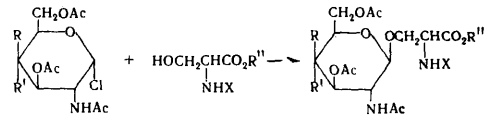
(LXXIII)

The employment of the bromide (XXXVIII) in the glycosylation of di-*N*-protected 2-deoxystreptamine resulted in the formation of a mixture of glycosides from which the isomer (LXXIV) was isolated in a low yield[121–123]. The related compound (LXXV) was also synthesised[124].



(LXXIV) (LXXV)

The Koenigs–Knorr reaction served for a long time as the main method for the synthesis of 2-acetamido-2-deoxyglycosides derived from hydroxyaminoacids. The condensation of the chloride (XIII) or its D-galacto-analogue (LXXVI) with esters of *N*-benzyloxycarbonyl- or *N*-(2,4-dinitrophenyl)-L-serine in the presence of silver carbonate or mercury cyanide led to the formation of the corresponding β-aminoglycosides [LXXVII, R and R' = H or OCOMe, R'' = Me or CH_2Ph, X = $COOCH_2Ph$ or 2,4-$(NO_2)_2.C_6H_3$] in yields up to 49%.[125–128] The glycosylation of the amide of *N*-benzyloxycarbonyl-DL-threonine with the chloride (XIII) was achieved under the same conditions[129]. It is noteworthy that the isolation of the glycosylation products is fairly laborious in many cases.

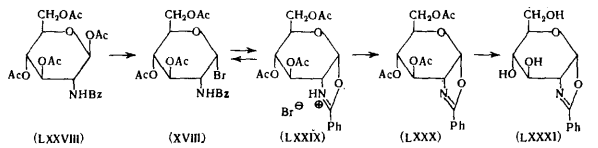


(XIII) or (LXXVI) (LXXVII)

Thus, despite the large number of studies enumerated above in which the classical version of the Koenigs–Knorr reaction or its modifications were employed, there have been virtually no systematic studies on the glycosylation by this method of partly protected saccharides and other "aglycone" components with a complex structure. Therefore, although the method can be regarded as fairly thoroughly developed, it is necessary to find special reaction conditions in each specific instance.

IV. 2-SUBSTITUTED GLYCO[2′,1′:4,5]-2-OXAZOLINES

The oxazoline derivatives of hexopyranoses, which are aza-analogues of sugar orthoesters, have been known for a long time as compounds obtained as side products when hydrogen bromide is allowed to react with acylated 2-amino-2-deoxysugars. The "oxazoline" derivative described by White[130] (cf. Micheel et al.[35]) was shown subsequently[34,131,132] to be 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-D-glucopyranose. Micheel and coworkers[63,133] succeeded for the first time in isolating the hydrobromide of 2-phenyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2′,1′:4,5]-2-oxazoline (LXXIX), formed when the *N*-benzoate (LXXVIII) is treated with hydrogen bromide in acetic acid. The bromide (XVIII) formed initially is rapidly converted into the oxazoline derivative (LXXIX):

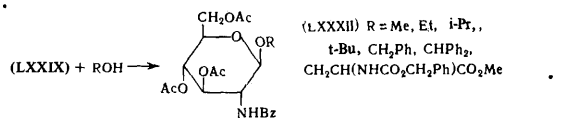


(LXXVIII) (XVIII) (LXXIX) (LXXX) (LXXXI)

Later it was established[134] that this process is reversible and that the equilibrium depends to a large extent on the solvent [as for the *O*-benzoylated analogue of the bromide (XVIII)]. In the instances described the α-chloride does not give rise to the oxazoline derivative[135]. It follows from Osawa's data[38] (see Scheme 1) that oxazoline derivatives are intermediates in the synthesis of *O*-acetylated 2-aroylamino-2-deoxy-α-D-glucopyranosyl chlorides from the corresponding β-acetates. After the acetates have been treated briefly with aluminium chloride or titanium tetrachloride in chloroform and also with hydrogen chloride in acetic anhydride, 2-arylgluco[2′,1′:4,5]-2-oxazolines were obtained in yields up to 75%; with increase of reaction time, the yield of the oxazoline derivatives fell and that of the α-chlorides increased.

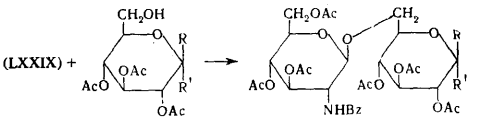
On treatment with pyridine, the hydrobromide (LXXIX) is converted into the free base (LXXX), which can be deacetylated to the oxazoline (LXXXI) without the rupture of the heterocyclic ring[135].

The oxazoline derivatives (LXXIX) and (LXXX) proved to be effective glycosylating agents in the synthesis of 1,2-*trans*-2-benzamido-2-deoxy-D-glucopyranosides. The reaction of compound (LXXIX) with primary, secondary, and tertiary alcohols and also with the methyl ester of *N*-benzyloxycarbonyl-L(D or DL)-serine in the presence of silver carbonate gave a 37–73% yield of the acetates of 2-benzamido-2-deoxy-β-D-glucopyranosides (LXXXII)[133,135,136]:



(LXXXII) R = Me, Et, i-Pr, t-Bu, CH_2Ph, $CHPh_2$, $CH_2CH(NHCO_2CH_2Ph)CO_2Me$

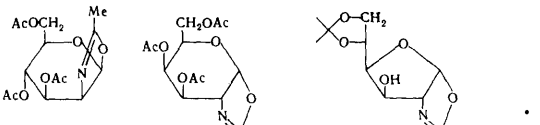
The possibility of using the oxazoline derivatives of sugars in the synthesis of disaccharides with 2-benzamido-2-deoxy-β-D-glucopyranosyl residues, for example (LXXXIV) and (LXXXV), was demonstrated for the first time in the reaction of the oxazoline (LXXIX) with glucose tetra-acetate (XIX) and the glucoside tri-acetate (LXXXIII)[137]:



(XIX, R = OAc) (LXXXIII, R′ = OMe) (LXXXIV, R = OAc), 55% (LXXXV, R′ = OMe), 51% R not specified and R′ = H

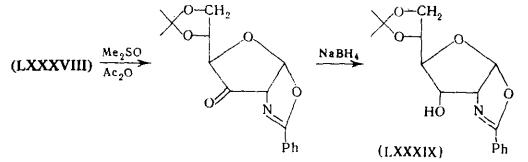
Despite the initial successes in the employment of oxazoline derivatives of sugars in the synthesis of *N*-benzoylaminoglucosides the development of the oxazoline method for the formation of the 1,2-*trans*-aminoglycosidic linkage was held back by the lack of reliable and general methods for the synthesis of the glycosylating agents themselves and in the first place of 2-methylglyco[2′,1′:4,5]-2-oxazolines which would open the way to glycosides and oligosaccharides containing 2-acetamido-2-deoxy-β-D-hexopyranosyl residues. The existing methods for the synthesis of oxazoline derivatives of sugars remained non-general for a long time.

A 2-methyl-substituted oxazoline of the D-manno-series (LXXXVI) was obtained by treating acetylated D-mannosamine with hydrogen bromide in acetic acid[133]. Fletcher and coworkers[138] observed the formation of the oxazoline (LXXXVI) and its D-galacto-analogue (LXXXVII), in yields of 11 and 26% respectively, as side products in the acetylation of *N*-acetyl-D-mannosamine and *N*-acetyl-D-galactosamine with acetic anhydride in the presence of a large amount of zinc chloride.



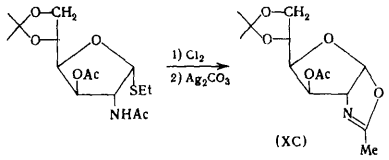
(LXXXVI) (LXXXVII) (LXXXVIII)

The oxazoline derivative of D-glucofuranose (LXXXVIII) was obtained by treating *N*-benzoyl-D-glucosamine with acetone in the presence of hydrogen chloride[139–141]. The oxazoline (LXXXVIII) was converted into the corresponding analogue of the D-allo-series (LXXXIX) by epimerisation at 3-C[142]:



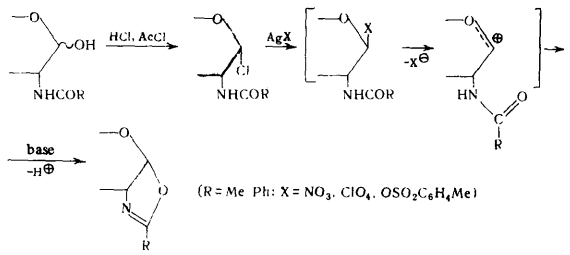
(LXXXIX)

2-Methyl-(3-*O*-acetyl-5,6-*O*-isopropylidene-1,2-dideoxy-α-D-glucofurano)[2′,1′ :4,5]-2-oxazoline (XC), which is the 2-methyl analogue of the oxazoline (LXXXVIII), was obtained for the first time by Wolfrom and Winkley[143] in 56% yield:

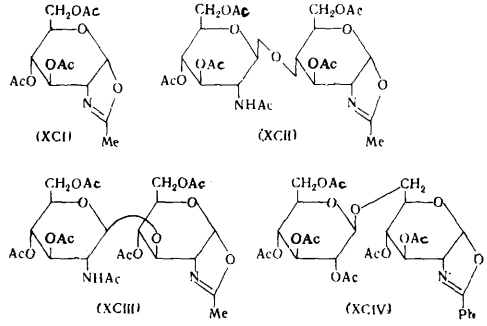


Examples of the employment of oxazoline derivatives of sugar in glycoside synthesis still remained few and were limited to the synthesis of aminoglycosides (including furanosides) derived from lower alcohols and phenol[140,142-145]. The oxazoline group was mainly used to protect the substituents at 1-C and 2-C in the synthesis of muramic acid and its derivatives[141,146-148].

A general method for the preparation of 2-substituted glyco[2′,1′ :4,5]-2-oxazolines was developed in 1968 in the authors' laboratory[149,150]. The starting compounds were *O*-acetylated 2-acylamino-2-deoxyglycosyl chlorides formed in high yields when *N*-acyl derivatives of 2-amino-2-deoxysugars are treated with hydrogen chloride in acetyl chloride[65]. Treatment of the chlorides with silver salts (nitrate, perchlorate, toluene-*p*-sulphonate) in anhydrous acetone or acetonitrile[151] in the presence of organic bases (pyridine, collidine) leads to the corresponding oxazoline derivatives. The reaction probably proceeds via the intermediate formation of a carbonium ion, which is then stabilised by conversion into an oxazoline. Best results were achieved when silver nitrate and collidine were used.



Oxazoline derivatives of mono- and di-saccharides [(LXXX), (LXXXVI), (LXXXVII), and the previously unknown compounds (XCI)–(XCIV)] were obtained by this method in 50–80% yields relative to the free *N*-acylamino-sugar.



It must be emphasised that this method of synthesis rules out the isolation of the intermediate aminoglycosyl chlorides. Some of the oxazoline derivatives obtained [(LXXX), (LXXXVI) and (XCI)] were deacetylated in methanol in the presence of triethylamine[150].

Table 3. Glyco[2′,1′ :4,5]-2-oxazolines.

Structure	Yield[a], %	M.p., °C	$[\alpha]_D^0$ and solvent	References
1	2	3	4	5
(1,2-Dideoxy-α-D-glucofurano)-2-oxazoline				
2-methyl-(3-*O*-acetyl-5,6-*O*-isopropylidene)-	56	96—97	+25 C	143
2-phenyl-(5,6-*O*-isopropylidene)-	61	159—160	+4 C	139
	~100	160—161,5		141
hydrochloride		125—128 d.		139
(3-*O*-acetyl)-		135—136	−16 C	139
(3-*O*-carbamoylmethyl)-		97—98,5	+0,2 C	141
(3-*O*-D-1-carbomoylethyl)-		192—193	+73 C	141
(3-*O*-L-1-carbomoylethyl)-		164.5—166	+6 C	141
(3-*O*-L-1-methoxycarbonylethyl)-		88—90	−31 C	147
(3-*O*-carboxymethyl)-		185—186	−22 C	146
		182—184	−23 C	141
(3-*O*-D-1-carboxyethyl)		163—164	+63 C	141
		163—164	+65 C	146,147
(3-*O*-L-1-carboxyethyl)		208—210	−34 C	146,147
		207—208	−38 C	141
(3-*O*-D-1-carboxypropyl)-		217—217,5	−34 C	141
(3-*O*-methyl)-		117—119	−15 C	146
(3-*O*-methanesulphonyl)-		141—142	+8 C	140
2-phenyl-(5,6-*O*-benzylidene)-		201—202	+64 C	229
(3-*O*-acetyl)-		88—89	+34 C	229
(1,2-Dideoxy-α-D-glucopyrano)-2-oxazoline				
2-methyl-		syrup	+13 C	150
(3,4,6-tri-*O*-acetyl)-	51	syrup	+10 C	149,150
	65	syrup	+7 C	154
(4,6-*O*-benzylidene)-		syrup	+3 C	229
2-*p*-methoxyphenyl-(3,4,6-tri-*O*-acetyl)-	74	106—108	+67 C	38
2-*p*-nitrophenyl-(3,4,6-tri-*O*-acetyl	76	142—143	+72 C	38
2-trifluoromethyl-(3,4,6-tri-*O*-acetyl)-	—	syrup	+5 C	107
2-phenyl		142	+48 C	135
		140—141	+48 C	150
(3,4,6-tri-*O*-acetyl)-	85	57	+45 P—W	133,135
	69	56	+52 C	38
	82	syrup		138
	98	syrup	+44 C	149,150
hydrochloride		135 d.	+39 P—W	38
hydrobromide	85	110 d.	+37 P—W	63,135
2-Methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-galactopyrano)-2-oxazoline	26	syrup	+26 C	138
	66	syrup	+26 C	153
	59	syrup	+82 C	151,157
2-Methyl-(1,2-dideoxy-β-D-mannopyrano)-2-oxazoline		166.5—167,5	+9 C	150
3,4,6-tri-*O*-acetyl)	11	133—134	−31 C	138
	82	132—133	−31 C	149,150
(4,6-*O*-benzylidene)-		172,5—174.5	−25 C	229
2-Phenyl-(1,2-dideoxy-α-D-allofurano)-2-oxazoline				
(5,6-*O*-isopropylidene)-		129—130	+76 C	142
3-keto-analogue		99—101	+380 C	142
2-Methyl-[4-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-3,6-di-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano]-2-oxazoline	59	189—190	−8 C	150
2-Methyl-[3-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-4,6-di-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano]-2-oxazoline	53	181—182	+8 C	166
2-Phenyl-[6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3,4-di-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano]-2-oxazoline	60		+60 C	149

[a] The yields are quoted only for those derivatives in which the oxazoline ring is formed.

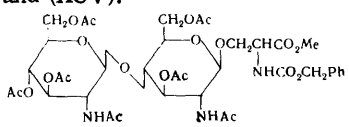
A modification of the method of Fletcher and co-workers[138], consisting of the treatment of the peracetates of 2-amino-2-deoxy-β-D-glucose and 2-amino-2-deoxy-β-D-galactose with anhydrous iron(III) chloride in methylene chloride, was proposed recently[152,153] (cf. Salo and Fletcher[154]). The high yields of the products—the oxazolines (LXXXVII) and (XCI)—and the simplicity of the process evidently make this method extremely promising.

Data for the oxazoline derivatives of sugars synthesised hitherto are summarised in Table 3.

V. OXAZOLINE SYNTHESIS OF 1,2-*trans*-2-ACETAMIDO-2-DEOXYGLYCOSIDES

2-Methylglyco[2′,1′:4,5]-2-oxazolines, which have become available recently, were investigated as glycosylating agents mainly in the glycosylation of "aglycone" components with complex structures. A detailed study was made of the employment of oxazoline derivatives of sugars in the synthesis of acetamidoglycosides, including aminosugar oligosaccharides, in the presence of acid catalysts—mainly toluene-*p*-sulphonic acid as well as other acids[155,156]. Alkyl[135,151,153,155-157] and aryl 2-acetamido-2-deoxy-β-D-hexopyranosides[158,159] are formed in high yields when alcohols and phenols are treated with the oxazolines (LXXXVII) and (XCI) in the presence of the above catalysts. Similarly the glycosylation of monoterpene alcohols with the oxazoline (XCI) led to the formation of (-)-bornyl and (-)-menthyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosides in yields of 40–43%.[159]

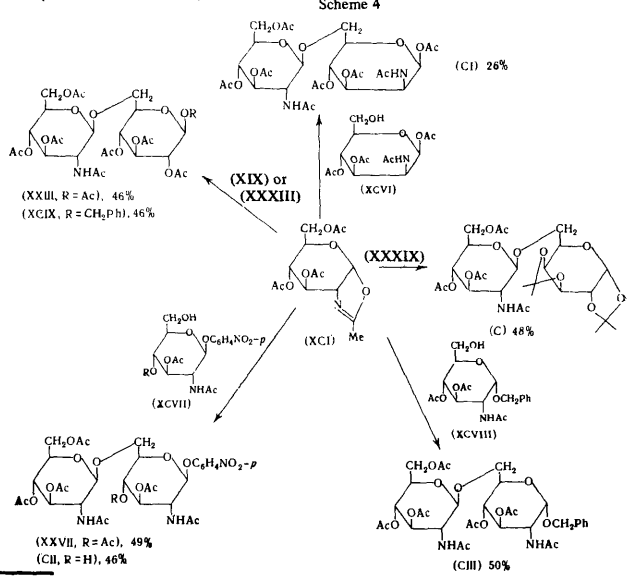
The effectiveness of the oxazoline method in the synthesis of compounds simulating the glycopeptide fragments of biopolymers was demonstrated in the glycosylation of *N*-benzyloxycarbonyl-L-serine esters by mono-[151,155] and disaccharide derivatives[160]. This led to the formation of high yields (55–75% for the monosaccharide and 40% for the disaccharide) of protected L-serine *O*-glycosides (LXXVII, R and R′ = H or OCOMe, R″ = Me or CH_2Ph, X = CO_2CH_2Ph) and (XCV).



(XCV)

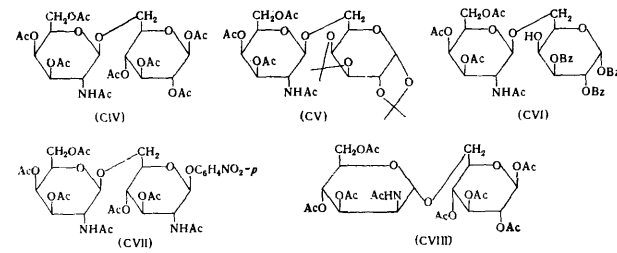
The results obtained using the oxazoline method in the synthesis of oligosaccharides ‡ are of greatest interest and value. Glycosylation of the primary hydroxy-group of derivatives of D-glucose [(XIX) and (XXXIII)][103,161], D-galactose (XXXIX)[161], D-mannose (XCVI)[152], and acetamido-D-glucose [(XCVII, R = H or COMe) and (XCVIII)][16,149,162] with the aid of the oxazoline (XCI) led to the formation of the corresponding disaccharide derivatives (XXIII), (XXVII) and (XCIX)–(CIII) in high yields—mainly about 50% (see Scheme 4).

Scheme 4



‡ See Table 2.

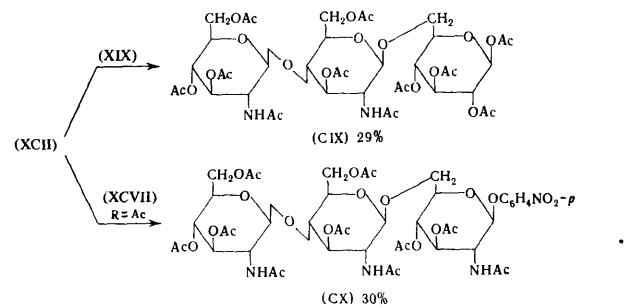
The oxazoline derivatives of the D-galacto-[151,153,157] and D-manno-series[161] proved just as effective in the synthesis of (1→6)-linked disaccharides. The protected disaccharides (CIV)–(CVIII) were obtained from them in 44–81% yield.



(CIV) (CV) (CVI)

(CVII) (CVIII)

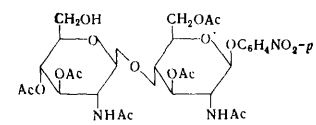
Glycosylation of the disaccharide (XCII) by oxazoline derivatives made it possible to increase the length of the oligosaccharide chain by two aminosugar residues in a single stage, as shown in the synthesis of the trisaccharide derivatives (CIX)[161] and (CX)[162]. This had not been achieved before by other glycosylation procedures.



(CIX) 29%

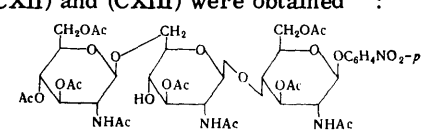
(CX) 30%

Like other glycosylating agents, oxazoline derivatives exhibit a higher reactivity in reactions with the primary hydroxy-groups of sugars than with the secondary groups, so that branched oligosaccharides, when the possibility of their formation was not ruled out altogether, were detected only in trace amounts[162,163]. This factor made it possible to employ as the glycosylated components derivatives of oligosaccharides with unprotected hydroxy-groups at 4-C and 6-C in the terminal monosaccharide residue [for example in compound (CXI)], which are readily obtained from the corresponding 4,6-*O*-benzylidene derivatives.

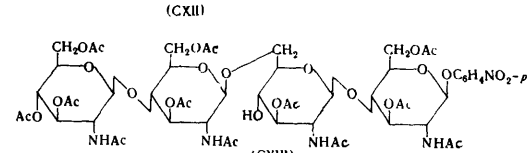


(CXI)

When oxazoline derivatives of the monosaccharide (XCI) and the disaccharide (XCII) were allowed to react with compound (CXI), the tri- and tetra-saccharide glycosides (CXII) and (CXIII) were obtained[164]:



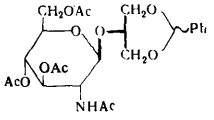
(CXII)

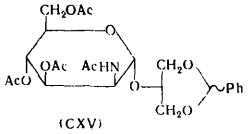


(CXIII)

The low yields of these products (not exceeding 15%) can be explained by the extremely low solubility of the glycosylated component (CXI) even in a polar solvent such as nitromethane. On the other hand, in highly polar solvents toluene-*p*-sulphonic acid catalyses the isomerisation of 2-methylglyco[2′,1′:4,5]-2-oxazolines to 2-acetamido-glycals[154], which apparently constitutes a competing process in the cases under consideration.

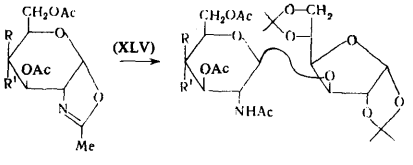
The effectiveness of the oxazoline method has been clearly demonstrated in the glycosylation of the secondary hydroxy-groups of polyols and monosaccharides. When the oxazolines (LXXXVI) and (XCI) were condensed with 1,3-*O*-benzylideneglycerol, protected 1,2-*trans*-aminoglycosides derived from benzylideneglycerol, (CXIV) and (CXV), were obtained[165,166] in yields which amounted to 34 and 31% respectively after the removal of the *O*-acetyl and benzylidene groups:


(CXIV)

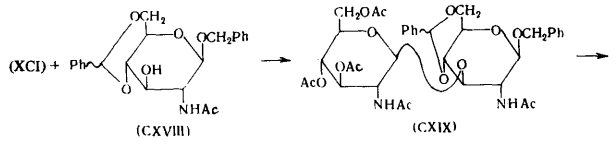

(CXV)

Derivatives of β-(1→3)-linked disaccharides (CXVI) and (CXVII) were obtained in yields of about 50% but the reaction of the oxazoline derivatives (LXXXVII) and (XCI) with diacetoneglucose (XLV)[151,157,166].

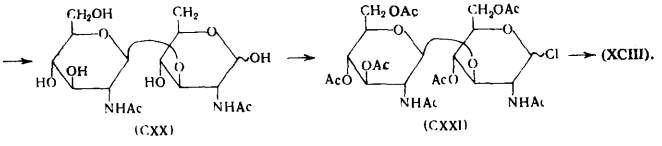
The glycosylation of the sterically hindered hydroxy-group at 3-C in the derivative (CXVIII) by the oxazoline (XCI) led to the protected disaccharide (CXIX) in 81% yield. The latter served as the starting compound in the synthesis of the oxazoline derivative of the β-(1→3)-linked disaccharide (XCIII).


(LXXXVII) or (XCI)

(CXVI, R = OAc, R′ = H)
(CXVII, R = H, R′ = OAc)


(CXVIII)

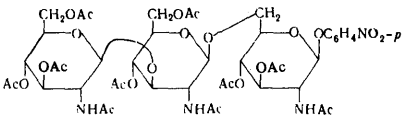
(CXIX)


(CXX)

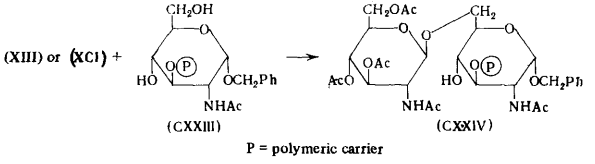
(CXXI)

(XCIII).

The disaccharide (CXX) was obtained by standard methods from (CXIX) and was then converted into the chloride (CXXI) and further into the oxazoline (XCIII) in an overall yield of 53% relative to (CXX).[166] The trisaccharide derivative (CXXII) was obtained in 78% yield by the glycosylation of *p*-nitrophenyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-β-D-glucopyranoside by the oxazoline (XCIII).[166] The above sequence of transformations demonstrates the possibility of synthesising oligosaccharides with different combinations of 1,2-*trans*-glycosidic linkages between aminosugar residues.


(CXXII)

The recently published study of Vignon and coworkers[163], who achieved the synthesis of a disaccharide on a polymeric carrier, made a significant contribution to the development not only of the oxazoline synthesis of aminoglycosides but also to the synthesis of oligosaccharides in general. The glycosylation by the oxazoline (XCI) [or the chloride (XIII) under the conditions of the Koenigs–Knorr reaction] of the acetamido-D-glucose derivative (CXXIII) linked to a polymeric carrier via an ester bond led to a high yield of the disaccharide derivative (CXXIV) on the carrier. After the treatment of the latter with sodium methoxide in methanol, the disaccharide glycoside was liberated.


(CXXIII) (CXXIV)

P = polymeric carrier

Apart from the advantages of solid-phase synthesis, known from the synthesis of peptides, this version of the oxazoline method for the preparation of aminoglycosides will probably make it possible to solve successfully the problem of synthesising higher oligosaccharides, the difficulties of which are associated with the low solubility of the glycosylated components[164].

In summing up the discussion of the oxazoline method for the synthesis of 1,2-*trans*-2-acetamido-2-deoxyglycosides, we may note that oxazoline derivatives of sugars permit the glycosylation of various types of hydroxy-compounds—alcohols, phenols, hydroxyaminoacids, polyols, and partly protected mono- and oligo-saccharides [as well as thiols (see below)]. The general nature of the reactions has been demonstrated for a number of important classes of natural aglycones. The application of glycosylating agents with a wide variety of structures and a series of different alcoholic components makes it possible to infer the stereospecificity of the reaction. On the other hand, one can conclude on the basis of these data that all the protecting groups tested are stable under the conditions of glycosylation with oxazoline derivatives of sugars, namely the acyl, alkylidene, and benzyl glycoside groups as well as the *N*-benzyloxycarbonyl group used in peptide synthesis.

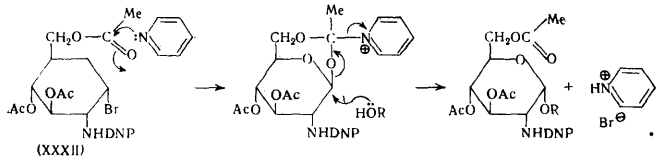
The results taken as a whole show that the oxazoline method is a general procedure for the formation of the 1,2-*trans*-aminoglycosidic linkage.

VI. STEREOSPECIFIC SYNTHESIS OF 1,2-*cis*-2-AMINO-2-DEOXYGLYCOSIDES

As in the series of neutral sugars, methods for the stereospecific synthesis of 1,2-*cis*-aminoglycosides are now in the stage of development only. Above it was stated that the formation of 1,2-*cis*-glycosides from acyl-halogeno-derivatives of sugars is prevented by the involvement of the acetoxy- or acylamino-groups. In those cases where this effect was suppressed by the introduction of "non-participating" substituents into the amino-group of the sugar, the stereospecificity of the glycosylation reaction was lost and the proportions of the anomeric glycosides formed varied within wide limits.

The separation of anomeric alkyl or aryl aminoglycosides presents no difficulties at present and is carried out by chromatographic methods[167-169]. Chromatography is also used to separate anomeric aminoglycosides with aglycones having a complex structure (including disaccharide derivatives), formed in the synthesis by different versions of the Koenigs–Knorr reaction. However, its scope is sharply reduced with increase in the length of the oligosaccharide chain, this effect being already observed for trisaccharide derivatives. For this reason, only stereospecific glycosylation permits the solution of the problem of synthesising higher oligosaccharides having the 1,2-*cis*-aminoglycosidic linkage.

The preferential formation of 1,2-*cis*-aminoglycosides was observed only in a few instances, for example in glycosylation by the bromide (XXXII) in the presence of pyridine[89,92], which the authors explain by the involvement of the acetoxy-group at 6-C:

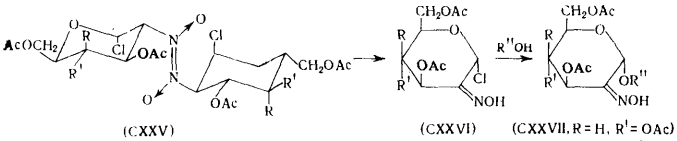


(XXXII)

Indeed, when 3,4-di-*O*-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-6-*O*-methyl-α-D-glucopyranosyl bromide was used as the glycosylating agent, the dominant reaction product was the 1,2-*trans*-glycoside[92] and in addition the reaction was significantly retarded. The replacement of the acetoxy-groups at 3-C or 4-C in the bromide (XXXII) by methyl groups does not alter the stereospecificity and rate of the reaction.

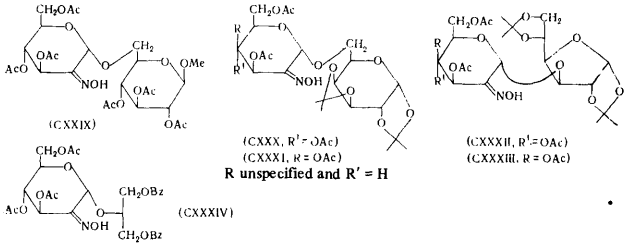
A similar effect of the involvement of the acetoxy-substituent at 4-C was observed recently[170] in a series of neutral sugars. Glycosylation by 2-*O*-benzyl-3,4-di-*O*-(*p*-nitrobenzoyl)-α-L-fucopyranosyl bromide led to α-L-fucosides with a high degree of stereospecificity.

The most promising method for the synthesis of 1,2-*cis*-aminoglycosides was proposed very recently by Lemieux and coworkers. The available[171,172] dimeric D-gluco- and D-galacto-nitrosyl chlorides (CXXV), which dissociate and isomerise in dimethyl formamide (DMF) to the corresponding hydroxyiminochlorides (CXXVI)[173], react with alcohols and phenols in the presence of pyridine to form high yields of 3,4,6-tri-*O*-acetyl-2-hydroxyimino-α-D-arabinohexopyranosides (CXXVII) and the corresponding α-D-lyxohexopyranosides (CXXVIII)[174-176]—the precursors of 2-amino-2-deoxy-α-D-glycosides:



(CXXV) (CXXVI) (CXXVII, R = H, R' = OAc)
(CXXVIII, R = OAc, R' = H)
(R'' = alkyl or aryl)

This method is suitable[174,176,177] also for the synthesis of 2'-hydroxyimino-derivatives of disaccharides [(CXXIX) – (CXXXIV)], which are formed in yields of 50–80%. The β-anomer was isolated in 9% yield only in the synthesis of (CXXXI).



(CXXIX) (CXXX, R' = OAc) (CXXXI, R = OAc) (CXXXII, R' = OAc) (CXXXIII, R = OAc)
R unspecified and R' = H
(CXXXIV)

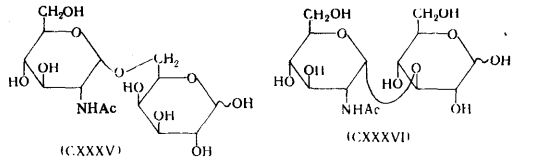
On the other hand, in the remaining cases the authors failed to observe the formation of β-anomers (but they did not rule out this possibility[176]).

The results of Miyai and Jeanloz[175] conflict with these data. They failed to observe the stereospecificity of the glycosylation of benzyl 2,3,4-tri-*O*-benzyl-β-D-galactopyranoside by the chloride (CXXV, R = H, R' = OCOMe) and obtained a mixture of α- and β-(1→6)-linked disaccharides in approximately equal amounts.

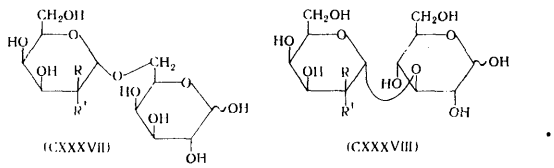
The preparative value of the method is reduced to some extent by the inadequate stereospecificity of the reduction of the hydroxyimino-derivatives to the corresponding 2-amino-2-deoxysugars. Depending on the conditions of the reduction of (CXXVII) and (CXXVIII), the ratio of the amino-α-D-glycosides formed, epimeric at 2-C, varied within a fairly wide range[175,178,179]. A high stereospecificity of the reaction was noted only in the hydrogenation of (CXXVII) on palladium in the presence of hydrazine or in the reduction of the *N*-acetate of compound (CXXVII) by diborane in tetrahydrofuran (THF), as a result of which the product contained 92–95% of the amino-α-D-glucoside and 5–8% of the amino-α-D-mannoside. The reduction of (CXXVII) or (CXXVIII) (as well as its *N*-acetate) by diborane or lithium tetrahydroaluminate in THF led to a mixture of the D-gluco- and D-manno-epimers [from (CXXVII)] and the D-galacto- and D-talo-epimers [from (CXXVIII)] in comparable amounts.

The same behaviour was noted[180] also in the reduction of the hydroxyimino-derivatives of disaccharides [(CXXX)–(CXXXIV)] by diborane in THF. The individual disaccharides (CXXXV) and (CXXXVI) were obtained in high yields only from compounds (CXXX) and (CXXXII) (after the removal of the protecting groups and *N*-acetylation). The reduction of (CXXXI) and (CXXXIII) under the same conditions led to mixtures of disaccharides [(CXXXII) and (CXXXVIII) with R = R' = H or NHCOMe) in which products with the D-talo-configuration of the aminosugar component predominated. They were separated by chromatography.

The reduction of (CXXIX) also leads to the formation of a mixture of disaccharide derivatives with the D-gluco- and D-manno-configuration of the non-reducing monosaccharide residue in proportions of approximately 1 : 1.[178]



(CXXXV) (CXXXVI)



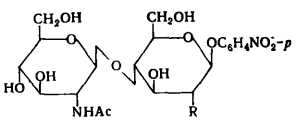
(CXXXVII) (CXXXVIII)

Despite the non-specific reduction of 2-hydroxyimino-derivatives of sugars in many cases, the method described is at present perhaps the only procedure for the synthesis of 1,2-*cis*-aminoglycosides with an aglycone having a complex structure. It is noteworthy that 2-hydroxyimino-2-deoxy-α-D-glycosides are the precursors of not only amino-α-D-glycosides but also of α-D-glycopyranosides[177,181], α-D-hexopyranosides[179], and 2-deoxy-α-D-glycosides[182], including disaccharide derivatives.

VII. ENZYMATIC SYNTHESIS OF AMINOSUGAR OLIGOSACCHARIDES

A detailed description of the synthesis of oligosaccharides containing aminosugar residues by enzymatic systems is outside the scope of this review. We wished to consider only those enzymatic methods for the formation of aminosugar oligosaccharides which are of interest from the preparative point of view. They are based on the well known transglycosylating ability of the lysozyme from hen egg protein (EC 3.2.1.17).

When lysozyme was allowed to act on di-*N*-acetylchitobiose in the presence of methanol, methyl 2-acetamido-2-deoxy-β-D-glucopyranoside was isolated[185]. Subsequently the same workers[186] obtained disaccharide glycosides (CXXXIX), which are formed when lysozyme acts on tetra-*N*-acetylchitotetraose in the presence of *p*-nitrophenyl β-glycosides derived from *N*-acetyl-D-glucosamine, D-glucose, and 2-deoxy-D-glucose as acceptors (see also van Eikeren and Chipman[187]). When penta-*N*-acetylchitopentaose was used as the donor of glycosyl residues and cellobiose as the acceptor, oligosaccharides with the formula $(GlcNAc)_nGlcGlc$§ (n = 1–3) were obtained[188,189].



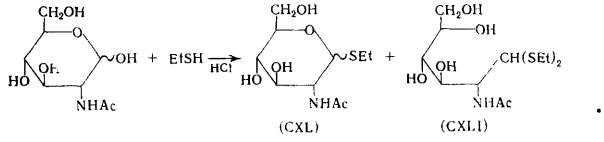
(CXXXIX, R = NHAc, OH, H)

The tetrasaccharide from the cell wall of the bacterium *Micrococcus lysodeikticus*, $(GlcNAc\text{-}MurNAc)_2$, is an active donor of glycosyl residues in lysozyme-catalysed reactions. When it was allowed to react with monosaccharide acceptors (*N*-acetyl-D-glucosamine, D-glucose, D-galactose, and D-xylose), the following trisaccharides were isolated[190–192]: GlcNAc-MurNAc-GlcNAc, GlcNAc-MurNAc-Glc, GlcNAc-MurNAc-β-(1→2)-Glc, GlcNAc-MurNAc-β-(1→2)-Gal, GlcNAc-MurNAc-Xyl, GlcNAc-MurNAc-β-(1→2)-Xyl, and GlcNAc-MurNAc-β-(1→3)-Xyl, the yield of the transglycosylation products reaching 15% (with respect to the donor). The transfer of the same glycosyl residue to oligosaccharides (di-*N*-acetylchitobiose and cellotetraose) proceeds similarly[188,192] and leads to the formation of the oligosaccharides GlcNAc-MurNAc-$(GlcNAc)_2$ and GlcNAc-MurNAc-$(Glc)_4$.

Transglycosylating activity is a characteristic property of glycosidases and endoglycanases, i.e. *O*-glycoside hydrolases, which catalyse the hydrolytic cleavage of the *O*-glycosidic linkage with retention of the configuration at the anomeric glycosidic centre of the substrate. An enhanced affinity of the active centres for the glycone part of the substrate is characteristic of enzymes of this type, and is responsible for the attachment of the activated glycosyl residue to them. The latter is then transferred to the acceptor. Apart from lysozyme, which has already been mentioned, in the preparative synthesis of aminoglycosides employing transglycosylating activity it is possible to use also other enzymes which cleave the aminoglycosidic linkage, for example α- and β-hexosaminidases. However, the available information on this subject is extremely limited.

VIII. SYNTHESIS OF *S*- AND *N*-AMINOGLYCOSIDES

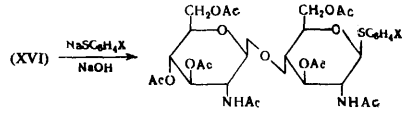
In contrast to neutral monosaccharides, *N*-acetyl-D-glucosamine is capable of giving rise to thioglycosides under the conditions of the Fischer synthesis of glycosides. Thus the anomeric ethyl 2-acetamido-2-deoxy-1-thio-D-glucopyranosides (CXL) were obtained in a low yield under controlled conditions[193], but the main reaction product was the mercaptal (CXLI):



(CXL) (CXLI)

Aminosugar *S*-glycosides are mainly synthesised by the methods used to prepare their neutral analogues[194]. The hydrolysis of the mercaptal (CXLI) in the presence of mercury(II) chloride and mercury(II) oxide gives a mixture of anomeric ethyl 2-acetamido-2-deoxy-1-thio-D-glucofuranosides, with the α-anomer predominating[195].

Different alkyl and aryl 2-amino-3,4,6-tri-*O*-benzoyl-2-deoxy-1-thio-β-D-glucopyranosides (in the form of the hydrobromides)[196] and their *N*-benzoyl analogues[39] have been obtained from the corresponding acylhalogeno-derivatives and thiols. Phenyl 1-thioglycosides of the disaccharide (CXLII, X = H, Me, or NO_2) and their 1-seleno-analogue[197] were synthesised similarly from the chloride (XVI)[197,198]:



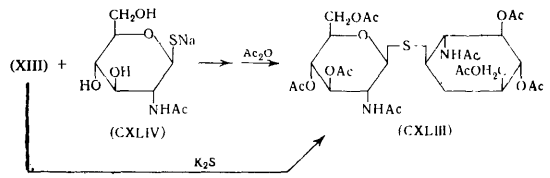
(CXLII)

§ For the significance of the abbreviations, see the footnote to Table 2. The unspecified positions of the glycosidic linkages are β-(1→4).

Ethyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-glucopyranoside is formed in the mercaptolysis of α-D-glucosamine peracetate in the presence of zinc chloride[183]. In this case the stereospecificity is due to the cooperative effect.

The oxazoline method is promising for the synthesis of 1-thioaminoglycosides. Phenyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-glucopyranoside and the thioglycoside (CXLII, X = H) were obtained in this way[158] in yields of 68 and 43% respectively.

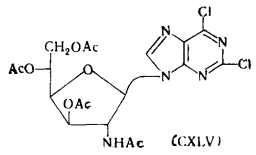
The thio-analogue of the non-reducing disaccharide (CXLIII) was obtained[61] in 50% yield by the reaction of the chloride (XIII) with the sodium salt of (CXLIV) or by treating the chloride (XIII) with potassium sulphide:



Either direct condensation of monosaccharides with aromatic amines[200-203] or aminoacids[203,204] or different versions of the Koenigs–Knorr reaction are used in the synthesis of the *N*-glycosides of 2-amino-2-deoxysugars, as for the *N*-glycosides of neutral sugars[199]. The use of acylhalogenosugars as glycosylating agents involves the same difficulties as in the synthesis of *O*-glycosides of 2-amino-2-deoxysugars.

O-Acylated glycosyl chlorides and bromides with different substituents at the nitrogen atom have been used in the synthesis of aminosugar nucleosides[205-218]. Mixtures of anomeric *N*-substituted aminoglycosides are formed as a rule from bromides with "non-participating" substituents at 2-C.

The synthesis of the nucleoside (CXLV) is so far the only instance[143] of the preparation of *N*-glycosides by the oxazoline method[135].



(CXLV)

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The data described permit the conclusion that the synthesis of 1,2-*trans*-aminoglycosides, including 2-amino-2-deoxysugar oligosaccharides, has now been developed in fair detail and there are a number of methods whereby they can be obtained on a preparative scale, among which the oxazoline method is the most convenient. Methods for the synthesis of 1,2-*cis*-aminoglycosides have been much less satisfactorily developed and the synthesis of polysaccharides made up of aminosugar residues has remained completely untouched. In this respect the synthetic chemistry of aminoglycosides still lags behind the synthetic chemistry of their neutral analogues[172,219].

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The Mechanism of Non-adiabatic Bimolecular Reactions

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The dynamics of bimolecular non-adiabatic elementary process in gases are discussed. The inelastic processes occurring in collisions between atoms and dia-atomic molecules and exchange and decomposition reactions are considered within the framework of the semiclassical description of collisions based on the instantaneous jump model of the reacting system between adiabatic potential energies surfaces.
The bibliography includes 121 references.

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1. INTRODUCTION

This review discusses the mechanisms of elementary non-adiabatic bimolecular gas-phase reactions, i.e. reactions involving a change in the electronic states of reactant molecules. These processes have been attracting increasing attention in connection with new research possibilities which have arisen as a result of applying the techniques of molecular beams and laser fluorescence which yield extremely detailed information about the initial states of the reactants and products. Non-adiabatic processes are much more common than might be supposed on the basis of the space devoted to them in recent books and reviews on elementary processes[1-3].

This paper is an attempt to fill part of the existing gap in the review literature on the mechanisms of elementary non-adiabatic reactions. The author has restricted the treatment to a discussion of the simplest (and therefore the best studied) non-adiabatic reactions—the reactions of atoms with diatomic molecules.

The review has been arranged as follows. Initially (Section 2) there is a brief discussion of the classification of non-adiabatic processes and general information about the mechanisms of non-adiabatic interaction is presented. The next section (Section 3) deals with the influence of non-adiabatic effects on the exchange of rotational and vibrational energies in processes without a redistribution of atoms. Sections 4 and 5 are devoted to non-adiabatic exchange and collisional dissociation reactions. The literature references include mainly recent studies associated directly with research on specific non-adiabatic processes. Instead of direct references to studies in the past years, recent books[1-4] in which the relevant processes are discussed and the original literature is given, are referred to.

2. DEFINITION OF NON-ADIABATIC PROCESSES

Adiabatic Potential Energy Surfaces

In the general case where an atom A collides with a diatomic molecule BC, the following elementary processes are possible:

$$A + BC \begin{cases} \rightarrow A + BC - \text{(elastic and inelastic collisions)} \\ \rightarrow AB + C \text{ (exchange)} \\ \rightarrow AC + B \text{ (exchange)} \\ \rightarrow A+B+C \text{ (dissociation).} \end{cases} \quad (1)$$

Analysis of the mechanism of any of these processes in the gas phase is based on the study of the dynamics of the elementary collision step. Such investigation yields the reaction cross-section which, together with the distribution of the reactant molecules between initial states, fully determines the rate of reaction (see Kondrat'ev and Nikitin[1], §8). The calculation of the cross-section constitutes a fairly difficult problem in classical or quantum mechanics and simplifying assumptions are always made. These simplifications concern two aspects of the problem. The first is associated with the attempt to exclude from consideration the dynamics of electron motion in the reacting system of atoms and molecules and to formulate the problem in terms of the motion of atomic nuclei alone. This is achieved by employing the adiabatic approximation[1,4], within the framework of which one introduces the concepts of the potential energy surfaces of the nuclei $U_n(R)$, which depend on the set of nuclear coordinates R and refer to a given electronic state n. Since the creation of the quantum theory of molecules, the calculation of potential energy surfaces has been one of its most important tasks (see the relevant reviews[5,6]).

Another aspect of the problem consists of the study of the dynamics of the motion of the nuclei of the reacting molecules, which is usually treated in terms of the motion of the characteristic point of the system along the specified potential energy surface from the region corresponding to the initial molecules (reactants) to that of the reaction products. This approach to the theory of elementary processes has developed strongly during the last 10–15 years and a major proportion of the important results have been obtained by computer calculations of reaction probabilities and cross-sections.

However, there is a whole class of chemical reactions which cannot, in principle, be interpreted in terms of the motion of the system along *one* fixed potential energy surface, i.e. a significant feature of the mechanism of these reactions is a change in the electronic state of the system. To investigate the dynamics of these reactions, called non-adiabatic, it is necessary to go beyond the framework of the adiabatic approximation. The theory corresponding to this generalisation can be formulated as follows. One of the formulations employs the adiabatic potential energy surfaces $U_n(R)$ as the zeroth approximation with additional allowance for the transitions between them (non-adiabatic transitions). This approximation will in fact be employed below.

Adiabatic potential energy surfaces are defined as the eigenvalues of the electronic Hamiltonian H_{el} of a system ABC with a fixed configuration of the nuclei. However, in terms of this general formulation, the problem of finding $U_n(R)$ and the corresponding adiabatic electronic functions φ_n usually cannot be solved. Any approximate solution is equivalent, in a certain sense, to the solution of the exact problem with a Hamiltonian H^0_{el} differing from H_{el}. The corresponding eigenfunctions φ^0_n and the eigenvalues $U^0_n(R)$ are associated with the so-called rough adiabatic approximation. If the difference between H_{el} and H^0_{el} is not great, then the $U^0_n(R)$ constitute a satisfactory approximation to the $U_n(R)_0$ in those regions of the configuration space of the nuclei where the difference $U^0_n(R) - U^0_{n'}(R)$ is appreciably greater than the matrix element $\delta H_{nn'}$ for the interaction ($\delta H = H_{el} - H^0_{el}$). Hence it follows that the regions of the intersections of the states of the rough adiabatic approximation, where the above condition is known not to hold, must be specially investigated since such an intersection can either also occur for adiabatic surfaces or be replaced by a close approach of the adiabatic surfaces (the so called quasi-intersection).

The general theory[7,8] and also its specific application to a three-atom system[4,9] establishes the characteristics of the intersection of the $U_n(R)$ and $U^0_n(R)$ states.

Depending on the effects which it is desirable to include in the study of the reaction dynamics, the Hamiltonian H^0_{el} is chosen with different degrees of approximation and the possibility of neglecting certain terms in H_{el} when specifying H^0_{el} is determined by the condition that these terms have little influence both on the structure of the adiabatic surfaces and on the probability of non-adiabatic transitions. In this connection we may mention the following approximations.

a. Neglect of magnetic interactions (spin–orbit and spin–spin). The energy of such an interaction varies from several hundredths of an electron-volt to 1 eV for heavy atoms (for example the iodine atom). In this approximation the overall electron spin is conserved so that any processes described by relation (1) should follow the Wigner rule: among the possible spin states of the products, there should be a state identical with one of the spin states of the initial reactants. Magnetic interactions can be neglected in constructing the potential energy surfaces for a system of light atoms. However, they must almost always be taken into consideration (systems comprising H and He atoms are an exception) in calculations of the probabilities of non-adiabatic transitions.

b. Neglect of electron correlation effects. Within the framework of this approach, based on the one-electron approximation, it is possible to formulate a number of simple rules for the qualitative construction of surfaces (for example the Woodward–Hoffmann principle of the conservation of orbital symmetry[11–13] or the employment of correlation diagrams for molecular orbitals[14]). Since the electron correlation energy is of the same order of magnitude as the energy of the splitting of the atomic states which arise from a single configuration (1–2 eV), the one-electron approximation is not applicable in a quantitative calculation of the surfaces. Nor can it be used to calculate the probability of non-adiabatic transitions.

c. Neglect of the change in electron correlation on mutual approach of the initial reactants. In constructing H^0_{el} within the framework of this approach account is taken first of the electron correlation in isolated atoms and molecules and the interaction between the colliding species is taken into account only in the following stage. This method, which is a generalisation of the Heitler–London method to include many-electron systems, yields the correct type of adiabatic states for large intermolecular distances[15]. We may note that the employment of this approximation for smaller distances leads to a qualitative proof of the familiar Polanyi–Semenov correlation[1] between activation energies and heats of reaction in a series of similar reactions.

Although for a fairly small perturbation δH the U_n^0 and U_n surfaces proved to be close in most of the configuration space of the nuclei, the corresponding states are specified by *different* sets of electronic quantum numbers. Therefore the classification of processes as adiabatic or non-adiabatic within the framework of any rough adiabatic approximation can frequently change when the approximation is refined. The consequent ambiguity in the definition of non-adiabatic reactions must be always borne in mind. However, the final result of the study of the dynamics—the calculation of the reaction probabilities or cross-sections—is independent of the ambiguity of the definition, provided that non-adiabatic transitions have been taken into account correctly in the solution of the problem.

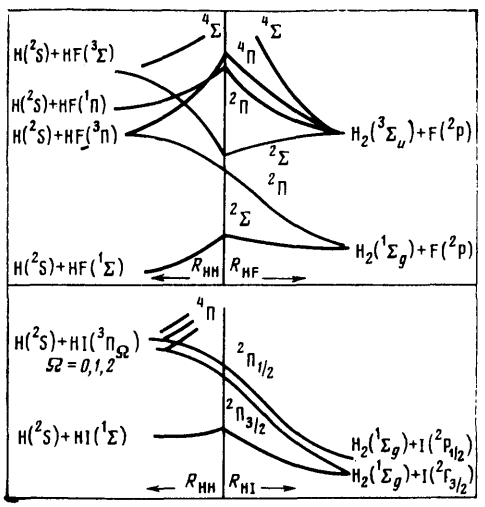

Figure 1. Correlation diagrams for the electronic terms of the reaction H + HF → H_2 + F (weak spin—orbital interaction, upper Figure) and H + HI → H_2 + I (strong spin—orbital interaction, lower figure) with a linear configuration of the nuclei.

Numerous examples of the correlation of the electronic states of a three-atom system are quoted in a review[16]. Here we shall mention only one example illustrating the influence of the spin-orbital interaction on the structure of the surfaces for an HHX system (X is a halogen atom). Fig. 1 presents the cross-sections of the surfaces of the linear HHF system which have been calculated by the semiempirical method of diatomic complexes in molecules[17]. The left-hand side of the Figure corresponds to the pathway $\infty > R_{HH} \geq R^{\circ}_{HH}$, $R_{HF} = R^{\circ}_{HF}$ and the right hand side corresponds to the pathway $R_{HH} = R^{\circ}_{HH}$, $R^{\circ}_{HF} \leq R_{HF} < \infty$. When the linear configuration of the nuclei breaks down, the $^2\Sigma$ and $^4\Sigma$ states (in the calculation of which the spin-orbital interaction is neglected, as in the case of the Π states, because it is small for the F atom) are classified as the $^2A'$ and $^4A'$ states in the C_S symmetry group, the corresponding energies being somewhat altered.

The $^2\Pi$ and $^4\Pi$ states are split as well as displaced and are classified as $^2A'$, $^2A''$, and $^4A'$, $^4A''$.

On passing from F to heavier halogens, account must be taken of the spin-orbit interaction in plotting the diagrams. The lower part of Fig. 1 illustrates qualitatively these changes in the disposition of the states for the HHI system which arise under these conditions. For example, the degeneracy of the state $^2\Pi$ is lifted; instead there arise two components $^2\Pi_{1/2}$ and $^2\Pi_{3/2}$, which are correlated with different states of the I atom. When the linear configuration is distorted, the states are not split further: they remain doubly degenerate with respect to the spin projections as a consequence of Kramers theorem[7].

Description of Non-adiabatic Transitions

Non-adiabatic transitions between potential energy surfaces are due to the dynamic interaction of electrons and nuclei. A consistent quantum theory formulates the problem of describing the transitions in terms of a system of coupled wave equations. In this formulation the problem can be solved (and has been solved successfully) for collisions of two atoms when the potential energy surfaces simplify into potential energy curves (a system of equations in a single variable R). The minimum dimensionality of the equations whose solution is significant in connection with the study of the dynamics of non-adiabatic reactions is two (linear collision of an atom with a diatomic molecule). However, this problem cannot be solved at present even on the best computers: the quantum solution has been obtained so far only for the two-dimensional adiabatic problem of the reaction of a hydrogen atom and an H_2 molecule. This factor and also the fact that even the solution of a real multidimensional adiabatic problem can be obtained only within the framework of the classical description necessitates the employment of semiclassical methods for calculating the probabilities of non-adiabatic transitions, the essential features of which are as follows.

The study of the problem of non-adiabatic transitions shows that the dynamic interaction is most vigorous in the region corresponding to the approach or intersection of the states. The main parameter determining the extent of the interaction is the ratio of the frequency of the oscillation of electrons between the levels, $\omega(R) = |U_n - U'_n|/\hbar$, to the "frequency" $1/\tau$ characterising the rate at which the nuclei traverse the region of interaction. If the parameter $\xi = \omega\tau$ is large, it is possible to neglect the non-adiabatic transitions[4,18,19]. Non-adiabatic transitions must be taken into account only in the regions of the configuration space of the nuclei where $\xi \leq 1$ or ξ becomes zero. The extent l of this region is then important. If the extent is small, i.e. l is appreciably smaller than the characteristic dimensions L which define the region of interaction of the three-atom system, then the semiclassical approximation suggests the following method for describing non-adiabatic transitions which makes maximum use of the simplicity of the classical description of the motion of the representative point in adiabatic regions. The representative point moves along the potential energy surface corresponding to the initial electronic states of the initial reactants until the attainment of the region of strong non-adiabatic coupling. In this region the system executes a jump from the initial surface to a neighbouring surface with a probability P_1, which depends on the parameters of the surfaces in this region; the probability that the system remains on the initial surface is $1 - P_1$. Subsequently the motion is

continued on two surfaces—the first and second surfaces—the probabilities $1 - P_1$ and P_1 being associated with the corresponding trajectories. The motion continues until each trajectory again reaches the non-adiabatic regions. In these regions each trajectory "branches" once more. The consecutive repetition of the steps involving the adiabatic motion on the surfaces and the corresponding jumps yields the semiclassical picture of the process. Clearly the trajectories characterised by different "histories" of the jumps between the potential surfaces and having different probabilities P_k contribute to the set of final states (for example to the energy range $\hbar\omega$ near the vibrational energy E_{vibr} of the molecule formed), which is identified in the semiclassical approximation with the population of the quantum level. Then the overall probability of the process is defined by the sum of the probabilities P_k.

Two general objections may be raised against the semiclassical method: (a) failure to include quantum effects in the adiabatic motion of the system on the surface, (b) inaccurate definition of the concept of the trajectory in the non-adiabatic region where the jump takes place, and (c) failure to consider interference effects in adding the probabilities (and not the probability amplitudes) in the final state. All these objections also apply to the semiclassical description of atomic collisions, the limits of applicability of which are well known. The information accumulated so far concerning the accuracy of the semiclassical method and ways for improving it[22] suggests that the semiclassical approach is the most promising in the study of the dynamics of non-adiabatic processes.

For a specific calculation of the overall probability of a non-adiabatic process, it is necessary to know the probabilities P_k of the individual transitions. The calculation of these quantities reduces to the solution of the system of equations for non-adiabatic coupling, which can be incorporated in a single computer program. However, it is possible to simplify the dynamic calculation significantly using in the transition probabilities calculated independently within the framework of specific models. A number of such models are known at present[18]. The simplest of these is the Landau—Zener model[1,4,19], which can be used to calculate P provided that the cross-sections of the adiabatic surfaces along the part of the projectory $\mathbf{R} = \mathbf{R}(t)$ in the region of the interaction can be fairly satisfactorily approximated by two coupled hyperbolae. States of this kind are known to arise naturally[1,4] when the surfaces U_1 and U_2 are obtained by diagonalisation of the second-order matrix in a basis set of the intersecting states of the rough adiabatic approximation. Then the expression for the probability of non-adiabatic transition is

$$P = \exp[-2\pi a^2/\hbar\,|F_{1R} - F_{2R}|\,v_R] \quad , \qquad (2)$$

where $2a$ is the minimum distance between the states U_1 and U_2, F_{1R} and F_{2R} are the slopes of the lines asymptotic to the hyperbolae along the section of the trajectory $\mathbf{R}$, and v_R is the rate of motion of the system in the region of the transition. It is seen from Eqn. (2), that, for low values of the parameter $2\pi a^2/\hbar\,|F_{1R} - F_{2R}|\,v_R$, the system executes transitions between the adiabatic states with a high degree of probability. Hence follows the usefulness of the concept of diabatic states or diabatic surfaces, defined as surfaces which are followed by the system with a high probability when the velocity is sufficiently high. Evidently the probability P' of the transition between the diabatic states is expressed in terms of P by the relation $P' = 1 - P$, so that we obtain for the Landau–Zener model

$$P' = 1 - \exp[-2\pi a^2/\hbar\,|F_{1R} - F_{2R}|\,v_R] \quad . \qquad (3)$$

For high velocities, the probability of the transition between the diabatic states is low and is given approximately by

$$P' = 2\pi a^2/\hbar\,|F_{1R} - F_{2R}|\,v_R \quad . \qquad (4)$$

In practical calculations upper and lower limits are imposed on the parameter $2\pi a^2/\hbar\,|F_{1R} - F_{2R}|\,v_R$, since unduly low probabilities of the transition (and hence of branching) between adiabatic or diabatic surfaces usually need not be taken into consideration. Bearing in mind these limitations and using the available estimates of the extent of the transition regions l,[18] it is possible to show that the condition $l \ll L$, for which the description of the transitions in terms of jumps is satisfactory, holds when the energies are less than 10 eV.

3. EFFECT OF NON-ADIABATIC CONDITIONS ON THE EXCHANGE OF ROTATIONAL AND VIBRATIONAL ENERGY

Energy exchange processes in the collisions between an atom A and a diatomic molecule BC are usually considered in terms of the trajectory on the potential energy surface, which for $R_{A\text{-}BC} \to \infty$ correlates with the electronic state of the uncoupled system A + BC. If the electronic states of A and BC are non-degenerate, such a correlation defines a single potential energy surface, which is used subsequently in the dynamic calculation. On the other hand, even if only one of the two species has a degenerate electronic state, the interaction between A and BC lifts the degeneracy. Thus several closely spaced potential energy surfaces arise and in the limit $R_{A\text{-}BC} \to \infty$ these are correlated with the degenerate electronic state of the uncoupled system A + BC. If is found that the existence of several close surfaces alters significantly the probabilities of the rotational and vibrational transitions compared with the simplest case of a single surface, where it is possible to employ the adiabatic approximation.

Rotational Transitions

Recent experiments on rotational transitions in the $Na_2^*(^1\Pi)$ [21,22] and $Li_2^*(^1\Pi)$ [23,24] molecules, induced by collisions with inert gas atoms, showed that, together with the $j' - j = \Delta j = \pm 2$ transitions (the usual selection rules for rotational transitions in diatomic molecules with identical nuclei), there is a high probability of transitions with $\Delta j = \pm 1$, and the cross-sections of the one-quantum transitions depend strongly on the sign of Δj. A quantum interpretation of this effect has been given[25,26]. Here we shall consider the simpler semiclassical interpretation based on symmetry considerations alone.

One of the integrals of motion of the moving atom + diatomic molecule system is the overall angular momentum J. In the semiclassical approximation the vector J is identified with the vector of the relative angular momentum l, which is valid subject to the condition $l \gg j$, where j is the angular momentum of the molecule. In this approximation the trajectory of the relative motion of A and BC must be regarded as planar and a reflection in this plane is an operation which commutes with a non-stationary Hamiltonian.

If the electronic state of the molecule BC is defined in such a way that it has a certain symmetry ϵ ($\epsilon = 0, 1$) with respect to reflection in the plane passing through the molecular axis [i.e. the electronic wavefunction acquires the multiplier $(-1)^{\epsilon}$ on reflection in this plane], then the overall wave function (the electronic-rotational function) acquires the multiplier $(-1)^{j-m+\epsilon}$ on reflection in the collision plane[7]. Since the reflection in this plane is an exact symmetry operation, the collision can give rise to transitions between states with the same symmetry relative to the collision plane. Therefore the initial quantum numbers j, m, and ϵ and the final numbers j', m', and ϵ' are linked by the relation $j - m + \epsilon = j' - m' + \epsilon' + 2p$, where m denotes a projection of j onto the axis perpendicular to the collision plane and $2p$ is an even number.

If the electronic state of the molecule is non-degenerate, then ϵ is defined unambiguously and $\epsilon = \epsilon'$. This condition does not alone impose any limitations on the variation of j and therefore for low anisotropy of the interaction the most probable transitions correspond to the minimum change in j, i.e. $\Delta j = \pm 1$. If the molecule BC contains identical atoms (B = C), then the interaction potential of A and B_2 has an additional symmetry, which forbids transitions involving a change in j by an odd number. It follows from this selection rule with respect to m and from the relations quoted above that j can change only by an even number. Therefore the minimum permissible change in j for diatomic molecules with identical nuclei in a non-degenerate electronic state is ± 2.

If the molecule BC is in a degenerate electronic state, then there are always two components of the electronic eigenfunction with different ϵ. Therefore, even for molecules with identical nuclei, transitions with $\Delta j = \pm 1$ are allowed, provided that ϵ changes simultaneously: under these conditions, the symmetry of the overall wavefunction remains unchanged in the transition.

Thus the degeneracy of the electronic state leads to a major effect in the rotational relaxation of diatomic molecules with identical nuclei—the appearance of transitions with $\Delta j = \pm 1$ as well as transitions with $\Delta j = \pm 2$.

Vibrational Transitions

An experimental study of the vibrational relaxation of diatomic molecules revealed a number of instances of "anomalously" rapid deactivation of vibrations in collisions. In this case the standard defining the "normal" rate of deactivation is the average probability $\langle P_{10} \rangle$ of the transition (the $v = 1 \rightarrow v = 0$ transition) for diatomic molecules with identical nuclei or for molecules with a low asymmetry in a single gas-kinetic collision with the molecules of the heat reservoir which are all of the same type. The theory of the vibrational–translational energy exchange ($T - V$ processes) (see, for example, Refs. 1, 3, and 4) predicts the following approximate relation between $\langle P_{10} \rangle$ and the temperature T of the heat reservoir, the frequency ω of the vibrations of the molecule being deactivated, the reduced mass μ of the colliding molecules, and the radius $1/\alpha$ of the action of the intermolecular potential:

$$\ln \langle P_{10} \rangle = -\frac{3}{2}(4\pi^2\omega^2\mu/\alpha^2 kT)^{1/3} + A , \qquad (5)$$

where A is a function of the above parameters, which shows a smaller dependence on them than the first term on the right-hand side of Eqn. (5). This relation constitutes the basis for the widely used semiempirical correlation of the $\langle P_{10} \rangle$ for different molecules over a wide temperature range[1]. Naturally, under these conditions a high accuracy is not achieved, but even approximate validity of Eqn. (5) is sufficient for subsequent discussion.

An illustration of "normal" VT processes may be provided by the following reactions which have been fairly fully investigated over a wide temperature range:

$$\begin{aligned} &N_2(v=1) + N_2(v=0) \rightarrow N_2(v=0) + N_2(v=0) , \\ &O_2(v=1) + O_2(v=0) \rightarrow O_2(v=0) + O_2(v=0) , \\ &CO(v=1) + CO(v=0) \rightarrow CO(v=0) + CO(v=0) . \end{aligned} \qquad (6)$$

The $\langle P_{10} \rangle$ for all these processes, summarised in Fig. 42 in Kondrat'ev and Nikitin's book[1], fall within the shaded band in Fig. 2, whose width makes it possible to estimate the accuracy of Eqn. (5). In this figure $-\lg \langle P_{10} \rangle$ is plotted as a function of the dimensionless parameter $(\omega^2\mu a_0^2/kT)^{1/3}$, where a_0 is the Bohr radius. According to Eqn. (5), the slope of the band should be $(\lg e)\frac{3}{2}(4\pi^2)^{1/3} \cdot (a_0\alpha)^{-2/3}$. Comparison of this quantity with the average slope shown in Fig. 2 yields $\alpha \simeq 3.2/a_0$, which is the usual value adopted in the theory of the vibrational relaxation of diatomic molecules.

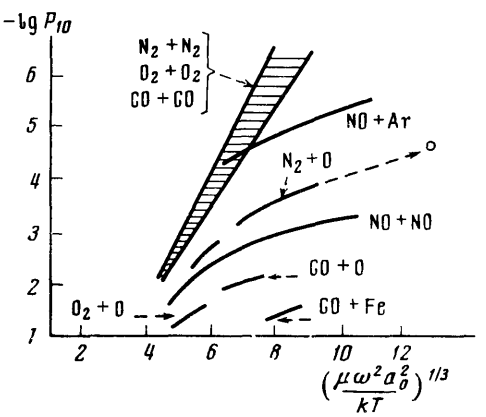

Figure 2. Probabilities of vibrational deactivation in "normal" and "anomalous" processes.

The experimental points for "anomalous" processes lie appreciably below this band. A number of anomalies have been explained by the contribution of VR processes, i.e. the transformation of the vibrational energy of the molecule into rotational energy (see Nikitin[4], §9). However, this explanation, which retains Eqn. (5) but alters the sense of the reduced mass μ, can be adduced only for processes where the reduced mass of the colliding species is much greater than the reduced mass of the molecule being deactivated. Finally, rapid relaxation can be caused by an exchange reaction if the latter is characterised by a low activation energy.

The processes with anomalously rapid relaxation known at present for which the VR mechanism is not effective are listed below (the references to the relevant experimental studies are indicated in square brackets):

$$\begin{aligned} &NO(v=1) + Ar \rightarrow NO(v=0) + Ar , && [27] \\ &NO(v=1) + NO \rightarrow NO(v=0) + NO , && [28, 29] \\ &CO(v=1) + Fe \rightarrow CO(v=0) + Fe , && [30] \\ &N_2(v=1) + O \rightarrow N_2(v=0) + O , && [31, 32, 33] \\ &O_2(v=1) + O \rightarrow O_2(v=0) + O , && [34] \\ &CO(v=1) + O \rightarrow CO(v=0) + O . && [33, 35] \end{aligned} \qquad (7)$$

The experimental $\langle P_{10} \rangle$, taken from the above investigations, are also illustrated in Fig. 2. Evidently the $\langle P_{10} \rangle$ for reactions (7) are much higher than the corresponding values for reaction (6). Thus the usual *VT* exchange model must be abandoned for reactions (7).

The only significant difference between reactions (6) and (7) is that in the first group both species involved are in a non-degenerate electronic state and in the second group one of the species has a degenerate electronic ground state. Accordingly, purely vibrational transitions are possible for the first group, while for the second group there is a possibility of both purely vibrational transitions and electronic-vibrational transitions in which the change in the vibrational state is accompanied by a transition from one adiabatic surface to another. The difference between the mechanisms of the purely vibrational and electronic-vibrational transitions can be understood most simply in terms of the model of an oscillator (molecule BC) excited by an external force (time dependent interaction between A and BC). The external force $F(t)$ acting on the oscillator consists of two components. The first component $F_a(t)$, which is comparatively large and varies with the characteristic collision time τ_c, is due to the relative adiabatic motion of A and BC. The second component $F_n(t)$, which is small and oscillates at the frequency of the splitting of the adiabatic states, arises from non-adiabatic transitions associated with the relative motion of the species. The effectiveness of these two components in exciting the oscillator is determined not only by their magnitude but also by their spectral composition, since only the Fourier component with the frequency ω excites (or deactivates) the oscillator.

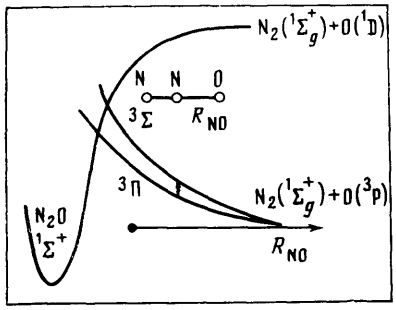

Figure 3. Electronic states of the N_2O system for a linear approach of N_2 and O.

The Fourier spectrum $f_a(\omega)$ of the component $F_a(t)$ may be bell-shaped with a characteristic width $\Delta\omega_c \simeq 1/\tau_c = \alpha u$ (u is the relative velocity of the molecules) and for $\omega \gg \alpha u$ the function $f_a(\omega)$ decreases exponentially:

$$f_a(\omega) = \int_0^\infty F_a(t)\cos\omega t\,dt \sim \exp[-\pi\omega/\alpha u] \text{ when } \frac{\omega}{\alpha u} \gg 1 \qquad (8)$$

The characteristic width of the Fourier spectrum of the component $F_n(t)$ is not determined by the condition that the frequency be equal to the reciprocal of the collision time (as for F_a) but by the maximum frequency ω_m corresponding to the transitions between the adiabatic states when A and BC move along a specific trajectory.

If the uncoupled A + BC system is in a non-degenerate state, then $F(t)$ has only one component $F_a(t)$. Under these conditions, the transition probability P_{10}, proportional to $|f_a(\omega)|^2$, varies approximately exponentially with the velocity subject to the condition $\omega/\alpha u \gg 1$. Such variation of P_{10} with the velocity in fact leads to the temperature variation of $\langle P_{10} \rangle$ in Eqn. (5), which is obtained after averaging P_{10} with respect to the relative velocities according to the Maxwell distribution. Then the parameter $(\mu\omega^2 a_0^2/kT)^{1/3}$, against which $\lg \langle P_{10} \rangle$ is plotted in Fig. 2, is equal to $(2\pi)^{-1/3}\omega a_0/u^*$, where u^* is the relative velocity of A and BC making the maximum contribution to the average transition probability.

If the uncoupled state A + BC is degenerate, it is necessary to take into account the contributions of $F_a(t)$ and $F_n(t)$. It is found[4] that, for fairly large values of $\omega\alpha/u^*$, the contribution of the force $F_a(t)$, which has a large absolute magnitude, is smaller than the contribution of $F_n(t)$, i.e. at fairly low temperatures the vibronic transitions prevail over the purely vibrational transitions. With increase of temperature (and hence with decrease of the parameter $\omega a_0/u^*$), the two contributions begin to compete and ultimately the purely vibrational transitions become more effective. Thus the theory explains the temperature variation of the "anomalous probabilities", which at high temperatures go outside the limit for the normal relation of the type of Eqn. (5).

Details of specific calculations of P_{10} for reaction (7) are quoted in the literature: NO + Ar,[37] NO + NO (Nikitin[4], §21), CO—Fe,[38] N_2 + O and O_2 + O,[39] and are discussed by Nikitin and Umanskii[40]. Here we shall mention only the following feature of the last two processes, in which there is a possibility of the formation of the intermediate complexes N_2O and O_3.

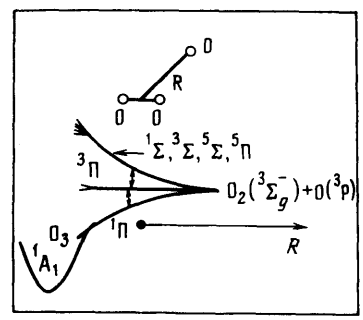

Figure 4. Electronic states of the O_3 system for a non-linear approach of O_2 and O.

The form of the states for the N_2O system (Fig. 3) shows that the vibronic transitions occur in the region where the vibration frequency is equal to the splitting of the electronic states (this region is designated by an arrow in Fig. 3), that is for energies appreciably lower than that of the intersection of the triplet states with the singlet ground state of NO_2. This rules out the possibility of forming a complex with an appreciable contribution of non-adiabatic effects in the region of the intersection of the state $^1\Sigma$ with the states $^3\Sigma$ and $^3\Pi$. This therefore throws doubt on the non-adiabatic relaxation mechanism proposed by Fisher and Bauer[41].

The form of the states for the system $O_2 + O$ (Fig. 4) shows that there is a state correlated adiabatically with the ^1A state of ozone. Therefore, in addition to adiabatic and non-adiabatic vibrational transitions involving the surfaces corresponding to the repulsion of O_2 and O, it is necessary to consider the energy redistribution as a result of the formation of the O_3 complex. Examination of the competition between various channels[39,40] based on different results[39,40] of numerical calculations on the dynamics of the O_3 system on the lower potential energy surface[42] shows that even at low temperatures the non-adiabatic and adiabatic mechanisms [but not described by Eqn. (5)] make comparable contributions.

In the CO + O system there is probably a situation intermediate between $N_2 + O$ and $O_2 + O$: the initial CO + O electronic state differs in spin from the CO_2 ground state (analogy with N_2O), but the CO + O interaction does not correspond to repulsion but to weak attraction (analogy with O_3). Clearly the theory of the relaxation of CO to O must take into account all the characteristics of this system, shown in the CO_2 decomposition reactions and in the recombination of CO and O (see, for example, Kondrat'ev and Nikitin[1] and Troe and Wagner[43]) as well as in isotope exchange reactions[44].

4. NON-ADIABATIC EXCHANGE REACTIONS

When the reacting molecules have a specified energy, he exchange reaction can usually be classified as one of he main types: the direct reaction (ricochet or explosive) or a reaction proceeding via a complex[1]. As a rule, the time of reaction is correlated with the general properties of the potential energy surface on which the reaction takes place. Since the involvement of several potential energy surfaces, frequently of completely different types, is characteristic of non-adiabatic reactions, the angular and energy distribution of the products can correspond to the existence of several reaction types. This was demonstrated for the first time in the reaction

$$Ba + Cl_2 \rightarrow BaCl + Cl\ , \qquad (9)$$

investigated spectroscopically[45,46] and by the method of molecular beams[47]. The product distribution was interpreted by postulating two potential energy surfaces correlated with the ground and excited states of the BaCl molecule.

The reactions proceeding via the formation of a long-lived complex can be described within the framework of a statistical approximation (see Kondrat'ev and Nikitin[1], Nikitin[4], and Nikitin and Umanskii's review[48]). In the simplest version of this approximation it is assumed that the distribution of the products between different electronic states, transitions between which are not forbidden by general conservation laws, is determined by a random redistribution law. However, this hypothesis is probably not valid. Calculation of the potential energy surfaces for the simplest reactions proceeding via a complex, such as

$$M + XM' \rightarrow MX + M' \qquad (10)$$

and

$$M + M'M'' \rightarrow MM' + M''\ , \qquad (11)$$

indicates a possible contribution of non-adiabatic effects (M, M', and M'' are alkali metal atoms and X is a halogen atom). In the first case[49] the surface leading to the excited state approaches very closely (to within 2–5 kcal mole^{-1}) the surface leading to the ground state and in the second case intersections actually occur. However, the relative contribution of the transition regions is very small, so that one cannot expect a statistical population of different electronic states. Similar processes can probably be described within the framework of a theory combining a statistical approach to the energy redistribution between different degrees of freedom for the motion of nuclei with a dynamic approach to the description of non-adiabatic transitions. Hitherto such a theory has not been developed. In this connection a purely dynamic approach is described below, in which reactions proceeding with and without a change in total spin are considered.

Reactions without a Change in Total Spin

The simplest reactions in which non-adiabatic effects are significant and which proceed in accordance with the Wigner rule are those between the inert gas atoms A^+ (A = He, Ne, Ar, Kr, or Xe) and hydrogen molecules. In these processes there may be competition between the exchange reaction

$$A^+ + H_2 \rightarrow AH^+ + H \qquad (12)$$

and the charge-transfer reaction

$$A^+ + H_2 \rightarrow H_2^+ + A\ . \qquad (13)$$

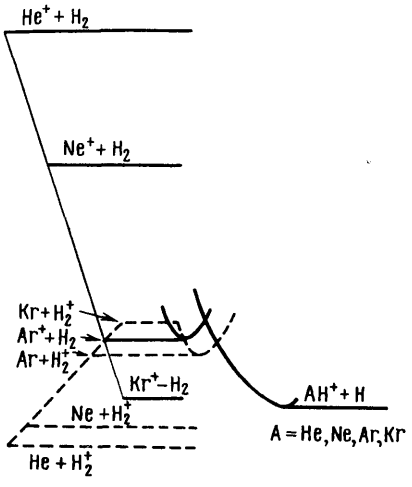

Figure 5. Correlation diagram for the electronic terms of the reactions $A^+ + H_2 \rightarrow A + H_2^+$ and $A^+ + H_2 \rightarrow AH^+ + H$.

The energy levels of the products and reactants are given in Fig. 5, where the energy minimum of the $AH^+ + H$ system (the continuous lines on the left refer to the $A^+ + H_2$ systems and the dashed lines to the $A + H_2^+$ systems) was chosen as the common zero for all the reactions. The correlation between the states on moving from left to right corresponds to motion along the reaction coordinate (12); the reaction pathway profiles then correspond to the rough adiabatic approximation. The parabolic rises on the left-hand side of the diagram correspond to the increase of energy on extension of the H—H bond (the rises for the $Ar^+ + H_2$ and $Ar + H_2^+$ systems are shown).

The potential energy surfaces for the system with A = He have the simplest structure because in this case the initial states are not degenerate and reactions (12) and (13) differ markedly in their energetics. Non-empirical[51,52] and semiempirical[53] calculations of the lowest surface yield a profile for the reaction pathway

$$He + H_2^+ \rightarrow HeH^+ + H, \qquad (14)$$

characterised by a shallow potential well (about 5 kcal mole^{-1}) and a rise equal to the endothermic heat of reaction. The calculations do not yield any indications concerning possible non-adiabatic effects. Experimental studies of reaction (14) in beams have shown[54,55] that the rise is overcome by the kinetic energy for low impact parameters and by the H_2^+ vibrational energy for high impact parameters. The theoretical study of the dynamics has been largely limited to a statistical approximation (see Nikitin and Umanskii's review[48]).

In his discussion of the cause of the low efficiency of the exothermic reaction (12) compared with the highly effective endothermic reaction (13) for A = He, Mahan[14] adduced general arguments showing that reaction (12) is non-adiabatic and that the potential surfaces which correlate with the initial states of the reactants and products, never approach one another. The same arguments remain in force also for A = Ne.[56]

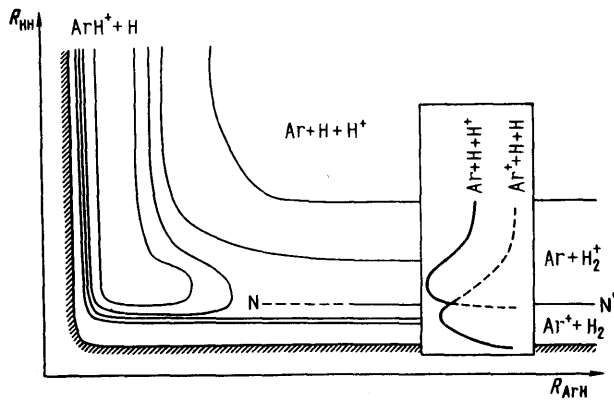

Figure 6. Schematic illustration of the potential energy surface for the collinear system ArH_2^+.

The situation changes significantly on passing to Ar and Kr. In this case the potential energy surfaces for reactions (12) and (13) are close, so that the Ar + H_2^+ and Ar^+ + H_2 diabatic states intersect when R_{HH} is varied and in the limit $R_{Ar-H} \rightarrow \infty$ the intersection is converted into a quasi-intersection for finite R_{Ar-H}. This is shown schematically in Fig. 6, where the lower adiabatic surface for the Ar—H—H linear system is illustrated. The insert illustrates the cross-sections of the surfaces of the ground and first excited states along the H—H coordinate. In adiabatic motion along this coordinate following the lowest surface the system reaches the Ar + H + H$^+$ plateau and for small H—H distances the profile of the cross-section yields the potential curve for the H_2 ground state in the repulsive region. In fact, for large R_{ArH}, the trajectory follows diabatic surfaces. In Fig. 6 this is reflected by the fact that, on approaching and intersecting the N—N′ line (which indicates the region of strong non-adiabatic interaction), the trajectory disappears from the figure or appears on it, depending on whether it approaches this line via the ground or excited state.

With decrease of R_{ArH}, the diabatic motion is increasingly replaced by adiabatic motion: in the region where the N—N′ line is shown dashed the trajectory continues to follow the lowest surface with an appreciable probability $1 - P_{12}$ also after passing through the region of non-adiabatic coupling. Finally, in the region of strong interaction, where the descent begins, the splitting between the states is high, P_{12} is close to zero, and the trajectory follows the lowest energy surface with a very high probability. Thus the dynamics is fully defined if the probability P_{12} of the non-adiabatic transition on the N—N′ line is specified. This treatment, proposed in a qualitative form by Gislason for the reactions discussed[58], was recently used as the basis for a more exact investigation of the dynamics by Chapman and Preston, who obtained a very good agreement with experiment for the cross-sections of reactions (12) and (13) (quoted by Tully[59]). When the energy is 3.36 eV, the charge-transfer cross-section appreciably exceeds the exchange cross-section (17.8 and 3.8 Å^2 respectively). However, Fig. 6 shows that the trajectories reflected from the region of turning of the dip, i.e. not leading to a reaction, result in charge transfer. Therefore dynamic calculations[60], carried out for a model adiabatic surface without taking into account non-adiabatic transitions and also the kinematic abstraction model[61] can be compared with the experimental results for the angular and energy distribution of the products.

A more complex situation arises in a reaction of the type

$$D^+ + DH \rightarrow H^+ + D_2 \qquad (15)$$

and in similar reactions for other hydrogen isotopes. Polanyi and coworkers[62] investigated the dynamics of this reaction on a non-empirical adiabatic surface. It was found, in agreement with the simplest ideas postulating the mechanism of a reaction proceeding via a stable intermediate complex, that the angular and energy distribution of the products agrees qualitatively with the predictions of the statistical theory. However, subsequent experiments[63] did not confirm the expected symmetry in the distribution of products with respect to forward and back scattering. A more detailed investigation of the structure of the surfaces showed that the surface employed in Polanyi's calculations[62] is in fact diabatic far from the potential well. It is necessary therefore to take into account the two lowest surfaces, as was done recently within the framework of semiempirical[64] and non-empirical[65] approximations. The adiabatic surface for the ground state of the H_3^+ linear system is illustrated qualitatively in Fig. 7, where the inserts show the cross-sections of the lowest (continuous line) and the first excited (dashed line) surfaces in directions perpendicular to the reaction coordinate. A surface of this type was used in recent calculations of the total and differential cross-sections of all the reactions pathways[59,66,67]:

$$D^+ + DH \begin{cases} \rightarrow H^+ + D_2 \text{ (channel } a \rightarrow b) \\ \rightarrow D + DH^+ \text{ (channel } a \rightarrow a^*) \\ \rightarrow H + D_2^+ \text{ (channel } a \rightarrow b^*) \end{cases} \qquad (16)$$

A satisfactory agreement was achieved with all the available experimental results for the differential cross-sections and the energy variation of the total cross-sections[59]. The calculated variation of the cross-sections

with the relative energy E_{transl} and for the zero-point DH level is shown in Fig. 8. This relation is simply correlated with the structure of the surfaces. The decrease of the cross-section $\sigma_{a\rightarrow b}$ of the adiabatic exchange reaction with increase of E_{transl} can be explained, by analogy with the usual adiabatic reactions, by an increase in reflection in the region of the turning of the trajectory. This effect is also shown by an increase of the charge-transfer cross-section $\sigma_{a\rightarrow b^*}$. Finally, the increase of $\sigma_{a\rightarrow b^*}$ for the non-adiabatic exchange reaction is due to the increase in non-adiabatic effects with increase of E_{transl}. If E_{transl} is sufficiently small, then the $a \rightarrow b^*$ pathway is unattainable according to the classical treatment. In this case the usual semiclassical description of the non-adiabatic transition is inapplicable and one must go outside the limits of this approximation in order to calculate the probability of the $a \rightarrow b^*$ reaction. One of the methods for extending the theory employs complex trajectories which can reach the non-adiabatic region at complex times. The probabilities of the $D^+ + DH \rightarrow H + D_2^+$ reaction were calculated in this way for low energies[68].

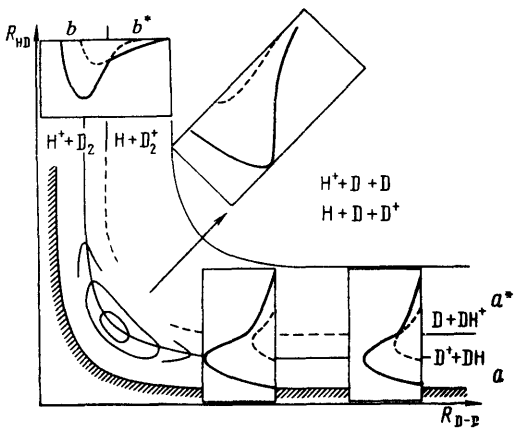

Figure 7. Schematic illustration of the potential energy surface for the collinear system HD_2^+.

Analysis of the dynamics of these reactions revealed the following important factor. Since the calculation of even the most detailed characteristic of the reaction (the differential cross-section) involves averaging with respect to at least two collision parameters (the initial phase of the vibrations and the azimuthal angle), the final result is comparatively insensitive to the transition probabilities along the lines of the quasi-intersection of the adiabatic surfaces. Therefore even comparatively rough estimates of the transition probabilities, carried out subject to the condition that the regions of the non-adiabatic transitions are unattainable on classical grounds, can yield satisfactory accuracy in the calculation of the cross-sections. This constitutes a significant difference between non-adiabatic processes involving three species and non-adiabatic atomic collisions; in the latter case the differential cross-section depends only on a single parameter (the impact parameter), which bears a single-valued (sometimes two-valued or three-valued) relation to the scattering angle[20]. Thus, whereas in the theory of non-elastic atomic collisions the main difficulty of the calculation of the cross-sections consists of the calculation of the transition probabilities, in molecular collisions the main problem involves the investigation of the motion of the system in the adiabatic regions of the configuration space.

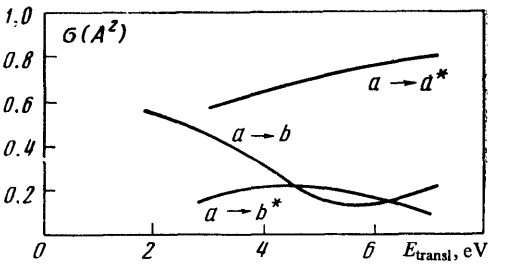

Figure 8. Variation of the cross-sections for reactions (16) with energy.

Another important difference between molecular non-adiabatic processes and atomic processes is that the vibration energy (and not the translational energy) can effectively induce transitions in molecular processes. With the potential energy surfaces for the H_3^+ ion, this is particularly clearly demonstrated by the calculation on the competition between the exchange and charge-transfer reactions[69]:

$$H + D_3^+ \begin{cases} \nearrow DH^+ + D \\ \searrow D_2 + H^+ \end{cases} . \qquad (17)$$

In this process the trajectory begins from the upper half of the pathway followed by the reactants (Fig. 7) subject to the condition that D_2^+ has undergone fairly intense vibrational excitation. Otherwise the trajectory of the reactants is not shown in Fig. 7 at all and their mutual approach, resulting in a transition from the diabatic to adiabatic D_2^+ vibrations, completely prevents the transition from the higher (dashed line) to the lower surface. Thus the probability of charge transfer, described by the transition of the system from the upper half of the reactant valley to the lower half, depends critically on the degree of vibrational excitation of D_2^+. The exchange process can proceed either adiabatically via singlet and triplet excited energy surfaces adjoining the D_2^+ diabatic terms in the initial process or via a non-adiabatic pathway along the lowest surface. In the first pathway it is necessary to overcome an energy barrier, which is not present in the second, but the latter includes a non-adiabatic transition. The competition between these possible processes determines ultimately the efficiency of the exchange.

Reactions Proceeding with a Change in Total Spin

If the set of the possible total spins of the reactants does not include any of the possible values of the total spin of the products, then the spin state of the system necessarily changes along the reaction pathway. The converse assertion is in general not valid: even if the

reaction satisfies Wigner's rule, the most effective reaction pathway need not necessarily correspond to an unchanged spin. An example of the latter process may be provided by the exothermic ion-molecule reaction

$$O^+(^4S) + N_2(^1\Sigma_g) \rightarrow NO^+(^1\Sigma) + N(^4S), \qquad (18)$$

which formally satisfies Wigner's rule.

In contrast to the majority of exothermic ion-molecule reactions, which usually proceed with large cross-sections and at low kinetic energies, the cross-section of reaction (18) is small for low energies and increases sharply with increase of E_{transl} and E_{vibr}. These features of the reaction can be understood qualitatively on the basis of correlation diagrams of electronic states (Fig. 9).

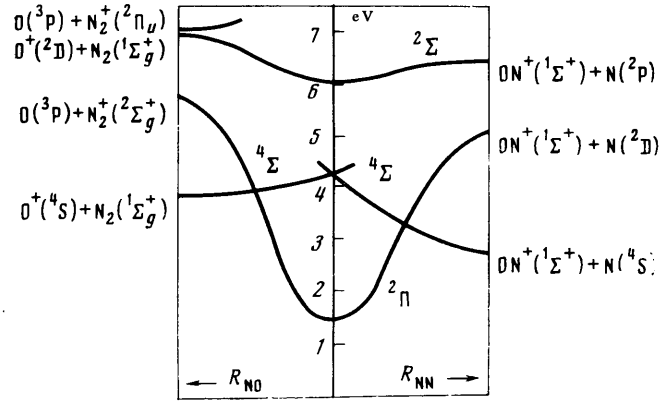

Figure 9. Correlation diagram for the electronic terms of the reaction $O^+ + N_2 \rightarrow NO^+ + N$.

The absence of activation energy in ion-molecule reactions is usually attributed to the fact that the repulsion of reactants due to the exchange interaction is fully compensated by polarisation attraction. However, if the repulsion is sufficiently marked, it can lead to a barrier even against the background of a strong polarisation interaction. Precisely this situation occurs in reaction (18). A non-empirical calculation of the cross-sections of the energy surfaces for the NNO^+ system has indeed shown[70] that in the initial and final pathways with a linear configuration the initial reactants and products repel one another ($^4\Sigma^-$ states). Possibly these two states are interconverted at short interatomic distances. The trajectory along the reaction pathway in an adiabatic mechanism (Fig. 9) requires that an activation barrier be overcome. The non-adiabatic pathway $^4\Sigma^- \rightarrow {}^2\Pi \rightarrow {}^4\Sigma^-$, in which the multiplicity of the system changes twice, can in principle compete with the above pathway. In this reaction mechanism the increase of the cross-section with the energy in the region of low energies can be explained by the existence of a small potential barrier at the point of intersection of the $^4\Sigma^-$ and $^2\Pi$ states in the initial pathway. After the N_2O^+ system has passed to the bonding state $^2\Pi$, it decomposes almost exclusively to the final state by a non-adiabatic transition at another point of intersection of the $^2\Pi$ and $^4\Sigma^-$ states[70].

With increase of the energy, the attainment of the region of the quasi-intersection of the $^4\Sigma^-$ states becomes possible. In this region the increase of the cross-section can be simply related to the increase of the transition probability with increase of E_{transl} and E_{vibr}. A rational calculation of the probability is possible only when the dynamic problem is solved. Since, however, the surface in this region is unknown, O'Malley[71] suggested that the system follows mainly the diabatic states and that the transition probability can be estimated by means of the first order perturbation theory in terms of the interaction corresponding to the quasisplitting. The change in the NN bond length is treated as the coordinate of the diabatic motion. In this case the profile of the reaction pathway has the form of a parabolic potential (the initial diabatic term corresponding to the N_2 vibrations), which is intersected by a monotonically decreasing potential (the final diabatic term describing the relative motion of N and NO^+) (Fig. 10). Within the framework of this one-dimensional model, the reaction probability $P(E_{transl}, E_{vibr})$ is proportional to the square of the overlap of the vibrational eigenfunctions and the wavefunctions for the continuous spectrum. For very low (thermal) energies, the overlapping of the functions of the vibrational ground state and those of the continuous spectrum is so slight that the entire diabatic mechanism is masked by the non-adiabatic mechanism $^4\Sigma^- \rightarrow {}^2\Pi \rightarrow {}^4\Sigma^-$.

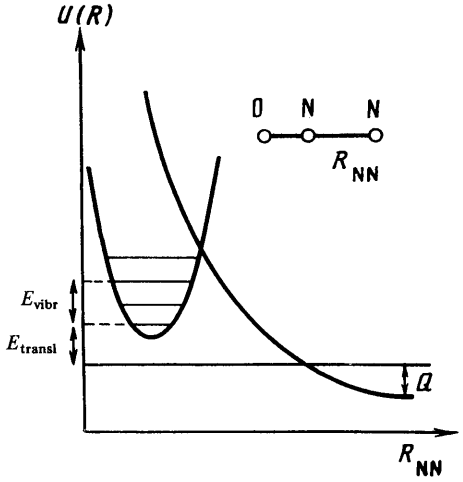

Figure 10. Illustration of the non-adiabatic mechanism of the reaction $O^+ + N_2 \rightarrow NO^+ + N$.

With increase of E_{vibr}, the overlapping will also increase and this is reflected in a sharp increase of the cross-section as a result of the contribution of the diabatic mechanism. On the other hand, the overlapping also increases with increase of E_{transl}. In the ground vibrational state, the cross-section reaches a maximum for values of E_{transl} such that the parabolic term intersects the repulsive term in the region of the minimum of the former. Finally, for a fixed E_{transl}, this mechanism predicts a less marked increase of the cross-section with

increase of E_{vibr} the higher the value of E_{transl}. All these conclusions, based on a simple model, were confirmed experimentally[72,73], which throws doubt on the adiabatic direct dislodgement mechanism put forward by Golubkov and Ivanov[74].

The mechanism of reaction (18) discussed above makes it possible to understand why the isotope exchange reaction

$$N'(^4S) + N_2(^1\Sigma_g) \rightarrow N'N(^1\Sigma_g) + N(^4S)\,, \qquad (19)$$

which is isoelectronic with reaction (18), occurs very slowly if at all[75]. Despite the existence of the stable complex N_3, transition to the latter is probably forbidden by the spin. On the other hand, isotope exchange reactions such as

$$\begin{aligned} O' + O_2 &\rightarrow OO' + O\,, \\ O' + CO &\rightarrow CO' + O \end{aligned} \qquad (20)$$

are very rapid: the first proceeds on the singlet surface of the O_3 ground state and the second on the triplet surface of CO_2. In many cases, for example for the reaction

$$N + NO \rightarrow N_2 + O\,, \qquad (21)$$

it is at present still impossible to interpret the mechanism unambiguously in view of the competition between the adiabatic and non-adiabatic pathways[76]. In general one may expect that, in reactions involving C, N, and O atoms and ions, non-adiabatic mechanisms should be extremely common (see, for example, Tully et al.[77] in connection with the reaction $N^+ + O_2 \rightarrow NO^+ + O$).

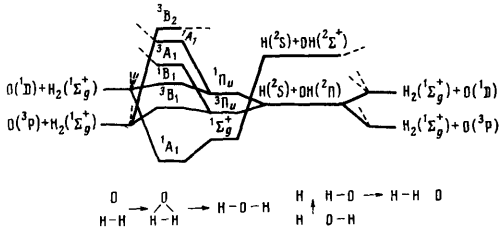

Figure 11. Correlation diagram for the electronic states of the reaction $O + H_2 \rightarrow OH + H$.

A dependence of the rate constant on the spin–orbit interaction in a number of similar reactions might constitute direct proof of a non-adiabatic mechanism infringing Wigner's rule. Unfortunately the activation energy also varies in many such series, so that it is fairly difficult to isolate the pure effect of the spin–orbit interaction. A reaction of the type

$$O(^3P) + HX(^1\Sigma) \rightarrow OH(^2\Pi) + X(^2P)\,, \qquad (22)$$

where X = Cl, Br, or I atoms, may be quoted as the only example which probably indicates the involvement of spin–orbit interaction[78]. Although formally there exists an adiabatic pathway along a triplet surface for these reactions, the correlation diagram for the states shows[79] that in the case of the non-linear configuration OHX the singlet surface lies below the triplet surface on the product side and the preferred reaction pathway at low temperatures involves a transition from the triplet surface $^3A'$ to the singlet surface $^1A'$. The transition probability for a fairly weak spin–orbit interaction is proportional to the square of the perturbation, which is determined by the fine splitting of the $^2P_{1/2}$ and $^2P_{3/2}$ states of the atoms X.[79] Thus the theory predicts a quadratic increase of the pre-exponential factor with increase of the splitting of the ^2P state, which is in qualitative agreement with experiment. For a more detailed investigation of the mechanism of reactions (22), it is necessary to have information about the details of the potential energy surfaces.

From this standpoint, the most complete information is available about the energy surfaces for the $O(^3P)$, $O(^1D) + H_2(^1\Sigma_g^+)$ system[80,81] (Fig. 11).

The study of the possible reaction pathways has shown that, although in the linear configuration the abstraction reaction

$$O(^1D) + H_2(\Sigma_g^+) \rightarrow OH(^2\Pi) + H(^2S) \qquad (23)$$

has a comparatively high activation energy (about 25 kcal mole^{-1}), there is probably no barrier for non-linear collisions. This instance of abstraction can be represented as decomposition of the vibrationally excited H_2O molecule in its ground electronic state, formed when $O(^1D)$ is inserted in the H–H bond. On the other hand, the abstraction reaction on the triplet surface,

$$O(^3P) + H_2(^1\Sigma_g^+) \rightarrow OH(^2\Pi) + H(^2S) \qquad (24)$$

has a potential barrier for all the configurations. If the $O(^3P) + H_2$ system reaches the line of intersection of the triplet and singlet surfaces before the region of the saddle point on the triplet surface, then, providing there is a fairly high transition probability, reaction (24) would occur without a change in spin. However, this probability is low for the H_2O molecule, as shown, in particular, by studies on the reaction

$$O^+(^4S) + H_2(^1\Sigma_g^+) \rightarrow OH(^2\Pi) + H^+ \qquad (25)$$

in molecular beams[82]. It has been found that reaction (25) proceeds via the direct mechanism, i.e. the H_2O^+ complex is not formed in the ground electronic state (Fig. 12).

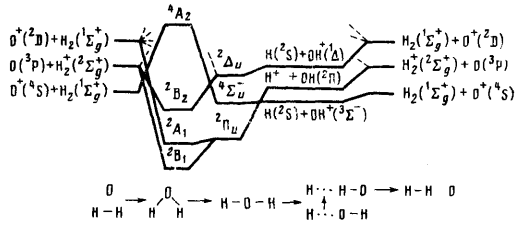

Figure 12. Correlation diagram for the electronic states of the reaction $O^+ + H_2 \rightarrow OH + H^+$.

For reactions involving heavier atoms, the spin–orbit interaction can be sufficiently strong to induce transitions between surfaces of different multiplicity [as happens in reaction (22)]. In this connection we may point to the reaction

$$O(^3P) + Br_2(^1\Sigma) \rightarrow OBr(^2\Pi) + Br(^2P)\,, \qquad (26)$$

which was recently investigated by the molecular beam method[83]. The angular and energy distribution of the

products shows that the reaction proceeds via the formation of the long-lived complex OBr_2. However, this complex can be formed only in its singlet state, so that the dynamic characteristics of the reaction show directly that the mechanism is non-adiabatic. A non-adiabatic mechanism should also be expected for reactions of excited oxygen atoms (see, for example, Pravilov and Vilesov's review[84]).

5. NON-ADIABATIC IMPACT DISSOCIATION

The impact dissociation of molecules BC in reaction (1) is understood as decomposition as a result of a single A + BC collision step. In this respect impact dissociation differs from thermal decomposition, which occurs as a result of many consecutive collisions of BC with the atoms or molecules of the heat reservoir. Many thermal non-adiabatic decomposition processes of triatomic molecules have now been studied[43] together with certain processes involving the thermal non-adiabatic decomposition of diatomic molecules into ions[85-87]. All these processes proceed via the stage of spontaneous non-adiabatic decomposition of an isolated molecule in the state which it attains after excitation. In this respect thermal non-adiabatic decomposition processes are analogous to processes involving spontaneous predissociation of molecules[88]: the only difference between them merely involves the excitation mechanism (by collision or by absorption of light), which has no direct bearing on decomposition.

In non-adiabatic impact dissociation the transitions take place between the potential energy surfaces of the system ABC and not between the terms of an isolated diatomic molecule BC, so that the excitation and decomposition cannot be treated independently.

Among all the non-adiabatic impact dissociation processes, the simplest is the predissociation of diatomic molecules induced by collisions. Molecules in an excited vibrational level of a bound excited electronic state, whose surface intersects that of the antibonding electronic state, usually undergo induced predissociation. If these states differ in parity or symmetry relative to reflection in the plane passing through the nuclei of BC, then spontaneous predissociation is impossible. Transitions between these states are induced by an external perturbation, which removes a corresponding symmetry operation of the Hamiltonian of an isolated molecule.

The induced predissociation of iodine in the $B^3\Pi(0_u^+)$ state has been investigated in greatest detail (see Mulliken[89] and the references quoted therein). The interpretation of the I_2 spectrum[89] and also non-empirical asymptotic calculations[90] yield the following pattern of states. The $0_u^+(B^3\Pi)$ state, which correlates with the $^2P_{1/2}$ and $^2P_{3/2}$ atomic states, is crossed by the $3_u(^3\Delta_u)$, $0_u^-(^3\Sigma_u^+)$, $0_g^+(^3\Sigma_g^-)$, $1_g(^3\Pi_g)$, and $2_g(^3\Pi_g)$ states on the side of the dissociation limit and by the $1_u(^1\Pi_u)$ and $0_u^-(^3\Pi_u)$ states on the side of the repulsive limb (all these states are correlated with the atomic states $^2P_{1/2}$ and $^2P_{3/2}$). The intersection with the 1_u state is responsible for the spontaneous dissociation of I_2 and the intersection with the states $0_u^-(^3\Sigma_u^+)$ and $0_u^-(^3\Pi_u)$ is responsible for the predissociation induced by the magnetic field; the intersection with the 0_g^+ state probably makes the main contribution to the predissociation induced by collisions. If it is supposed that the perturbing effect of the third particle reduces solely to the removal of the prohibition of the transition between the states†, which should now be regarded as diabatic from the standpoint of the classification adopted here, and that the transition probability is low, then the dissociation rate constant k should be correlated with the average parameter $2\pi a^2/\hbar|F_{1R} - F_{2R}|v_R$ in Eqn. (4). Calculations show that, for a fixed vibrational state of I_2, the constant k is proportional to $\alpha_A^2 R_0^{-9}$, where α_A is the polarisability of the other species A involved in the I_2 + A collision and R_0 is the gas-kinetic radius of the pair (in one of the earlier studies[92] it was erroneously suggested that k be correlated with the parameter $I_A\alpha_A\mu^{1/2}R_0^{-3}$). The available experimental results confirm this correlation.

However, this type of treatment is not sufficiently general, since no account is taken of the perturbing effect of the A species on the motion of the I atoms. Allowance for this perturbing effect in fact implies the solution of the dynamic three-particle problem, which was recently investigated within the framework of the classical[93] and semiclassical[94] approximations without taking into account non-adiabatic transitions.

Whereas the phenomenon of induced predissociation has been known for a comparatively long time, the study of non-adiabatic impact dissociation of molecules, which are in the lowest vibrational states before collision, is only just beginning. These processes include the dissociation of the salts NaBr,[95] CsI,[96] and TlX [97,98] (X = halogen atom) into ions in collisions with inert gas atoms and also the dissociation of the molecules X_2 in collisions with caesium[99] and potassium[100-103] atoms. The competition between the different possible non-adiabatic channels was also investigated for the latter processes[102,103]:

$$M + XY \rightarrow \begin{cases} M^+ + XY^- \\ M^+ + X + Y^- \\ M^+ + X^- + Y, \end{cases} \qquad (27)$$

(here M is an alkali metal atom and X and Y are halogen atoms). For relative kinetic energies exceeding the thresholds of the chemi-ionisation processes (27), these channels are the main ones and the competing exchange association processes involving the formation of neutral products,

$$M + XY \rightarrow \begin{cases} MX + Y \\ MY + X \\ M + X + Y, \end{cases} \qquad (28)$$

are comparatively ineffective. The main characteristics of the dynamics of reaction (27) and (28) can be explained qualitatively by the electronic harpooning mechanism[1]. Within the framework of this concept, two functions of the rough adiabatic basis—the function of the covalent state ψ_c (M + X_2 system) and the function of the ionic state ψ_i ($M^+ + X_2^-$) system‡—are adduced in the description of the reaction. Two potential energy surfaces correspond to these wavefunctions—the covalent (U_c) and ionic (U_i) surfaces. If the energy of the unbound system M + X + X is adopted as the starting point of the calculation, then, for large distances R between M and the centre of gravity of XX, the potentials U_c and U_i are

$$U_c = c(r, \gamma)/R^6 + \ldots$$
$$U_i = [I_M - A_{X_2}(r)] - e^2/R + \ldots \qquad (29)$$

† In terms of this approximation, the induced predissociation of diatomic molecules is analogous to the radiationless transitions induced by collisions in polyatomic molecules[91].

‡ For simplicity, the case where X = Y will be considered henceforth.

(where r is the internuclear distance in XX, γ is the angle between the vectors **r** and **R**, and $A_{X_2}(r)$ is the electron affinity of XX). The U_c and U_i surfaces intersect along a line given by the following equation when all interactions other than Coulombic are neglected:

$$e^2/R = I_M - A_{X_2}(r) \ . \qquad (30)$$

If account is taken of the interaction between the covalent and ionic states, the intersection is replaced by a quasi-intersection, so that the line defined by Eqn. (30) gives the location of the region of the possible non-adiabatic coupling. The minimum splitting between the states is equal to twice the matrix element of the interaction

$$V_{ic} = C(R, r, \gamma)\exp[-(A_{X_2}(r)/I_n)^{1/2} \cdot R/a_0]\cos^2\gamma \ . \qquad (31)$$

The variation of V_{ic} with the coordinates is specified mainly by the last two multipliers of this expression, which depend on their arguments to a greater extent than does the coefficient $C(R_r, \gamma)$.[104] A characteristic feature of the interaction is the equality of V_{ic} to zero when $\gamma = \pi/2$, i.e. when MX_2 has the configuration of an equilateral triangle. This corresponds to the familiar case of the conical intersection of the states[4,7].

In the products channel the interaction between the states rapidly attains its asymptotic value corresponding to the interaction of the covalent and Coulombic states of an isolated molecule. In terms of the coordinates R_{MX} and R_{XX}, the line of the quasi-intersection in the products channel,

$$R_{MX} = R^0_{MX} \ , \qquad (32)$$

on which the splitting of the adiabatic terms is constant, becomes straight.

In the region of strong interaction of all three particles, the line of the quasi-intersection, defined by Eqn. (30), is continually converted into the straight line defined by Eqn. (32). The position of this line and the general characteristics of the two lowest U_c and U_i surfaces for the collinear configuration of the M + X + X atoms are illustrated in Fig. 13. As in the previous Figures, the inserts show the cross-sections of the lowest (continuous lines) and highest (dashed line) adiabatic surfaces. The quasi-intersection line is represented by a continuous curve in the output channel in conformity with the fact that, for energies such that chemi-ionisation is possible, the system in this channel is characterised by diabatic behaviour (the trajectory of the representative point does not cross the continuous line). In the initial channel, part of this line is shown dashed (there is an appreciable probability of adiabatic motion of the system), which when produced yields the limit of the sharp descent on the adiabatic surface. In this region non-adiabatic transitions are unlikely, since the splitting of the states is large.

Various approximations for the description of the energy surfaces of the ground state of the MXX system are now known[105-108] and also semiempirical[109] and non-empirical calculations have been made for the simple LiFF system[110,111].

The dynamics of adiabatic reactions (28) was investigated in a series of studies with an exact solution of the classical dynamic problem[105-108,112], as well as within the framework of simplified approaches[113,114]. The qualitative dynamic pattern corresponds to the vertical transition $X_2(r) \rightarrow X_2^-(r)$ in the field of the ion M^+ retained in the vicinity of X_2^- by Coulombic attraction ("the electron harpoon"). The stripping mechanism with participation of the spectator[1], which was proposed in earlier investigations and was shown by subsequent investigations, not to be fully justified, constitutes the limiting simplification of the mechanism described above.

The relevant studies on the dynamics of non-adiabatic reactions (27) are only just beginning. Important information about the variation of the adiabatic terms can be derived from the study of non-elastic and atomic collisions accompanied by the formation of ions[115-117]:

$$M + X \rightarrow M^+ + X^- \ . \qquad (33)$$

In particular the matrix element for the interaction between the ionic and covalent terms[116], which determines the oscillatory structure of the differential cross-section of reaction (33), can be estimated in this way. The interpretation of the differential cross-section of the reaction involving charge transfer to the molecule [the first reaction (27)] is more difficult, since it is then necessary to take into account the effect of the rotation and vibration of the molecule X_2. It is found that the characteristics of the differential cross-sections can be understood if rotation alone is taken into account[118].

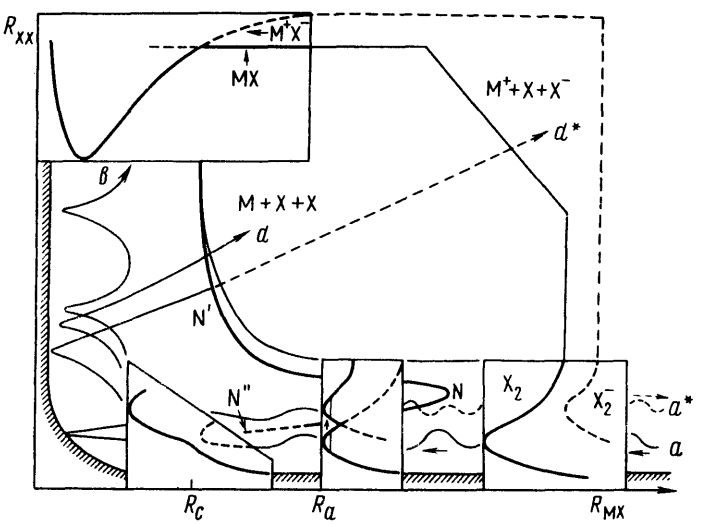

Figure 13. Schematic illustration of the potential energy surface for the collinear system MX_2.

However, the energy dependence of the total charge-transfer cross-section near the threshold depends significantly on the vibrations of X_2. The experimental threshold for the formation of the ion is equal to the difference between the ionisation potential of M and the adiabatic electron affinity A_a of the molecule X_2. This is at first sight inconsistent with the hypothesis of the vertical transition $X_2 \rightarrow X_2^-$ leading to the formation of ions subjected to a strong vibrational excitation. The non-vertical transition corresponding to the affinity A_a also corresponds to the transition between the potential minima of X_2 and X_2^-. This is possible, for example, as a result of tunneling between two potential wells (the potentials of the X_2 and X_2^- vibrations) for distances between the reactants such that the energy levels of the ground vibrational states in the diabatic potentials of the molecule and ion are the same. This transition, occurring when $R \simeq R_a$,

is indicated by an arrow in Fig. 13. Its probability is proportional to the Franck-Condon factor $S_{00}[X_2(v = 0) \rightarrow X_2^-(v = 0)]$ and determines the cross-section directly above the threshold. The energy dependence of the cross-section should be correlated with the variation of the overlap integrals S_{0v} with the number v of the vibrational level of X_2^-, which may be excited on electron transition[119].

However, it is possible to put forward also another mechanism to account for the threshold variation of the cross-section[120-121]. According to this mechanism, involving the classical approximation, the trajectory follows the minimum in the reactant valley (the initial trajectory a), reaching a sharp break in the states at $R \simeq R_C$ in the region of the quasi-intersection of the covalent and ionic states [the coordinate of the break R_C corresponds to the vertical transition $X_2 \rightarrow X_2^-$ when the reactants approach one another, and is determined from Eqn. (30) in which one must put $r = r_e$]. After reaching the break, the trajectory corresponds to the extension of the bond in the ion X_2^-, i.e. to the onset of dissociation of the ion. However, before this process reaches completion the collision of M^+ with one of the atoms of X_2^- leads to marked deactivation of X_2^- as a result of which the ion loses energy and M^+ is strongly accelerated. The ion M^+ begins to move along the reactant valley in the opposite direction and can intersect the line N'NN" of the quasi-intersection of the surfaces in the region where the motion is almost diabatic. The final result of such collision (the trajectory a^* corresponding to the highest state) is the formation of the ions M^+ and X_2^-, the reaction threshold being determined by the adiabatic electron affinity of X_2 despite the fact that the electron transition is a vertical process. This mechanism predicts a correlation between the energy dependence of the cross-section and the probability of the deactivation of the ion X_2^- on collision with M^+ as a result of the brief exchange interaction. Naturally, elucidation of the true mechanism of the formation of ions requires a more thorough investigation of the collision dynamics.

With increase of the energy above the molecular ion formation threshold, the atomic ion formation threshold is reached. One of the trajectories (trajectory d^*) leading to such products is illustrated in Fig. 13. The velocity along the quasi-intersection line N'N is so high that the probability of the non-adiabatic transition is close to unity. Under these conditions, the formation of neutral atoms in adiabatic dissociation (trajectory d) and of neutral molecules in adiabatic exchange (trajectory d) is unlikely.

Possibly a large number of surfaces must be adduced in order to refine further the mechanism of such reactions. This is indicated by the results of a study of processes involving the formation of the products $X + Y^-$ and $X^- + Y$ in reaction (27).[103] Moreover, if one is dealing with impact dissociation under the influence of an inert atom (for example the reaction $TlCl + Ar \rightarrow Tl^+ + Cl^- + Ar$), then it is absolutely essential to take into account several potential surfaces for a correct interpretation of the experimental results.

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The Chemisorption of Oxygen on Group IB Metals and Their Surface Oxidation

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The modern views on the kinetics and mechanism of the chemisorption of oxygen on group IB metals and their surface oxidation (up to the appearance of an oxide phase) are described. Processes occurring in the temperature range from 0° to 300-400°C, which are of interest in connection with problems of catalysis and radioelectronics, are mainly considered. The bibliography includes 123 references.

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I. INTRODUCTION

Group IB metals are catalysts of mild, partial oxidation[1,2]. Catalytic oxidation processes are usually regarded as occurring in stages and it is believed that one of the stages is chemisorption of oxygen[1-4]. The overall rate of the catalytic process on metallic catalysts in general and on group IB metals in particular usually depends significantly on the rate of adsorption of oxygen[5]. This is one of the reasons why much attention is being devoted to the study of the kinetics and mechanism of the chemisorption of oxygen on copper, silver, and gold. Another reason is the requirement for pure materials in the radioelectronics industry[6] and the consequent necessity for assessing the possible contamination of the metals by oxygen under various conditions and also for assessing the effect of the chemisorption of oxygen on the properties of the finished articles. The third reason for studying the above processes is the effect of small amounts of oxygen on various mechanical characteristics such as creep (see, for example, Ostrovskii et al.[7]), strength (see, for example, Gupta[8] and Ahlers[9]), the self-diffusion coefficient (see, for example, Cabane[10]), etc. The chemisorption of oxygen on gold is also of special importance in connection with the problem of reference electrodes in measurements of the changes in contact potentials during the adsorption of oxygen on various surfaces.

II. CERTAIN CHARACTERISTICS OF THE SURFACE INTERACTION OF COPPER, SILVER, AND GOLD WITH OXYGEN

The phase interactions of copper, silver, and gold with oxygen differ sharply in the thermodynamic sense. Table 1 presents the standard free energies of formation ΔG_{f_0} and the standard heats of formation ΔH_{f_0} of copper, silver, and gold oxides from the elements, both at 25°C.[11] It follows from the table that, in the temperature range considered, the metal-oxygen equilibrium involving copper is sharply displaced towards the formation of the oxide and in the case of gold towards the metal. The equilibrium position for silver depends on the oxygen pressure and temperature. Thus the equilibrium oxygen pressure over Ag_2O at 201°C is 1.526 atm, while at 174°C it amounts to 0.596 atm.[12] Nevertheless oxygen is chemisorbed on the pure surfaces of all the metals considered even at pressures much lower than 1 mmHg. The problem of the chemisorption of oxygen on gold remained open for a long time. It had been concluded[13] that oxygen is not chemisorbed, but subsequently it was shown[14] that the method of measurement used in the earlier study[13] was insufficiently sensitive. The widely held view that oxygen is not chemisorbed on gold was also supported by other results[15,16], where the degree of adsorption was not measured directly but it was observed that the electronic work function of gold does not change when the latter is in contact with oxygen at room temperature. However, it was shown later[17-22] and also in earlier studies[23,24] that gold in powder form[18,19,22-24] and in the form of a wire[17], films[20], and foil[21] can chemisorb oxygen.

Table 1. Thermochemical parameters of the oxidation processes.

Oxide	State	ΔH_{f_0}, kcal mole^{-1}	ΔG_{f_0}, kcal mole^{-1}	Remarks
CuO	crystalline	−37.1	−30.4	See also Refs.37 and 38
Cu_2O	ditto	−39.84	−34.98	See also Refs.37 and 38
Ag_2O	»	−7.31	−2.59	See also Ref.12
Ag_2O_2	»	−6.3	—	
Au_2O_3	»	19.3	39.0	

For many years it was not established reliably whether or not oxygen is chemisorbed on gold, since studies of the chemisorption of oxygen on group IB metals encounter a number of the difficulties described above, one of which is common to many metals and others are specific to the metals of the given Group.

1. The presence of admixtures of light elements, in the first place hydrogen and oxygen, and also of catalyst and

adsorption poisons such as sulphur, chlorine, etc. Oxygen may be present owing to the contact of the specimen with air before its introduction into the apparatus or as a result of its contact with the residual gas in the evacuated apparatus. In order to remove oxygen from copper[25], silver[26-28], or gold[19], prolonged treatment by heating with hydrogen or carbon monoxide is necessary. However, there is then a risk of the contamination of the surface layer of the specimen with hydrogen or carbon. At the same time the presence of oxygen on the surface lowers the degree and the initial rate of its adsorption and the presence of hydrogen can lead to an unduly high value of the observed degree of adsorption, since some of the oxygen is consumed in the oxidation of hydrogen. The presence of very small amounts of catalyst poisons as impurities on the surface can also alter its adsorption properties[29,30]. It is then necessary to take into account the ability of many non-metallic impurities in metals to migrate rapidly towards the surface[31-34].

2. The presence of small amounts of impurities comprising other metals. For example, it is known that the addition of very small amounts of nickel to copper sharply enhances its catalytic properties[35], while mercury vapour can alter sharply the adsorption and other properties of gold[36].

3. The possibility of the oxidation of lubricant vapour during the experiments on the adsorption of oxygen[19]. An impression may be created that oxygen is adsorbed to a greater extent than is in fact the case if one does not take into account the fact that part of it is consumed in the formation of water and carbon dioxide. The physical properties of the adsorbent such as the electron work function, electrical conductivity, etc. can also change as a result of the oxidation of the lubricant on the surface.

The need to work under the conditions of high purity leads to a sharp decrease of the specific surface. This imposes more stringent requirements for the purity of the adsorbant and gas employed and for the sensitivity of the method of measurement.

III. KINETICS OF THE PROCESSES

Here we shall consider mainly adsorption and surface oxidation, where the rate of absorption of oxygen is limited by adsorption and not by diffusion in the solid specimen. These processes can occur under different conditions. Such an approach makes it possible to assess the magnitude of the adsorption rate constants. These constants are needed in the derivation of kinetic equations for heterogeneous catalytic oxidation processes involving a mechanism comprising a number of stages and also for the calculation of the degree of contamination of the test metals by oxygen under the conditions of contact with the latter.

1. The Copper–Oxygen System

Above 0°C, copper can sorb irreversibly more than one monolayer of oxygen. Even at −195°C a very thin oxidised layer is formed on copper as a result of the chemisorption of oxygen[39]. This implies that the process is not limited to chemisorption alone, but that oxygen can penetrate also deeper layers of the metal. Thus the rate of sorption of oxygen can depend on at least two processes: the adsorption process proper as a result of which oxygen appears on the surface and another process leading to the generation of copper atoms on the surface capable of adsorbing new portions of oxygen. On contact between copper and oxygen, an induction period is initially observed, during which the formation of the oxide phase cannot be observed on the surface with the aid of the electron microscope[40]. During this period, oxygen is adsorbed and dissolved in the metal phase. The solubility of oxygen in the massive metal (s, in parts per million) up to 750°C is given by the equation[41]

$$\lg s = 2{,}2875 - (956.4/T). \qquad (1)$$

Solubilities close to those given by Eqn. (1) have been published[42]. The standard enthalpy of solution of oxygen in copper $\Delta H^{\circ}_{298} = -10$ kcal mole^{-1} [43] and the free energy of the process up to 750°C can be calculated from the equation $\Delta G = 4360 \pm 14.18\,T$.[41]

The appearance of nuclei of the oxide phase with dimensions less than 100 Å can be observed on the copper surface at the end of the induction period. Copper(I) oxide or Cu_2O_3, which has the structure of the former with a large number of defects, are mainly formed at temperatures up to 600–800°C.[44-47] At higher temperatures copper(II) oxide is also produced[48,49].

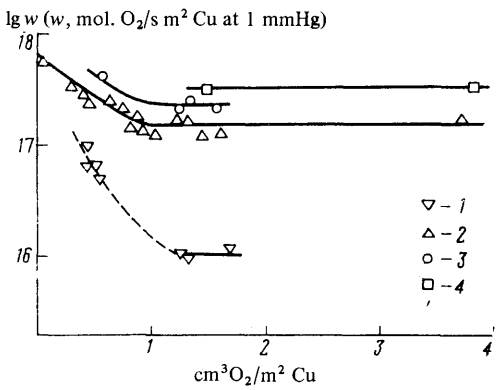

Figure 1. Variation of the rate of sorption of oxygen by copper with the degree of oxidation at different temperatures[18,50] (°C): 1) 55; 2) 105; 3) 125; 4) 135.

There have been comparatively few studies on the rate of adsorption of oxygen in the stages corresponding to the very beginning of the oxidation. Table 2 presents the results of those where measurements were made of the rate per unit surface of the specimen. It also includes the results of the determination of the activation energy. The kinetics of the earliest stage in the sorption of oxygen by copper have been investigated[18,50]. The preliminary reduction of the copper(II) oxide powder was carried out for 190 h at 300–330°C, with subsequent evacuation for 80 h at 350–400°C. Fig. 1 shows results from the study of the dependence of the rate of oxygen sorption on the degree of oxidation at different temperatures. Oxygen was admitted in portions at an initial pressure of 0.13 mmHg. The kinetics of the sorption of oxygen are described by the equation

$$r_i = 4.1 \times 10^{23} \sqrt{\frac{T}{273}} \cdot P_{O_2}\, e^{-11800/RT} \qquad (2)$$

Table 2. Kinetic data for the copper–oxygen system.

Temp., range, °C	Rate constant: k, mol. O_2 s^{-1} m^{-2} $mmHg^{-1}$	Rate constant: degree of oxidation σ, cm^3 O_2/m^2 Cu	Activation energy E, kcal $mole^{-1}$	Kinetic equation	Rate of sorption of oxygen, 10^{-15} mol. O_2/s m^2 Cu mmHg	References
50—110[a]			15.5	$r = kP_{O_2}e^{-E/RT}$		61
55—135	$4{,}1\cdot10^{23}\sqrt{\frac{T}{273}}$	1—4	11.5	ditto	10 (55°), 330 (135°), 2000 (extrapolation to 200°), 45 (55°)[c] 350 (125°)[c]	18
55—135	$4{,}6\cdot10^{21}\sqrt{\frac{T}{273}}$	0.6	7.5	»[b]		50
25—200	$1{,}1\cdot10^{22}\sqrt{\frac{T}{273}}$	$0.25 < \sigma < 0.8$	7.3	»	52 (25°)[d] 1900 (150°)[d] 4800 (200°)[d]	51
50—400			5.6 — 5.9		500 (150°)[e]	62
300—600			21.8			44
150—800			21[f]			40
25—200			3.5 [(110)face]			53

[a] Pressure 76 torr. Copper sheet specimen subjected to preliminary oxidation to give a content of about 10 cm^3 O_2/mm^2 Cu.
[b] With decrease of σ from 1.0 to zero, the activation energy and k both fall.
[c] In the range $\sigma < 1.0$ cm^3 O_2/m^2 Cu the rate of adsorption decreases with increase of σ.
[d] In the range $\sigma < 0.2$ cm^3 O_2/m^2 Cu the rate of adsorption decreases with increase of σ.
[e] The average rate of adsorption for adsorption from zero to about 20 cm^3 O_2/m^2 Cu.
[f] Specimen oxidised to give a content of about 35 cm^3 O_2/m^2 Cu.

for degrees of oxidation in the range 1–4 cm^3 O_2/m^2 Cu. On further sorption of oxygen, the kinetics change sharply. When the degree of oxidation σ is less than 1 cm^3 O_2/m^2 Cu, the activation energy and the pre-exponential factor diminish with decrease of the degree of oxidation in such a way that the rate of sorption of oxygen increases at the same time (Fig. 1). Qualitatively similar behaviour was observed in another investigation[51]. The quantitative discrepancies between the results of the two studies[50,51] are probably due to the fact that in the investigation of Shakhovskaya et al.[51] the copper was cleaned in a different way before the oxygen sorption experiments (treatment for several hours at 250°C). The kinetic parameters obtained in the remaining studies whose results are presented in Table 2 are known to refer to surface-oxidised copper specimens which usually contained nuclei of the oxide phases.

The effective activation energies listed in Table 2 for such cases were influenced by diffusion phenomena; these results will be discussed in the section on the mechanism of oxygen sorption. At the end of the induction period the kinetics for the surface-oxidised specimens are no longer described by a simple equation of type (2) and as a rule the process is treated within the framework of the theory of Cabrera and Mott[52], although this does not account for a number of the observed phenomena and relations, for example the discontinuity of the oxidised layer, the differences between the rates of oxidation on different crystal faces, etc.[42] According to the kinetic measurements of Ostrovskii and Kalistratova[50], up to the sorption of 4 cm^3O_2/m^2 Cu (2.5×10^{19} mol./g Cu) the rate of sorption is proportional to the oxygen pressure (the specific surface of copper was 0.3 m^2g^{-1}). This suggests that in these experiments the diffusion of oxygen did not limit the rate of the process, i.e. oxygen was sorbed until the instant of the appearance of the oxide phase. In a study[40] on non-porous copper about 35 cm^3 O_2/m^2 (5×10^{16} mol./g Cu) was sorbed during the induction period at 150°C. This value is close to the solubility of oxygen in massive copper. Comparison of the results of Ostrovskii and Kalistratova[50] with those of Ertl[53] shows that porous copper can sorb (per unit weight of the metal) several orders of magnitude more oxygen than massive specimens. However, when the limiting degree of sorption of oxygen, occurring up to the formation of a new phase, is referred to unit surface area, this quantity differs much less. Although the specific surfaces differ by a factor of several thousands, in the case under consideration the degrees of sorption of oxygen referred to 1 m^2 differ by less than an order of magnitude. This is evidence for unusual properties of the surface layer of copper with respect to the sorption of oxygen. The main bulk of the oxygen dissolved in copper at low temperatures is probably located in the layer near the surface.

The rates of sorption of oxygen by different copper faces are different, but not as a rule by more than an order of magnitude. Gwathmey and Lawless[54] and later others[48,50] concluded that the (100) face sorbs oxygen fastest. Jardinier–Offergeld and Bouillom[56] observed the highest rate constant for the sorption of oxygen and the shortest induction period at 511°C for the (111) face. The induction period for the (110) face was longer than for the (111) face and for the (100) face it was longer still. The information available about the relative rates of sorption of oxygen by the (100) and (110) faces is contradictory[56–58]. Since the results were obtained at different temperatures, it may be that the discrepancies are due to marked differences between the activation energies for the sorption of oxygen on different faces[59].

2. The Silver–Oxygen System

Table 1 shows that the decrease of free energy in the oxidation of massive silver under standard conditions is small. In the oxidation of a cryptocrystalline powder the decrease of free energy may be somewhat greater, but, when the crystal size exceeds 10^{15} Å^3, which is usually the case for silver powders of films, comminution has little influence on the equilibrium position. At an oxygen pressure of the order of several mmHg or below only a two-dimensional adsorption structure is observed on the silver

surface[60], but no oxide phase. At temperatures above 0°C silver strongly sorbs considerable amounts of oxygen. Together with chemisorption, oxygen may dissolve in the bulk of the metal. The dissolution of oxygen in massive silver has been investigated[63-66]. The rate of dissolution and the solubility of oxygen are proportional to the square root of pressure. The heat of solution of oxygen in silver is about 12 kcal mole^{-1}.[67,68]

The formation of a monolayer adsorbed on non-porous specimens requires less oxygen than can dissolve in the specimen according to solubility data. However, the corresponding values have comparable orders of magnitude. The volume of oxygen corresponding to the formation of a monolayer on porous specimens can be much greater than the volume corresponding to the solubility, measured per unit weight of massive specimens. Nevertheless there are data[69] showing that, even at an oxygen pressure of about 0.2 mmHg, the decrease of oxygen pressure on contact with silver corresponds to the sorption of several oxygen monolayers. It is believed[69] that the surface layers of silver can sorb additional amounts of oxygen in the tetrahedral vacancies of the crystal lattice. Possibly the sorption of oxygen by the surface layers of copper described above is of the same type. The rate of the process described in the literature[69], which has been called "deep adsorption", is two–three orders of magnitudes lower than the rate of chemisorption of oxygen on silver. For this reason, the experimental rate of chemisorption should not be significantly influenced by this process.

The main results of the studies of the chemisorption of oxygen on silver are presented in Table 3. In selecting the studies quoted in the table the same criteria were applied as in the selection of the studies in Table 2. Comparison of the data in Tables 2 and 3 shows that the rate of sorption of oxygen by silver is two–three orders of magnitudes lower than the rate of sorption by copper. The rates of sorption of oxygen by silver obtained in different studies differ within the limits of a single order of magnitude when the comparison is made at the same temperature and degree of oxidation. Examination of the complete set of investigations of the chemisorption of oxygen on silver lead to the conclusion that three adsorption regions should be distinguished as a function of the degree of oxidation. The adsorption in these three regions is probably described by different kinetic equations. The first region corresponds to a change in the degree of oxidation σ up to 0.10–0.12 cm^3 O_2/m^2 Ag, i.e. within the limits of surface coverage by an oxygen monolayer constructed in such a way that an oxygen atom is bound to two silver atoms (AgS_2O, where Ag^S is a silver atom on the surface). The second region corresponds to $0.12 < \sigma < 0.22$–0.26, i.e. extends up to the adsorption of an oxygen monolayer in which an oxygen atom is bound to one silver atom (Ag^SO or $Ag^S{}_2O_2$). The third region corresponds to the adsorption of a greater amount of oxygen. The absorption in the first region was investigated in greatest detail in three studies[63,70,71], where measurements were made from σ = 0.05 cm^3 O_2/m^2 Ag. Other workers[71,72] described the results of studies on the kinetics in this region obtained at a pressure of about 10^{-2} mmHg, in terms of an equation of the type

$$r = Ce^{-b\Gamma}Pe^{-E/RT}, \qquad (3)$$

where $C = 10^{-9}$ mole s^{-1} cm^{-2} and $b \simeq 2.6 \times 10^{10}$ cm^2 mole^{-1} at 20°C. The rate of adsorption is proportional to the pressure. According to Temkin and Kul'kova[69], the activation energy for adsorption in this region is 7–8 kcal mole^{-1}, increasing to 10 kcal mole^{-1} when σ = 0.135 cm^3 O_2/m^2 Ag. According to other results[70], the activation energy depends in a complex way on temperature and on the degree of oxidation. The adsorption in the second region has also been studied[28,70]. According to the present author's results[28], the adsorption kinetics in the range $0.14 < \sigma < 0.21$ are described by the simple equation

$$r = kP(1-\theta)\cdot e^{-E/RT}, \qquad (4)$$

where $\theta = 0$ when σ = 0.13 cm^3 O_2/m^2 Ag and $\theta = 1$ when σ = 0.26 cm^3 O_2/m^2 Ag and $k = 7 \times 10^{11}$ mol. O_2 s^{-1} cm^{-2} mmHg^{-1} at 110°C. The activation energy for adsorption in this region, estimated[28] from the theory of the absolute rates of heterogeneous reactions[72], is 12 kcal mole^{-1}. In the third region the rate of adsorption is limited by surface diffusion[70] or diffusion in the surface layer[69]. The activation energy for the adsorption of oxygen is 22–29 kcal mole^{-1}.[70,73]

Table 3. Kinetic data for the silver–oxygen system.

Temp., range, °C	Rate constant: k, mol. O_2 s^{-1} m^{-2} mmHg^{-1}	Rate constant: Degree of oxidation σ, cm^3 O_2/m^2 Ag	Activation energy E, kcal mole^{-1}	Kinetic equation	Rate of adsorption of oxygen, 10^{-15} mol. O_2/s m^2 Ag mmHg	References
180—300			22 ÷ 29			73
100			3; 8; 22[a]		5 (100°, σ=0.10) 1 (100°, σ=0.18)	70
132—218			13[b]			79
23—200		0.03—0.08	8.2; 7.5; 10.2[c]	$r = Ce^{-ab}$ [d] (in the range $0.03 < \sigma < 0.08$)	6 (100°, σ=0.05) 1 (100°, σ=0.08) 0.25(100°, σ=0.25)	71
110	$7\cdot10^{15}$	0.13—0.21	12[e]	$r = kP(1-\theta)$[f] (in the range $0.145 < \sigma < 0.21$)	0.72(110°, σ=0.13) 0.36(110°, σ=0.18)	28
20		0.05—0.13		$r = Ce^{-ab}$ (in the range $0.05 < \sigma < 0.09$)	1 (20°, σ = 0.11)	80

a 3 kcal mole^{-1} is the activation energy for the adsorption of oxygen in the form of charged atoms, 8 kcal mole^{-1} is the activation energy for the adsorption of oxygen in the form of charged molecules, and 22 kcal mole^{-1} is the activation energy for surface migration.
b The activation energy for conduction in the silver film in contact with oxygen.
c 8.2 kcal mole^{-1} for σ = 0.09, 7.5 kcal mole^{-1} for σ = 0.10, and 10.2 kcal mole^{-1} for σ = 0.135.
d a and b are constants.
e Calculated using the theory of absolute reaction rates following Temkin[72].
f $0.1 < \theta < 1.0$; $\theta = 0.1$ when σ = 0.143 and $\theta = 1.0$ when σ = 0.26.

The rate of adsorption of oxygen and the maximum degree of adsorption are significantly influenced by the presence of electronegative elements as impurities in the silver. Thus 25% surface coverage of silver by chlorine reduces the rate of subsequent adsorption of oxygen[30] and surface coverage by sulphur even to the extent of several percent greatly reduces the degree and rate of adsorption of oxygen[29,74]. A theory of these phenomena has been discussed from the standpoint of the effect of mutual influence in chemisorption[75]. With the aid of added sulphur,

chlorine, selenium, and tellurium labelled with radioactive isotopes, it was established[31-33,76] that admixtures of electronegative elements (10^{-4}–10^{-1} at.%), uniformly distributed throughout the bulk of silver, diffuse to the surface during the pelleting of the catalyst at 200–300°C. Therefore, even when the concentration of the impurities is of the order of 10^{-3} at.% with respect to the specimen as a whole, the surface concentration can be of the order of several per cent, which, as stated above, influences significantly the adsorption of oxygen.

The total amount of oxygen which can be sorbed by pure silver per unit surface area is about one order of magnitude less than the amount of oxygen which can be sorbed by copper. At the same time oxygen hardly oxidises silver at pressures below 100–200 mmHg, but diffuses fairly rapidly through it. Therefore diffusion through silver can be used for the thorough separation of small amounts of oxygen[7] from hydrogen, nitrogen, and the inert gases, which are not adsorbed on silver.

Table 4. Kinetic data for the gold–oxygen system.

Temp., range, °C	Rate constant: k, mol. O_2 s^{-1} mm^{-2} $mmHg^{-1}$	Rate constant: degree of oxidation σ, cm^3 O_2/m^2 Au	Activation energy E, kcal $mole^{-1}$	Kinetic equation	Rate of sorption of oxygen, 10^{-15} mol. $O_2/s\,m^2$ Au mmHg	References
50—400	$4.4\cdot10^{15}$ (120°)	0.015—0.083	3.2		7.3 (120°, σ=0.05) 0.94 (120°, σ=0.08)	17
25—150			~3			14
90—140	$22\cdot10^{15}$ (140°)	0.03—0.091	4.15[a] 10.5[c]	$r=kP(1-\theta)^4\left(\frac{2}{2-\theta}\right)^3$[b]	27 (140°, σ=0.05) 2.9 (140°, σ=0.09)	19
150—380			16÷20[d]		13 (150°, σ=0.06) 0.080(150°, σ=0.23)[e]	22

[a] Estimate obtained with the aid of the theory of absolute rates of heterogeneous reactions for the initial rate of adsorption.
[b] $\theta = 1$ when $\sigma = 0.13$ cm^3/m^2 Au and $\theta = 0$ when $\sigma = 0$; equation valid up to $\sigma = 0.09$.
[c] For $\sigma = 0.20$ cm^3/m^2 Au.
[d] Calculated from the results of the extrapolation of the experimental rates of adsorption for $\sigma = 0.06$–0.23.
[e] Result of the extrapolation of the relation between the rate and degree of adsorption.

3. The Gold–Oxygen System

The solubility of oxygen in gold at 300–900°C is only 5×10^{-4} cm^3 O_2 per gram of gold[78]. This is nevertheless more than the volume of oxygen required to adsorb a monolayer on the surface of 1 g of the massive metal. On the other hand, for porous gold with a specific surface of the order of 0.1 m^2g^{-1} the solubility is orders of magnitude smaller than the volume of oxygen needed to form a monolayer. The chemisorption of oxygen at 100–150°C corresponds to the formation of a surface monolayer with one oxygen atom for each gold atom[19]. Therefore in the study of the chemisorption of oxygen its dissolution can be virtually ignored. The results of the few studies on the kinetics of the chemisorption of oxygen on gold are presented in Table 4, which shows that similar rates of chemisorption are obtained in different investigations[14,19,22] at low surface coverages. The rate is two orders of magnitude lower than the rate of sorption of oxygen by copper at the same temperature and is close to the rate of sorption of oxygen by silver. With increase in the degree of adsorption, the rate of the latter decreases sharply. The adsorption of oxygen on gold containing not more than one silver atom for each 2000 gold atoms has been studied[19]. Thus the adsorption of oxygen on gold cannot be attributed to adsorption on the silver impurity. In order that gold can adsorb oxygen, it is very important to prevent contact with mercury vapour, since otherwise the capacity to adsorb oxygen is lost[36]. Preliminary treatment of gold before the study of the adsorption of oxygen is important, since the adsorbed oxygen and water, present apparently in the form of hydroxy-groups, are removed with much difficulty. Treatment with hydrogen for 100 h at 350°C and then evacuation at the same temperature and for the same period proved convenient for the purification of the adsorbant[19]. The treatment with hydrogen was carried out at low pressures to facilitate the diffusion of the resulting water to the trap where it was frozen out. The activation energy for the chemisorption of oxygen at a low degree of adsorption does not exceed 3–5 kcal $mole^{-1}$ as can be seen from the data in Table 4 and as has been shown by Endow et al.[21] With increase in the degree of adsorption, the activation energy rises[19,21,22]. The kinetics of the adsorption of oxygen up to the sorption of the amount corresponding to about 0.7 of a monolayer are described by the equation

$$r = kP(1-\theta)^4\left(\frac{2}{2-\theta}\right)^3, \qquad (5)$$

where $k = 2 \times 10^{16}$ mol. O_2 s^{-1} m^{-2} at a pressure of 1 mmHg, $\theta = 0$ when $\sigma = 0$, and $\theta = 1$ when $\sigma = 0.13$ cm^3 O_2/m^2 Au. Eqn. (5) was derived[81] for the case where the adsorbate molecule occupies four sites in adsorption on a homogeneous surface. In the adsorption of oxygen on gold this corresponds to the formation of Au_2SO. At a higher surface coverage the rate of adsorption is limited by the rate of rearrangement of the surface oxide layer, the observed activation energy for adsorption increases, and the reaction order with respect to oxygen pressure gradually falls. When the volume of the adsorbed oxygen approaches that corresponding to the formation of a monolayer of the surface oxide AuSO, the rate virtually ceases to depend on the pressure[19].

IV. CHANGES IN CERTAIN PHYSICAL PARAMETERS OF THE METALS DURING THEIR SURFACE OXIDATION

1. Heat of Adsorption

The heat of adsorption of oxygen on copper has been studied using powders[25,82] and films[83,84]. Russell and Bacon[82] observed a slow decrease in the heat of adsorption at 0°C in a Bunsen calorimeter from 92 kcal/mole O_2 with increased degree of adsorption. However, the portions of oxygen used were too large to determine the dependence of the differential heat of adsorption Q_d on the degree of adsorption. Later the variation of Q_d with surface coverage was investigated[83] with the aid of a Beeck calorimeter at 25°C and in another study[25] with the aid of a FOSKA calorimeter[85] at 100–130°C. The results obtained in these two studies[25,83] are presented in Fig. 2. The initial heat of adsorption at 25° and 100°C is about 115 kcal $mole^{-1}$. It then falls to the level of 82–90 kcal/mole O_2. At 25°C the decrease occurs at $\sigma = 0.08$ cm^3 O_2/m^2 Cu and 100°C at a degree of adsorption as low

as $\sigma = 0.04$ cm^3 O_2/m^2 Cu. After this the heat of adsorption remains almost constant both at 25° and 100°C up to the adsorption of a monolayer or a little more. Then at 25°C it falls to 58 kcal mole^{-1} when $\sigma = 1.0$ cm^3 O_2/m^2 Cu.

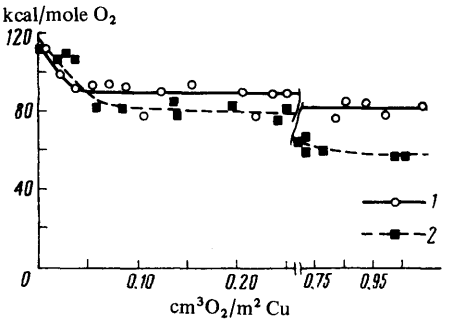

Figure 2. Variation of the heat of sorption of oxygen by copper with the degree of oxidation: 1) to the left of the discontinuity at 100° or 110°C; to the right of the discontinuity at 130°C according to Ostrovskii[25]; 2) at 25°C according to Starostina et al.[80]

It is believed[83] that the decrease is caused by the adsorption of oxygen on a surface layer of copper(I) oxide. At 100–110°C[25] the heat of adsorption decreases to only 82 kcal mole^{-1}, which is equal, within the accuracy of measurement, to the heat of oxidation of copper to the Cu_2O phase (Table 1). Thus at 100–110°C, where the rates of diffusion processes in the copper specimen undergoing oxidation are much higher than at 25°C, the region of enhanced heat of adsorption is narrower than at 25°C and after the oxidation of 1–2 copper monolayers the heat of reaction corresponds to the heat of oxidation to the oxide phase. It has been found that the heat of adsorption of oxygen on a copper film at room temperature is 110 kcal mole^{-1} regardless of the surface coverage[84]. The heat of adsorption of oxygen on silver has been determined calorimetrically[29,86,87] and also from the adsorption-chemical equilibrium involving water vapour[88,89], from the difference between the activation energies for adsorption and desorption[90], and from adsorption isosteres[73]. The results obtained in different studies agree. Fig. 3 presents the results of direct calorimetric measurements[87] at 110°C. Evidently the initial heat of adsorption is about 125 kcal mole^{-1}. Similar values were obtained in studies on the adsorption-chemical equilibrium involving water vapour: 108 kcal mole^{-1} [88] and 115 kcal mole^{-1}.[89] The heat of adsorption corresponding to almost complete monolayer coverage is about 15 kcal mole^{-1} according to Benton and Drake[90], which is close to the value obtained by Kul'kova and Temkin[89]. The isosteric heat of adsorption of oxygen on silver is 21 kcal mole^{-1},[91] and on silver containing 0.08% Ni and 0.13% Cu at oxygen pressures of several hundred mmHg it increases from 17 kcal mole^{-1} as the equilibrium pressure is reduced. For comparison, we may note that the heat of decomposition of Ag_2O is 14.7 kcal mole^{-1}.[12,92] It has been shown[87] that the heat of adsorption decreases appreciably in the presence of even small amounts (of the order of 1% of the monolayer) of a sulphur impurity on the surface of silver.

The heat of chemisorption of oxygen on gold has been determined in only two studies[18,19]. It was shown[19] that, in contrast to the heats of chemisorption on copper and silver, the heat of chemisorption of oxygen on gold is independent of the degree of surface coverage within the limits of experimental error (about 4%) and amounts to about 103 kcal/mole O_2.

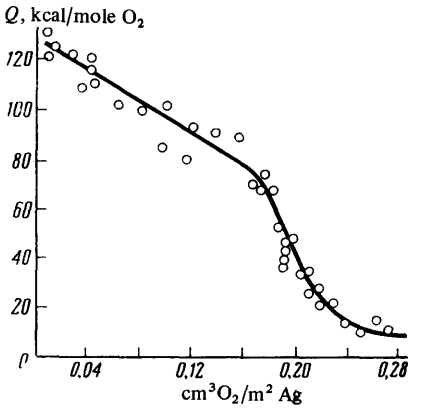

Figure 3. Variation of the heat of sorption of oxygen by silver with the degree of oxidation[84].

Thus almost all the oxygen adsorbed on a carefully cleaned gold surface is very firmly bound to the surface. It has been shown[19] that it can be removed only with much difficulty in the form of water after treatment by hydrogen with heating.

2. The Electronic Work Function

Table 5 presents the results of measurements of the maximum change in the electronic work function following the adsorption of oxygen on copper, silver, and gold. Evidently the electronic work function increases with adsorption or remains unchanged (on gold). The increase is evidence that the oxygen becomes negatively charged on adsorption. The maximum change in electronic work function after the adsorption of oxygen on this metal apparently depends on temperature, the amount of adsorbed oxygen, and to a large extent on the method of measurement employed. With increase of the amount of oxygen, the electron work function initially rises and then either remains unchanged or actually falls somewhat. If the oxygen is admitted onto the surface in portions, then after the introduction of each portion there is initially a rapid increase in the electronic work function and then a decrease. The decrease can actually amount to more than half of the initial rapid increase of the electron work function for the given portion of oxygen. The decrease in the electronic work function is usually explained by the diffusion of oxygen into the bulk of the specimen. However, one cannot rule out the possibility that it is partly due to the desorption from the surface of the water formed because the metals can contain hydrogen in the form of hydroxy-groups, owing to their previous history. Moreover the slow changes can be caused in many

instances by the processes occurring at the reference electrode. Table 5 shows that the smallest differences between the maximum changes in the electron work function on interaction with oxygen are observed for copper.

Table 5. Maximum increase in electron work function after the chemisorption of oxygen on Group IB metals.

Metal	Maximum increase in electron work function, V	Temperature of measurements, °C	Method	References
Copper	0.30	+20	d.	107
Copper	0.40[a] 0.8[b]	+25	v.c.(Au)	108
Copper	0.55	0—25	d.	109
Copper	0.27	+80	v.c.(Mo-gl.)	51
Silver	0.60	—	v.c.(Au)	110
Silver	0.20	+220	v.c(Au)	97
Silver	0.30	+25	v.c.(Au)	93
Silver	0.75 0.75 0.65	+23 +100 +200	v.c.(Mo-gl.)	71 111
Silver	1.04	+25	d.	95
Silver	0.90 1.1	+20,100 +200	v.c.(Au)	96
Silver	0.3 0.7	+20 +330	v.c.(Mo-gl.)	94
Gold	0.12	+25	d.	112
Gold	0	+25	v.c.(W)	16
Gold	0 0.7	+25 +400	v.c.	113
Gold	0	+25	ph.	99
Gold	0.30	+25	d.	20
Gold	(>0.35) (>0.55) (>0.65)	+150 +250 +350	v.c.(Mo-gl.)	22

[a] At a pressure below 1 mmHg.
[b] At a pressure of 50 mmHg.
Methods: d. = diode; ph. = photoelectric emission; v.c.(Au) = vibrating condenser with gold reference electrode; v.c.(W) = ditto with tungsten reference electrode; v.c.(Mo-gl.) = ditto with molybdenum electrode enclosed in glass.

In this case the electron work function amounts to 0.30–0.55 V close to room temperature when the oxygen pressure is below 1 mmHg. The increase in the electronic work function following an increase in oxygen pressure to 50 mmHg may be because at this high pressure and 25°C the surface is completely saturated by oxygen which cannot diffuse sufficiently rapidly into the bulk of the specimen and at low pressures part of the surface remains free as a result of the dissolution of oxygen. The results of measurements of the changes in the electron work function after the adsorption of oxygen on silver in different investigations differ very considerably. For example, when the adsorption of oxygen and the measurements of the change in electron work function were carried out at room temperature, the observed change in the electron work function ranged from 0.3 V in some studies [93,94] to about 1.0 V in others [95,96]. The results obtained at 100°C agree somewhat better, ranging from 0.65 to 1.1 V (except for the results of Enikeev et al. [93]). The measurements of the electronic work function of gold on contact with oxygen do not yet yield a final conclusion as to whether or not oxygen influences the electron work function. This is aggravated by the fact that the failure to take into account various experimental characteristics may have a decisive influence on the result for gold. For example, the formation of a gold film by atomising gold in an atmosphere of hydrogen [20], can lead to the occlusion of the gas by the film with subsequent formation of water when the film interacts with oxygen, whereas inadequate reduction of the initial gold hydroxide may lead to a distortion of the results for the adsorption of oxygen by the desorption of water, etc. According to the theory of the role of the surface electron gas in adsorption phenomena developed by Temkin and coworkers [27,98], the heat of adsorption being independent of the degree of surface coverage, as observed by Dobrovol'skii and Ostrovskii [19], should correspond to a constant electron work function in adsorption of oxygen on gold, which was in fact observed in careful investigations [16,19].

3. Electrical Conductivity and Other Properties

The electrical conductivity of thin copper, silver, and gold films decreases as a result of their contact with oxygen. The temperature coefficient of the resistance of copper decreases after the admission of oxygen [100-102]. At 0°C the introduction of oxygen into the space over degassed copper leads to a rapid increase of resistance. After some time the resistance ceases to change or begins to decrease. With increase of oxygen pressure above a certain limit, a slow increase of the resistance is again observed. The changes are irreversible, the electrical conductivity of the film is not restored after evacuation. Similar changes were observed also when oxygen was brought into contact with silver [102-104]. After a film 255 μm thick was exposed at 0°C to oxygen at a pressure of 0.1 mmHg, the resistance increased rapidly by 0.4% and then by a further 0.4% over 1 h. [104] At 200–300°C the resistance of a thin silver film increases in oxygen in proportion to the square of the time [103].

After the exposure of gold films 182 μm thick to oxygen at a pressure of 0.1 mmHg and 0°C, their resistance increases slowly to an extent reaching 2‰ after 1 h. [104] A decrease of the conductivity of gold in the presence of oxygen is observed also at higher temperatures (150–200°C) [105].

The adsorption of oxygen on copper or silver films about 50 Å thick alters the Hall potential [106]. As stated above, the oxygen impurity in copper and silver at a concentration of the order of 10^{-4}% greatly increases the self-diffusion coefficient of the metal [10].

V. THE MECHANISM OF THE PROCESSES IN THE SURFACE OXIDATION OF METALS

1. The Problem of Creating Clean Surfaces

A discussion of the problem of creating clean surfaces cannot be separated from a discussion of the oxidation mechanism, since the explanation of the phenomena observed in the sorption of oxygen is frequently determined by the presence of impurities in the specimens or at any rate depends significantly on them. The problem of the elimination from copper, silver, or gold of heavy element impurities which may influence the sorption of oxygen can now be solved comparatively readily because of the availability of sensitive and reliable analytical methods such as spectroscopic analysis, activation analysis, etc. Moreover, this is facilitated by the fact that,

in the storage and preparation of the specimens in vacuum apparatus, they are as a rule not subjected to additional contamination by heavy element impurities. It is much more difficult to determine the content of light element impurities, in the first place such as hydrogen, nitrogen, oxygen, and their compounds. In Group IB metals the problem is somewhat facilitated by the fact that these metals hardly sorb nitrogen and hydrogen. However, compounds of the above elements, including their oxides, can be adsorbed by Group IB metals.

Table 6. Heats of adsorption of the vapours of the principal impurities contaminating copper, silver, and gold.

Metal	Heat of adsorption, kcal mole^{-1}			
	CO	H_2O	CO_2	H_2S
Copper	16—17[83] 17.5[114] 9.3[115]	12[116]		
Silver		14.9[117]	17.5[118] (on Ag_2O)	78 ± 10*[29]
Gold	8.7[115]	14[19,86] 14.5[117]	14[19,86]	

* The interaction of the silver surface with hydrogen sulphide at 100°C proceeds in accordance with the equation $H_2S + (\ ) = H_2 + (S)$, where ( ) is a bivalent adsorption centre on the surface and (S) a chemisorbed sulphur atom[29].

Table 6 presents the heats of adsorption of certain substances contaminating the above adsorbents. Evidently the heats of adsorption are low and it would seem that *in vacuo* the surface should be rapidly cleaned. However, the problem is more difficult. Impurities in amounts greatly exceeding the volume of one monolayer can be present within the bulk of the crystals whence they can diffuse over a long period to the surface and contaminate it. Various sulphur- and chlorine-containing impurities, etc. diffuse rapidly to the surface on heating[32], but cannot be desorbed on heating *in vacuo*, since the bond energy between them and the surface is high (for example the bond energy of the sulphur atoms adsorbed on the surface of silver is 78 ± 10 kcal mole^{-1}).[29] The specimens obtained by reducing salts precipitated from aqueous solutions can contain considerable amounts of water and the acid residues of the salts undergoing decomposition, which are eliminated slowly owing to kinetic barriers which hinder their rapid diffusion to the surface. For example, the removal of residual water from gold obtained by the reduction of gold hydroxide at 350°C *in vacuo* takes place over hundreds of hours[19]. The elimination of oxygen present in the metal during the cleaning of the surface before the study of the adsorption of oxygen constitutes a special problem. Usually the metal is treated for this purpose with hydrogen or carbon monoxide and the water or carbon dioxide formed are evacuated. The cleaning of powdered copper in a static apparatus at 170°C requires treatment with hydrogen for hundreds of hours[25] and the cleaning of gold at 350°C requires many tens of hours[19]. The study of adsorption in an ultrahigh vacuum on sputtered metal films facilitates the solution of some of the problems enumerated above, but new problems are created because the surface of the films is very small compared with the surface of the powders and therefore very small amounts of impurities are sufficient to contaminate it (see, for example, Savchenko[119]). Nevertheless, the present review has shown that in those cases where sufficient attention was devoted to the cleaning of the specimens, the results obtained in the study of the oxidation of the surface of powders were analogous to those obtained in the study of the oxidation of the surface of thin films.

2. The Mechanism of the Sorption of Oxygen

The nature of the interaction of oxygen with copper, silver, and gold surfaces is in many respects similar, but each of the three systems has its specific features. The most striking common feature is that a definite amount of oxygen is sorbed by the metals above room temperature with a heat exceeding significantly the heat of formation of the corresponding oxides. Moreover, copper and silver can sorb considerable amounts of oxygen in their surface layers (deep adsorption) without the formation of an oxide phase. With increase of the specific surface, the maximum amount of such oxygen per unit weight of the metal increases and for specimens with a high surface area can be several orders of magnitude greater than the amount corresponding to the solubility of oxygen in the given metal determined for non-porous specimens. Even if the heat of deep adsorption exceeds that of the oxidation of the metal to an oxide phase, it does not do so by more than 10%. Most of the oxygen estimated in the determination of its solubility in such metals is probably concentrated in the surface layers. At the same time some oxygen can be present also in the bulk of the copper and silver, since its diffusion through a layer of the metal can be observed. The sorption of oxygen by porous gold is limited to a monolayer. The initial specific rates of sorption of oxygen on the metals under consideration have similar orders of magnitude when the comparison is made at 100–200°C. The initial heat of adsorption lies between 100 (gold) and 125 (silver) kcal/mole O_2 with an average error of the measurements in the range 5–7 kcal mole^{-1}. At the same time the variation of the rate of sorption of oxygen on copper, silver, and gold with the amount sorbed and the dependence of the heat of sorption on the amount sorbed on these metals are specific to each metal.

The sum total of the above results for the sorption of oxygen by copper shows that on clean copper oxygen is adsorbed and passes into the bulk of the metal. The collision of oxygen molecules with a surface coated by a layer of adsorbed oxygen probably stimulates an endothermic activated transfer of oxygen to the surface layer of the specimen with further adsorption on the liberated site. The heat of adsorption greatly exceeds the heat of oxidation to an oxide phase, while the heat of transfer of oxygen from the gas phase to the surface layer is close to the heat of oxidation of copper to an oxide phase. Therefore the initial heat of sorption of oxygen corresponds to the heat of adsorption, but, as the surface is covered, the heat of sorption approaches the heat of oxidation of copper to an oxide phase (Fig. 3). An increase of temperature increases the probability that the oxygen colliding with an unoxidised surface site is transferred directly to the surface layer. This explains why more oxygen is sorbed with a heat significantly exceeding the heat of oxidation of copper to an oxide phase at room temperature[83] than at 100°C.[25] Thus, in order to explain all the results obtained for the sorption of oxygen by copper up to the formation of nuclei of a new phase, it is necessary to assume that three processes can occur when oxygen molecules collide with the copper surface. In the collision

between an oxygen molecule and unoxidised surface sites there is a possibility of (1) the adsorption of the oxygen on the surface and (2) deep adsorption. When an oxygen molecule collides with oxidised surface sites, a third process is possible—the adsorption of the molecule with transfer of another molecule previously adsorbed to the surface layer. The rates of each of these processes are proportional to the oxygen pressure in the gas phase. The rates of the first two processes decrease with decrease of the fraction of unoxidised surface. The rate of the third process increases as the surface monolayer is oxidised and can fall slowly as oxygen is sorbed after the completion of the oxygen monolayer when diffusion in the surface layers begins to have an effect. The second process does not require an additional activation energy as compared with the first (the energy liberated in the adsorption step at any temperature is sufficient to transfer oxygen to the surface layer and the fate of a given species is determined solely by the direction of the impulse), since otherwise the decrease of the rate, illustrated in Fig. 1, would cease for different amounts of sorbed oxygen at different temperatures. The activation energy for adsorption is much lower than the activation energy for the third process. Thus on polycrystalline materials it amounts to 7.5 kcal mole^{-1} for the sorption of 0.6 cm^3 O_2/m^2 Cu [18,50] and to 7.3 kcal mole^{-1} for the sorption of between 0.25 and 0.80 cm^3 O_2/m^2 Cu [51]; on the (110) face, under the conditions of the formation of the adsorption layer, the activation energy is 3.5 kcal mole^{-1} [53]. Fig. 1 shows that, as oxygen is sorbed up to 1 cm^3 O_2/m^2 Cu, the activation energy rises. Extrapolation of the curves to the initial conditions yields very similar rates at different temperatures, i.e. the initial activation energy for adsorption is close to zero. The activation energy for the third process is 11.5 kcal mole^{-1} in the sorption of 1–4 cm^3 O_2/m^2 Cu [18,50] or 15.5 kcal mole^{-1} in the sorption of about 10 cm^3 O_2/m^2 Cu. [61] Under these conditions, the rate of sorption of oxygen is still proportional to the pressure. On further sorption of oxygen, the activation energy rises to 21.8 kcal mole^{-1} [44] or 21 kcal mole^{-1} [40] on sorption of about 35 cm^3 O_2/m^2 Cu. Within the limits of experimental error, these activation energies are equal to the activation energy for the diffusion of copper ions in the surface oxide film (20.1 kcal mole^{-1}). [120] The activation energies quoted in some studies [40,44,120] were obtained under conditions where the rate of sorption of oxygen is almost independent of its pressure in the gas phase. In other words, under these conditions, the rate of reaction is limited by diffusion in the solid. On further oxidation, nuclei of the oxide phase appear and an increased rate of sorption of oxygen characteristic of this stage is observed.

On silver as well as on copper, oxygen is adsorbed and passes into the bulk metal. As for copper, the heat of adsorption on silver greatly exceeds the heat of oxidation to an oxide phase and the heat of deep adsorption is close to the heat of oxidation of the metal. However, the difference between the initial heats of adsorption of oxygen on silver (about 125 kcal/mole O_2) and the enthalpy of formation of Ag_2O (about 15 kcal/mole O_2) is in this case much greater than the difference between the corresponding values for copper. The dependence of the differential heat of adsorption of oxygen on the degree of adsorption (Fig. 3) shows that the heat of adsorption of oxygen greatly exceeds the heat of oxidation to an oxide phase up to almost complete surface coverage, in which there is one oxygen atom for each surface silver atom (0.26 cm^3 O_2/m^2 Ag). An increase in the electronic work function of silver following the adsorption of oxygen is also observed up to virtually monolayer surface coverage [111]. The rate of deep adsorption of oxygen on silver at 250°C is three orders of magnitude slower than the average rate of monolayer adsorption [69] and deep adsorption should not affect the results of the study of the adsorption of oxygen up to the limit of one monolayer. At the same time deep adsorption can influence the catalytic properties of silver in oxidation reactions. The results of studies of the adsorption of oxygen on silver are described in terms of the hypothesis that adsorbed oxygen exists in two forms, one of which corresponds to the formation of a two-dimensional surface oxide Ag_2SO and the other to the formation of $AgSO$ (or Ag_2SO_2). Many workers have used ideas of this type [5,73,77,81]. In this connection we may point to the existence of the compound AgO, which is not a peroxide [121], and of the surface compound of silver and oxygen, which was identified as a superoxide [122]. Oxygen is adsorbed initially with formation of the surface oxide Ag_2SO. The adsorption of oxygen as Ag_2SO has the highest heat and involves the main change in the electronic work function. The adsorption of oxygen as $AgSO$ begins only after the surface has been largely covered by oxygen as Ag_2SO. The adsorption of oxygen on a reduced surface proceeds in accordance with the equation

$$4\,Ag^S + O_2 \rightarrow 2\,Ag^S\!\!<\!\!\overset{O}{}\!\!>\!\!Ag^S, \qquad (6)$$

and on a surface coated by Ag_2SO according to the equation

$$2\,Ag^S\!\!<\!\!\overset{O}{}\!\!>\!\!Ag^S + O_2 \rightarrow 4\,\overset{O}{\|}\,Ag^S. \qquad (7)$$

In the intermediate range of coverages the following reactions can also occur:

$$2\,Ag^S + O_2 \rightarrow 2Ag^S \xrightarrow{+2Ag^S} 2\,Ag^S\!\!<\!\!\overset{O}{}\!\!>\!\!Ag^S, \qquad (8)$$

$$Ag^S\!\!<\!\!\overset{O}{}\!\!>\!\!Ag^S Ag^S + O_2 \rightarrow 3\,\overset{O}{\|}\,Ag^S \xrightarrow{+2Ag^S} 3\,Ag^S\!\!<\!\!\overset{O}{}\!\!>\!\!Ag^S. \qquad (9)$$

The maximum degree of adsorption of oxygen on silver before the rate drops by 2–3 orders of magnitude corresponds to the saturation of a monolayer with one oxygen atom per surface silver atom. Thus it was possible to assume that oxygen is adsorbed in the form of $AgSO$ (or Ag_2SO_2). However, the heat of adsorption of oxygen on an oxygen-free surface differs from the heat of adsorption at monolayer coverage by more than 100 kcal mole^{-1}, a sharp decrease of the heat of adsorption being observed near the degree of adsorption corresponding to one oxygen atom per silver atom on the surface. Moreover, as adsorption proceeds until the attainment of the above surface coverage, the electronic work function of silver rises, but subsequent adsorption has little influence on it; the depolarisation of dipoles cannot explain this type of variation of electronic work function with surface coverage. Under conditions close to complete surface coverage by oxygen with one oxygen atom per two silver atoms, there is also a change in the kinetics of the adsorption of oxygen (Table 3). These findings can be explained by assuming that oxygen is adsorbed on the surface in the two forms indicated above. The existence of two forms of oxygen on silver was also postulated to account for its catalytic properties. The heat of adsorption of oxygen in the form of Ag_2SO is high, decreasing with surface coverage (Fig. 3). The rate of adsorption decreases exponentially under these conditions [71,80]. The bond between oxygen and silver in the surface oxide Ag_2SO is polar with the negative end of the

dipole directed to oxygen (Table 5). Further adsorption of oxygen, leading to the conversion of adsorbed oxygen from Ag_2SO into $AgSO$, involves a small heat change and the electronic work function of silver does not alter. Under these conditions, the rate of adsorption of oxygen falls linearly, to a first approximation, as the concentration of Ag_2SO on the surface decreases[28]. The adsorption terminates when the surface is covered by an $AgSO$ monolayer. Further sorption of oxygen proceeds slowly and is due to deep adsorption†. The introduction onto the surface of impurities comprising electronegative elements such as sulphur, selenium, etc. reduces the rate of adsorption of oxygen[29,30,74], and the heat of its adsorption[28], via the mechanism of the mutual influence of adsorbed species. Admixtures of the above elements, introduced into the bulk of the specimen, act similarly, since they can migrate rapidly to the surface[32].

The oxygen adsorbed on gold hardly penetrates into the bulk of the crystal lattice at temperatures below 150°C. The sorption of oxygen is limited to a monolayer. To describe the results of adsorption studies, it is assumed, as for the adsorption on silver, that the oxygen can exist in two forms on the surface: as Au_2SO and $AuSO$. The heat of adsorption of oxygen on a clean gold surface with formation of Au_2SO is equal, within the limits of experimental error, to the heat of adsorption of oxygen with formation of $AuSO$ on a surface coated by Au_2SO. A clean gold surface is homogeneous with respect to the adsorption of oxygen. The heat of adsorption is constant over a wide range of variation in the extent of surface coverage by a monatomic oxygen layer. It amounts to about 100 kcal $mole^{-1}$, while the enthalpy of oxidation of gold to an oxide phase is positive (Table 1). Up to 70% surface coverage by the Au_2SO species, the adsorption kinetics are described by Eqn. (5), which corresponds to the adsorption of each O_2 molecule on four adjacent atoms of the homogeneous gold surface. Subsequent adsorption involves mainly the formation of $AuSO$. Only two surface sites are required for the adsorption of an oxygen molecule in the form of $AuSO$. Therefore the rate of adsorption depends less strongly on the degree of surface coverage than the rate of adsorption in the form of Au_2SO. The rate of adsorption remains proportional to pressure, but Eqn. (5) does not hold. On further increase of the degree of adsorption, the order of the adsorption process with respect to oxygen pressure diminishes, since the observed rate of adsorption begins to depend on the rate of surface migration. Data on the electronic work function of gold in the adsorption of oxygen are contradictory, as can be seen from Table 5. In studies[16,99] carried out under the cleanest conditions using different methods for the measurement of the electronic work function, no changes in the latter were observed when gold came into contact with oxygen. The change in surface potential observed[20] on bringing gold into contact with oxygen can be attributed to the fact that the fusion of gold and the sputtering of the film were carried out in an atmosphere of hydrogen. The adsorbed oxygen might interact with the occluded hydrogen on the surface of the film, generating a charge on the latter.

† In a recently published study[123] the hypothesis of the existence of Ag_2SO and Ag_2SO_3 was used to explain the results of an investigation of the heteroexchange of oxygen on silver.

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Surface Properties of Aqueous Salt Systems

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Use of the Gibbs method and of a layer of finite thickness to calculate the thermodynamic characteristics of surface layers is examined. The chief properties of surface layers have been calculated for 35 aqueous salt systems from experimental data. The influence of the nature of the dissolved salt on the properties of solutions and surface layers is discussed on the basis of the calculated results. A list of 87 references is included.

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I. INTRODUCTION

Considerable experimental information has been accumulated on the surface tension of aqueous salt systems, but its processing is far from complete. Calculation is usually confined to finding the adsorption, although modern thermodynamics enables the composition and the entropy characteristics of the surface layer also to be calculated from sufficiently complete surface-tension data. These characteristics in turn make it possible to elucidate the effect of the nature of the ions on the structure and the properties of the surface layers.

The aim of the present paper is to generalise available published information from unified points of view by basing the thermodynamic calculations on a rigorous scheme and comparing characteristics of the same type for various aqueous salt systems. The most reliable published data on the surface tensions of solutions containing singly and multiply charged ions have been used for the calculations. A total of 35 aqueous salt systems have been considered.

II. SURFACE PHENOMENA IN AQUEOUS SALT SYSTEMS

1. Experimental Investigations of Surface Tension

Nearly linear increases in the surface tension of the solution with salt concentration were observed [1-6]. Quincke [2] formulated the empirical rule that solutions of different chlorides have roughly the same surface tension at the same volume concentration of the chloride ion. An attempt to extend this rule to other halides was less successful.

Whatmough [4] suggested that, when several salts were present together in solution, they made additive contributions to the surface tension.

More accurate results [7-9] revealed a fairly complicated relation between surface tension and solution composition. The earlier empirical relations were found to lack generality and be applicable only to dilute solutions. Nevertheless, the hypothetical linear composition dependence of the surface tension of a salt solution was used [10] to estimate by extrapolation the surface tension of a supercooled melt of the pure salt. This hypothesis, which is only an approximation, has been used also to solve several applied problems requiring no great accuracy in the calculation of surface tension [11,12].

An important contribution to developing ideas on the structure of the surface layer was made by Langmuir [13]. He assumed that the surface of a salt solution is covered by a film of water, below which the salt concentration is constant, and calculated the thickness of the film by means of the formula

$$\tau = -1000\,\Gamma_{1(2)}/c \qquad \text{(II, 1)}$$

where $\Gamma_{1(2)}$ is the adsorption of the salt and c the molar concentration of the solution. Extension of similar calculations to various aqueous salt systems showed [9,14,15] that the film thickness depends on the nature of the salt, but in all cases examined diminishes from 5–3 Å at low concentrations to 2 Å at high concentrations. Comparison with the size of a water molecule led to the important conclusion that the ions of a dissolved salt enter the surface monolayer when the solution is sufficiently concentrated.

Adsorption of a solute changes the potential difference between the solution and the surrounding medium. The dependence of this potential difference on solution composition was investigated by Frumkin [16,17], who discovered that most salt solutions give a small potential difference at their air interface, with the outer region of the double layer charged negatively. This indicates that anions are arranged on the average closer to the air than are cations. With solutions of the same concentration the negative charge increases in the sequence of anions

$$F^- < Cl^- < Br^- < I^- < CNS^-.$$

The reason is that less strongly hydrated ions pass more readily (and hence in greater quantity) into the surface layer, thus conferring a higher charge on the surface. According to Frumkin the nature of the cation has little effect on the surface charge.

Comparison of the adsorptions calculated by means of the relation

$$RT\Gamma_{1(2)} \approx 0.5\,(\sigma_0 - \sigma) \qquad \text{(II, 2)}$$

(in which R is the gas constant, T is the temperature, and σ and σ_0 are the surface tensions of the salt solution and pure water respectively) with the results of electrometric measurements indicated that the greater the adsorption of the salt the more strongly charged was the surface of the solution.

Pavlov [18] used empirical relations to calculate the surface tensions of salt solutions, and in many cases observed satisfactory agreement with experimental values obtained

by other workers. Having used incorrect premises in calculating the adsorption of the salt, he obtained positive values of $\Gamma_{1(2)}$.

In a study of the surface properties of aqueous salt systems Rebinder[19] directed attention to the behaviour of water as a surface-active compound. He obtained the complete surface-tension isotherm for the aqueous silver thallium(I) nitrate system at 90°C (the salt $AgTl(NO_3)_2$ melts at 82.5°C, above which temperature it is completely miscible with water). The surface-tension isotherm is well described by Shishkovskii's equation

$$\sigma - \sigma_0 = b \ln (ac + 1) \qquad \text{(II, 3)}$$

where a and b are constants, c is the concentration of water, and σ and σ_0 are the surface tensions of the molten salt and of the solution respectively.

Yashkichev[20] suggested a qualitative interpretation of results for the surface tension of salt solutions according to which the effect of the salt was governed by two factors acting in different directions. The first such factor was the effect of ions in disrupting the mutual order of the water molecules, which with negatively hydrated ions would tend to diminish surface tension. The other factor was the negative adsorption of ions, interaction of whose fields with water molecules of the surface layer should strengthen the tendency of the molecules to be drawn into the interior of the solution, which would correspond to an increase in surface tension. Such an explanation is, of course, greatly oversimplified and insufficiently informative, since negative adsorption of a salt is the starting point of the argument, but this does not provide sufficient grounds for such an assumption.

A series of studies[21-25] on foams, films, and drop entrainment from electrolyte solutions has shown that the stability of a foam depends on the nature of the dissolved salt and is increased by the presence of strongly hydrated ions. The critical rupture thickness on the spontaneous thinning of films of electrolyte solutions is inversely proportional to the concentration and energy of hydration of the ions. In several cases separation of electrolytes has been observed during drop entrainment[25].

2. The Jones–Ray Effect

A prolonged controversy ensued from the papers by Jones and Ray[26-28], who discovered by the capillary-rise method a minimum in the surface-tension isotherms for 13 aqueous salt systems. A depression of surface tension reaching 0.02 dyn cm^{-1} was observed in all cases in dilute solutions (below 0.002 N). The positive adsorption of the salt corresponding to this depression was explained by preferential attraction between salt ions and water molecules on the solution surface (at higher concentrations the forces retaining ions in solution increase more rapidly and the adsorption becomes negative).

According to Langmuir[29] the Jones–Ray effect is a consequence of the experimental technique: a film of water which may be several hundreds of ångströms thick would be present on the internal surface of the capillary, and would be thicker for salt solutions than for pure water. Such a film leads to a change in the effective radius of the capillary, which influences the measured results.

Langmuir's view was criticised[30], and the Jones–Ray effect was then confirmed[31] for aqueous potassium chloride by the ring-detachment method. Dole[32] also tried to obtain theoretically an equation for a surface-tension isotherm passing through a minimum. The deduction involved the postulated presence, on the surface of a dilute solution, of a monomolecular layer of water, whose interaction with the ions of the salt was far stronger than the interionic interaction in the solution. In order to bring into line with the experimental results, furthermore, it was postulated that only negative ions could be adsorbed and only on certain active centres (one per 10^5 water molecules). The calculated surface tensions were close to the experimental values, but Dole's postulates were too arbitrary to serve as evidence.

Bikerman[33] discussed the Jones–Ray effect in terms of the surface tension as the sum of three contributions. The work required for a water molecule to escape to the surface was assumed to be independent of concentration. The second term resulted from the lower salt concentration at the surface than in the bulk of the solution, so that formation of a surface layer entailed an increase in the bulk concentration of the solutions; this process was replaced in the calculations by compression of the ionic gas, and the corresponding work was computed solely on the basis of electrostatic interaction. The third term represented the work required to separate positive and negative ions. Calculations based on this scheme gave minimum surface tension for dilute potassium chloride solutions, but the third term was calculated from Jones and Ray's results. Moreover, the postulates involved (e.g. the assumed concentration independence of the first term) restrict considerably the concentration range in which the formulae might be applied.

The phenomena associated with the Jones–Ray effect was carefully examined by Passoth[34], who measured the surface tension by a modified maximum bubble pressure method enabling the time of formation of the bubble to be varied within wide limits. When the bubble formed slowly, the effect was observed with sodium and potassium chloride solutions, but no effect was observed when the rate was increased. Passoth concluded that the inner walls of the capillary were coated with a liquid film, whose thickness depended on solution concentration with slow formation of the bubble. Estimated thicknesses of this film were consistent with Langmuir's results.

A recent examination of the thermodynamic conditions of concentration buffering has shown that the Jones–Ray effect is impossible. It must thus be accepted that the effect is spurious, and is connected with the method adopted for measuring surface tension[34,36].

3. Use of Thermodynamics in the Analysis of Surface Phenomena in Aqueous Salt Systems

Two chief methods—the Gibbs method and the method of a layer of finite thickness—can be distinguished in the thermodynamics of surface phenomena. The former is based on the concept of a geometric surface, and utilises excess functions[37]. The excess entropy $\bar{S}$ and the excess mass of the ith component $\bar{m}_i$ are defined by the relations

$$\bar{S} \equiv S - s_v^{(\alpha)} V_\alpha - s_v^{(\beta)} V_\beta \qquad \text{(II, 4)}$$

$$\bar{m}_i \equiv m_i - \rho_i^{(\alpha)} V_\alpha - \rho_i^{(\beta)} V_\beta \qquad \text{(II, 5)}$$

where S is the entropy of the system, m_i is the mass (or the number of moles) of the ith component, $\rho_i^{(\alpha)}$ and $\rho_i^{(\beta)}$ are the densities of the ith component in the coexisting α and β phases, $s_V^{(\alpha)}$ and $s_V^{(\beta)}$ are the bulk entropy densities in these phases, and the sum of the volumes of regions of the system mutually separated by a dividing surface gives the total volume $V = V_\alpha + V_\beta$. The values of the excess

quantities depend on the position chosen for the dividing surface. The surface density of the excess of mass is termed the absolute adsorption

$$\Gamma_i \equiv \bar{m}_i/A \qquad \text{(II, 6)}$$

(in which A is the area of the dividing surface); while the combination

$$\Gamma_{i(j)} \equiv \Gamma_i - \Gamma_j \frac{\rho_i^{(\beta)} - \rho_i^{(\alpha)}}{\rho_j^{(\beta)} - \rho_j^{(\alpha)}} \qquad \text{(II, 7)}$$

is the Gibbs relative adsorption, which is invariant with respect to displacement of the dividing surface. The relative adsorption $\Gamma_{i(j)}$ is numerically equal to the absolute adsorption Γ_i for a dividing surface corresponding to the condition $\Gamma_j = 0$. Gibbs obtained the adsorption equation

$$d\sigma = -\bar{s}_{(j)}dT - \sum_{i \neq j} \Gamma_{i(j)}\, d\mu_i \qquad \text{(II, 8)}$$

where σ is the surface tension, μ_i is the chemical potential of the ith component, and $\bar{s}_{(j)}$ is defined by the relation

$$\bar{s}_{(j)} \equiv \frac{\bar{S}}{A} - \Gamma_j \frac{s_v^{(\beta)} - s_v^{(\alpha)}}{\rho_j^{(\beta)} - \rho_j^{(\alpha)}} \qquad \text{(II, 9)}$$

In the case of electrolyte solutions Eqn. (II, 8) contains electrode potentials instead of chemical potentials.

The chief merit of the Gibbs method is its mathematical simplicity. An important disadvantage, however, is that the use of geometric surfaces excludes consideration of the thickness of the surface layer, which is one of the principal problems of the theory of surface phenomena. An important role in the discussion of this problem was played by the method of a layer of finite thickness[38-40], an account of whose development and a modern presentation will be found in a monograph[41].

Displacement of the equilibrium in a two-phase n-component system with a planar surface is described by the set of equations[41]

$$\begin{cases} a\,d\sigma = s_{a\sigma}\,dT + v_{a\sigma}\,dP - \sum_{i=1}^{n-1}\sum_{k=1}^{n-1} (x_i^{(\sigma)} - x_i^{(\alpha)})\, g_{ik}^{(\alpha)} dx_k^{(\alpha)} \\ a\,d\sigma = (s_{a\beta} - s_{a\sigma})\,dT - (v_{a\beta} - v_{a\sigma})\,dP - \sum_{i=1}^{n-1}\sum_{k=1}^{n-1} (x_i^{(\alpha)} - x_i^{(\beta)})\, g_{ik}^{(\alpha)} dx_k^{(\alpha)}, \end{cases} \qquad \text{(II, 10)}$$

where

$$\bar{s}_{a\sigma} \equiv s^{(\sigma)} - s^{(\alpha)} - \sum_{i=1}^{n-1} (x_i^{(\sigma)} - x_i^{(\alpha)}) \left(\frac{\partial s}{\partial x_i}\right)^{(\alpha)} \qquad \text{(II, 11)}$$

$$v_{a\sigma} \equiv v^{(\sigma)} - v^{(\alpha)} - \sum_{i=1}^{n-1} (x_i^{(\sigma)} - x_i^{(\alpha)}) \left(\frac{\partial v}{\partial x_i}\right)^{(\alpha)} \qquad \text{(II, 12)}$$

$$s_{a\beta} \equiv s^{(\beta)} - s^{(\alpha)} = \sum_{i=1}^{n-1} (x_i^{(\beta)} - x_i^{(\alpha)}) \left(\frac{\partial s}{\partial x_i}\right)^{(\alpha)} \qquad \text{(II, 13)}$$

$$v_{a\beta} \equiv v^{(\beta)} - v^{(\alpha)} - \sum_{i=1}^{n-1} (x_i^{\beta} - x_i^{(\alpha)}) \left(\frac{\partial v}{\partial x_i}\right)^{(\alpha)} \qquad \text{(II, 14)}$$

$$g_{ik} \equiv \left(\frac{\partial^2 g}{\partial x_i\, \partial x_k}\right)_{P,T}^{(\alpha)} \qquad \text{(II, 15)}$$

a is the molar surface, x_i is the mole fraction of the ith component, g is the molar Gibbs thermodynamic potential, and the s and v are molar entropies and volumes. The superscripts α and β denote the coexisting bulk phases, and σ indicates the surface layer. Physically the quantities $s_{a\sigma}$ and $s_{a\beta}$ represent entropy effects, and $v_{a\sigma}$ and $v_{a\beta}$ volume effects of transitions from the α phase to the surface layer and to the β phase respectively, i.e. effects accompanying formation of 1 mole of surface layer and of phase β from an infinite quantity of phase α. The quantities $s_{a\sigma}$ and $v_{a\sigma}$ are differential molar effects of adsorption. In the case of a liquid–vapour (α–β) equilibrium the quantities $s_{a\beta}$ and $v_{a\beta}$ are differential molar effects of vaporisation.

III. CALCULATION OF THERMODYNAMIC PROPERTIES OF SURFACE LAYERS

1. Calculation of Relative Adsorptions

For a strong uni-univalent electrolyte dissolved in water (the KA–H_2O system) the equation to the Gibbs adsorption isotherm is

$$-d\sigma = \Gamma_K + d\bar{\mu}_{K^+} + \Gamma_{A^-} d\bar{\mu}_{A^-} + \Gamma_{H^+} d\bar{\mu}_{H^+} + \Gamma_{OH^-} d\bar{\mu}_{OH^-} + \Gamma_{H_2O} d\mu_{H_2O} \qquad \text{(III, 1)}$$

where σ is the surface tension, Γ and $\bar{\mu}$ are the absolute adsorption and the electrochemical potential of the corresponding ion, and Γ_{H_2O} and μ_{H_2O} are the absolute adsorption and the chemical potential of undissociated water. Besides taking into account the phase equilibrium conditions, we should consider Eqn. (III, 1) in combination with the condition of equilibrium in the dissociation of water

$$\mu_{H_2O} = \bar{\mu}_{H^+} + \bar{\mu}_{OH^-} \qquad \text{(III, 2)}$$

and the condition of electrical neutrality

$$\Gamma_{H^+} + \Gamma_{K^+} = \Gamma_{OH^-} + \Gamma_{A^-} \qquad \text{(III, 3)}$$

According to thermodynamics the number of components in a given mixture is strictly defined, but their choice is arbitrary. For convenience we shall henceforward select as components the neutral substances HA and KA (almost completely absent from the bulk of the solution), and introduce for them, by analogy with (III, 2), the conditions

$$\mu_{KA} = \bar{\mu}_{K^+} + \bar{\mu}_{A^-};\ \mu_{HA} = \bar{\mu}_{H^+} + \bar{\mu}_{A^-} \qquad \text{(III, 4)}$$

From Eqns. (III, 1–4) we then obtain

$$-d\sigma = (\Gamma_{A^-} - \Gamma_{K^+})\, d\mu_{HA} + \Gamma_{K^+} d\mu_{KA} + (\Gamma_{OH^-} + \Gamma_{H_2O})\, d\mu_{H_2O} \qquad \text{(III, 5)}$$

and after allowing for the phase equilibrium conditions and eliminating $d\mu_{KA}$ we find that

$$-d\sigma = \Gamma_{A^-(K^+)} d\mu_{HA} + (\Gamma_{OH^-(K^+)} + \Gamma_{H_2O(K^+)})\, d\mu_{H_2O} \qquad \text{(III, 6)}$$

where the additional subscript (K^+) indicates conversion to relative adsorptions (with respect to the cation K^+).

The coefficient of $d\mu_{HA}$ in Eqns. (III, 5 and 6) represents the non-equivalence of adsorption of cation and anion of the dissolved electrolyte. If the compound HA is volatile, this coefficient can in principle be evaluated from the dependence of the surface tension on the vapour pressure of HA. When the non-equivalence of adsorption of the ions can be neglected, the first term on the right-hand side of (III, 5 and 6) vanishes, and the coefficient of $d\mu_{H_2O}$ becomes equal to the total adsorption of water in molecular and dissociated forms. These two adsorption equations then become formally identical with those for systems of non-electrolytes:

$$-d\sigma = \Gamma_1 d\mu_1 + \Gamma_2 d\mu_2 \qquad \text{(III, 7)}$$

$$-d\sigma = \Gamma_{2(1)} d\mu_{(2)} \qquad \text{(III, 8)}$$

where $\Gamma_1 \equiv \Gamma_{KA} = \Gamma_{K^+}$ and $\Gamma_2 \equiv \Gamma_{H_2O} + \Gamma_{OH^-}$. Analogous formulae are obtained also for a solution of a weak electrolyte (when Γ_1 becomes the total adsorption of the electrolyte in molecular and dissociated forms). Formulae (III, 7 and 8) are obviously valid not only for an aqueous uni-univalent electrolyte but also for electrolytes of any type.

From (III, 8) the relative adsorption of water $\Gamma_{2(1)}$ can be calculated by means of the formula

$$\Gamma_{2(1)} = -\frac{1}{RT}\left(\frac{d\sigma}{d\ln a_2}\right)_T \qquad \text{(III, 9)}$$

where a_2 is the activity of water. If the salt is non-volatile and the vapour approximates to an ideal gas, we can use isothermal data on the vapour pressure P over the solution to calculate

$$\Gamma_{2(1)} = -\frac{P}{RT}\left(\frac{d\sigma}{dP}\right)_T \qquad \text{(III, 10)}$$

The relative adsorption of the salt $\Gamma_{1(2)}$ is easily found from formula (II, 8):

$$\Gamma_{1(2)} = -x_1^{(\alpha)}\Gamma_{2(1)}/(1-x_1^{(\alpha)}) \qquad \text{(III, 11)}$$

where $x_1^{(\alpha)}$ is the mole fraction of the salt in the solution. In Eqn. (III, 10) the vapour is regarded as ideal, but in (III, 11) the vapour density is neglected, so that both relations are valid only far from the critical point.

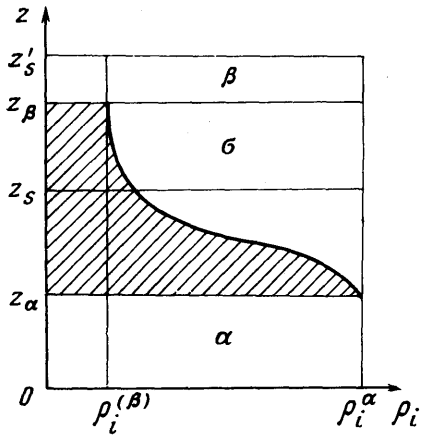

Figure 1. Density profile of ith component in surface layer.

2. Calculation of Composition of Surface Layer

Relation between adsorption and composition of surface layer

If the z-axis is directed perpendicularly to the surface from phase α towards phase β, the quantity $m_1^{(\sigma)}/A$ (the shaded area in **Fig. 1**) in a surface layer of thickness $\tau \equiv z_\beta - z_\alpha$ will be given by

$$m_1^{(\sigma)}/A = {}^{(\sigma)}_{m}x_1^{(\alpha)}/A = \Gamma_1 + \rho_1^{(\alpha)}\tau - (\rho_1^{(\alpha)} - \rho_1^{(\beta)})(z_\beta - z_s) \qquad \text{(III, 12)}$$

and similarly

$$m_2^{(\sigma)}/A = m^{(\sigma)}(1-x_1^{(\alpha)})/A = \Gamma_2 + \rho_2^{(\alpha)}\tau - (\rho_2^{(\alpha)} - \rho_2^{(\beta)})(z_\beta - z_s) \qquad \text{(III, 13)}$$

where

$$m^{(\sigma)} = m_1^{(\sigma)} + m_2^{(\sigma)},\quad x_1^{(\sigma)} = m_1^{(\sigma)}/m^{(\sigma)};$$

$m_i^{(\sigma)}$ is the number of moles of the ith component in the surface layer, and z_S is the coordinate of the dividing surface. These relations hold for any position of the dividing surface, not necessarily within the surface layer.

Passing to the relative adsorption

$$\Gamma_{2(1)} \equiv \Gamma_2 - \Gamma_1(\rho_2^{(\alpha)} - \rho_2^{(\beta)})/(\rho_1^{(\alpha)} - \rho_1^{(\beta)}) \qquad \text{(III, 14)}$$

and remembering that $A/m^{(\sigma)} = v^{(\sigma)}/\tau$, we obtain from (III, 12 and 13) the required relation

$$x_1^{(\sigma)} = \frac{x_1^{(\alpha)} - x_1^{(\beta)}\varkappa}{1-\varkappa}(1 - v^{(\sigma)}\Gamma_{2(1)}/\tau) - \frac{v^{(\sigma)}(x_1^{(\alpha)} - x_1^{(\beta)})}{v^{(\beta)}(1-\varkappa)} \qquad \text{(III, 15)}$$

where

$$\varkappa \equiv \rho^{(\beta)}/\rho^{(\alpha)} = v^{(\alpha)}/v^{(\beta)},\quad \rho = \rho_1 + \rho_2;$$

and v is the molar volume. Equation (III, 15) shows that conversion from relative adsorptions to mole fractions in the surface layer necessitates specification of the thickness and the molar volume of the latter—two parameters which characterise unambiguously the situation of the surface layer in the system.

In the case of equilibrium between solution and vapour with neglect of the density of the latter $\varkappa \to 0$ formula (III, 15) simplifies to[42,43]

$$x_1^{(\sigma)} = x_1^{(\alpha)}(1 - v^{(\sigma)}\Gamma_{2(1)}/\tau), \qquad \text{(III, 16)}$$

which coincides also with the expression for adsorption from a binary liquid solution at its interface with a solid[44].

Use of thermodynamic equations to calculate composition of surface layer

In order to calculate $x_1^{(\sigma)}$ by means of Eqn. (III, 16) it is first necessary to find the Gibbs relative adsorption. However, it can be calculated also by use of the thermodynamics of surface layers, e.g. from the constant-pressure temperature dependence of surface tension, an equation for which is obtained by fixing the pressure in Eqns. (II, 10) and eliminating one of the derivatives, e.g. $(dx_{n-1}/dT)_P^{(\alpha)}$. For a binary system we then have

$$a\left(\frac{d\sigma}{dT}\right)_P = -s_{\alpha\sigma} + \frac{x_1^{(\sigma)} - x_1^{(\alpha)}}{x_1^{(\beta)} - x_1^{(\alpha)}}s_{\alpha\beta} \qquad \text{(III, 17)}$$

which holds in practice even in the presence of a foreign gas (e.g. air[45]) in the system. In the case of a non-volatile salt ($x_1^{(\beta)} = 0$) we find from (III, 17) that

$$x_1^{(\sigma)} = x_1^{(\alpha)} - \frac{(d\sigma/dT)_P \cdot v^{(\sigma)}/\tau + s_{\alpha\sigma}}{s_{\alpha\beta}}x_1^{(\alpha)} \qquad \text{(III, 18)}$$

where $v^{(\sigma)} = a\tau$, which enables the composition of the surface layer of a binary solution to be calculated from the constant-pressure temperature dependence of surface tension. The differential molar entropy effects in (III, 18) are defined[41]

$$s_{\alpha\sigma} = -(d\sigma/dT)^{(\alpha)}_{x_1}\, v^{(\sigma)}/\tau;\quad s_{\alpha\beta} = RB/T$$

the constant B being evaluated from the temperature dependence of the vapour pressure $\ln P = A - B/T$. Surface-tension isobars are found from the composition dependence of σ and P, and are then differentiated to determine $(d\sigma/dT)_P$.

The composition of a surface layer of given thickness can be calculated also from isothermal data on the dependence of surface tension on solution composition. For a binary system the surface-tension isotherm

$$a\,d\sigma = \left[(x_1^{(\beta)} - x_1^{(\alpha)})\frac{v_{\alpha\sigma}}{v_{\alpha\beta}} - (x_1^{(\sigma)} - x_1^{(\alpha)})\right]g_{11}^{(\alpha)}dx_1^{(\alpha)} \qquad \text{(III, 19)}$$

follows from (II, 10).[46] When liquid–vapour (α–β) equilibrium is established far from the critical point, it can be assumed that

$$|v_{\alpha\beta}| \gg |v_{\alpha\sigma}| \qquad \text{(III, 20)}$$

and the first term in square brackets can be neglected. From (III, 19) we then obtain

$$x_1^{(\sigma)} = x_1^{(\alpha)} \frac{(d\sigma/dx_2^{(\alpha)})_T v^{(\sigma)}}{g_{11}^{(\alpha)} \cdot \tau} \qquad \text{(III, 21)}$$

The quantity $g_{11}^{(\alpha)}$ is calculated by means of the formula

$$g_{11}^{(\alpha)} = \frac{RT}{1 - x_1^{(\alpha)}} \frac{\partial \ln a_1}{\partial x_1^{(\alpha)}},$$

where a_1 is the activity of the first component. The molar volume is determined to a first approximation with no salt present in the surface layer. On the assumption of the same composition dependence of molar volume in the surface layer and in the solution, the calculated values of $x_1^{(\sigma)}$ are then used to make a second approximation refining the value of $v^{(\sigma)}$, and so on.

It follows from formulae (III–16, 18, and 21) that calculation of the composition of the surface layer requires that its thickness τ should be specified. Thermodynamics imposes certain restrictions on the choice of this quantity.

3. Estimation of Minimal Possible Thickness of Surface Layer

It has been shown[44,47] in the thermodynamics of surface phenomena that conditions of stability impose limitations on the thickness of the surface layer. These conditions can be used to find the minimum possible thickness for every mixture composition at every temperature. The requirement that the compositions of solution and surface layer should vary in parallel

$$(dx_1^{(\sigma)}/dx_1^{(\alpha)}) \geqslant 0$$

can be used as such a condition for binary systems. Application of this inequality to Eqn. (III, 15) and the assumption that molar volumes are additive yield

$$\tau \geqslant \Gamma_{2(1)} [v^{(\alpha)} - x_1^{(\alpha)}(v_1 - v_2)] + x_1^{(\sigma)} d\Gamma_{2(1)}/dx_1^{(\alpha)} \qquad \text{(III, 22)}$$

On the other hand, it follows from the self-evident inequality $0 \leqslant x_1^{(\sigma)} \leqslant 1$ that

$$\tau \geqslant \Gamma_{2(1)} v_2 \qquad \text{(III, 23)}$$

where v_1 and v_2 are the molar volumes of the components, and

$$v^{(\alpha)} \equiv v_2 + (v_1 - v_2) x_1^{(\alpha)}$$

is the additive molar volume of phase α. Analogous relations (but written for an equimolecular surface) were obtained for films adsorbed on a solid[44].

Use of other stability conditions for surface layers of finite thickness also leads to inequalities of the type (III, 22 and 23). The minimum possible thickness is then found directly from data on the composition of the surface layer[41,46].

4. Calculation of Excess Entropy

Considerable interest attaches not only to relative adsorption and the composition of the surface layer but also to the entropy characteristics of the latter, especially in connection with its structure. Calculations of these characteristics for binary liquid solutions were first published by the Reviewers[43,45]. The excess entropy depends by definition (II, 4) on the position of the dividing surface. However, the quantity $\bar{s}(j)$, introduced by analogy with the relative adsorption, is invariant with respect to displacement of the dividing surface and according to (II, 9) is equal to the excess entropy for a surface corresponding to the condition $\Gamma_j = 0$.

To obtain a relation for calculating the excess entropy we make use of an equation linking the molar entropies of solution and surface layer of finite thickness $s^{(\alpha)}$ and $s^{(\sigma)}$ with the temperature derivative of the surface tension. For a liquid–vapour equilibrium in a binary system, with the density of the vapour phase neglected, this equation becomes[41]

$$s^{(\sigma)} = s^{(\alpha)} - \frac{A}{m^{(\sigma)}} \left(\frac{d\sigma}{dT}\right)_{x_1^{(\alpha)}} + \left(\frac{\partial s}{\partial x_1}\right)^{(\alpha)} (x_1^{(\sigma)} - x_1^{(\alpha)}) \qquad \text{(III, 24)}$$

According to a general rule[41] a similar relation should apply to the excess functions. On passing to the latter $m^{(\sigma)}/A$ is replaced by the sum of the absolute adsorptions $\Gamma_1 + \Gamma_2$, and $x_1^{(\sigma)}$ by $\Gamma_1/(\Gamma_1 + \Gamma_2)$. Hence the entropy of the surface layer $s^{(\sigma)} \equiv S^{(\sigma)}/m^{(\sigma)}$ is replaced by $\bar{s}/(\Gamma_1 + \Gamma_2)$, where $\bar{s}$ is the excess entropy per unit surface. From this we obtain

$$\bar{s} = s^{(\alpha)}(\Gamma_1 + \Gamma_2) - (d\sigma/dT)_{x_1^{(\alpha)}} + (\partial s/\partial x_1^{(\alpha)})[\Gamma_1 - x_1^{(\alpha)}(\Gamma_1 + \Gamma_2)] \qquad \text{(III, 25)}$$

Passing to relative adsorptions, we find from (III, 25) that

$$\bar{s}_{(1)} = -(d\sigma/dt)_{x_1^{(\alpha)}} + [s^{(\alpha)} - (\partial s/\partial x_1)^{(\alpha)} x_1^{(\alpha)}]\,\Gamma_{2(1)} \qquad \text{(III, 26)}$$

$$\bar{s}_{(2)} = -(d\sigma/dT)_{x_1^{(\alpha)}} + [s^{(\alpha)} + (\partial s/\partial x_1)^{(\alpha)}(1 - x_1^{(\alpha)})]\,\Gamma_{1(2)} \qquad \text{(III, 27)}$$

whence

$$\bar{s}_{(2)} = \bar{s}_1 + \bar{s}^{(\alpha)}(\Gamma_{1(2)} - \Gamma_{2(1)}) \qquad \text{(III, 28)}$$

In the practical application of formulae (III, 26 and 27) to the calculation of excess entropies from experimental values of $(d\sigma/dT)_{x_1(\alpha)}$ the molar entropy of the solution is first calculated by means of the formula

$$s^{(\alpha)} = s_1 x_1^{(\alpha)} + s_2(1 - x_1^{(\alpha)}) + (\Delta h - \Delta g)/T \qquad \text{(III, 29)}$$

where Δh is the molar heat of mixing, which can be determined from calorimetric data, and Δg is the molar Gibbs free energy of mixing.

5. Calculation of Molar Entropy of Surface Layer

Calculation of molar entropy of surface layer from data on excess entropy

As in the calculation of composition, the entropy of the surface layer can be calculated either from excess Gibbs functions or directly by means of formulae relating to the surface layer. To obtain relations between the excess entropy and the molar entropy of the surface layer we return to Fig. 1, replace the density profile by the entropy profile, and write down the consequent self-evident relation

$$\bar{s} = S^{(\sigma)}/A - s_v^{(\alpha)}\tau + (s_v^{(\alpha)} - s_v^{(\beta)})(z_\beta - z_s) \qquad \text{(III, 30)}$$

Considering (III, 30) together with (III, 12) and passing to molar quantities

$$S^{(\sigma)} = s^{(\sigma)} m^{(\sigma)},\ s_v^{(\alpha)} = \frac{s^{(\alpha)}}{v^{(\alpha)}},\ s_v^{(\beta)} = \frac{s^{(\beta)}}{v^{(\beta)}},\ \rho_1^{(\alpha)} = \frac{x_1^{(\alpha)}}{v^{(\alpha)}},\ \rho_1^{(\alpha)} = \frac{x_1^{(\beta)}}{v^{(\beta)}}$$

we find from (II, 9) that

$$s^{(\sigma)} = \frac{v^{(\sigma)}}{\tau}\bar{s}_{(1)} + \frac{\varkappa\,(x_1^{(\alpha)}s^{(\beta)} - x_1^{(\beta)}s^{(\alpha)})\,v^{(\sigma)}/v^{(\alpha)} + (s^{(\alpha)} - s^{(\beta)\varkappa})\,x_1^{(\sigma)}}{x_1^{(\alpha)} - x_1^{(\beta)\varkappa}} \quad \text{(III, 31)}$$

where $x_1^{(\sigma)}$ is defined by (III, 15) with the same meaning of κ. Thus formula (III, 31), when considered in combination with (III, 15), enables the molar entropy of the surface layer to be calculated from its excess entropy. We again stress that the thickness and the molar volume of the surface layer must be specified: these two parameters define unambiguously the position of the surface layer in the heterogeneous system.

On passing to a solution–vapour ($\alpha-\beta$) system and neglecting the vapour density, we find from (III, 15 and 31) that

$$s^{(\sigma)} = s^{(\alpha)} + (\bar{s}_{(1)} - \Gamma_{2(1)}s^{(\alpha)})\,v^{(\sigma)}/\tau \quad \text{(III, 32)}$$

which can be used to calculate the molar entropy of the surface layer from the excess functions.

Calculation of molar entropy of surface layer from entropies of coexisting phases

The molar entropy of the surface layer $s^{(\sigma)}$ can be calculated directly from the thermodynamic equations for a layer of finite thickness. A suitable formula can be obtained from the definition (II, 11) of the differential molar entropy effect of adsorption. For a binary system we have

$$s_{\alpha\sigma} = s^{(\sigma)} - s^{(\alpha)} - (\partial s/\partial x_1)^{(\alpha)}\,(x_1^{(\sigma)} - x_1^{(\alpha)}) \quad \text{(III, 33)}$$

Taking into account the above expression for $s\alpha\sigma$, we hence obtain Eqn. (III, 24), which is quite convenient for calculating $s^{(\sigma)}$ from the entropy of the solution $s^{(\alpha)}$ and the temperature variation of surface tension.

The entropy of the surface layer can be calculated also by means of the formula

$$s^{(\sigma)} = s^{(\beta)} - s_{\alpha\beta} + s_{\alpha\sigma} - (\partial s/\partial x_1)^{(\alpha)}\,(x_1^{(\beta)} - x_1^{(\sigma)}) \quad \text{(III, 34)}$$

obtained by subtracting (II, 11) from (II, 13). Since the salt is non-volatile, $x_1^{(\beta)} = 0$, and we finally obtain[45]

$$s^{(\sigma)} = s^{(\beta)} - RB/T - (d\sigma/dT)_{x_1^{(\alpha)}}v^{(\sigma)}/\tau + (\partial s/\partial x_1)^{(\alpha)}x_1^{(\sigma)} \quad \text{(III, 35)}$$

The molar entropy of the vapour $s^{(\beta)}$ is evaluated from the formula

$$s^{(\beta)} = s_0^{\beta} - R\ln P \quad \text{(III, 36)}$$

where $s_0^{(\beta)}$ is the entropy of 1 mole of water vapour at 1 atm, and P (in atm) is the aqueous vapour pressure over the solution.

Among Eqns. (III–24, 32, and 35) the most convenient for practical application is (III, 24), which gives the smallest calculated error[43,48]. However, the use both of this equation and of (III, 32) requires the availability of calorimetric data, from which $s^{(\alpha)}$ can be calculated, and then the entropy of the surface layer. Adsorption data are also required when Eqn. (III, 34) is applied. However, formula (III, 36), which involves calculating the entropy of phase β and the entropy effect $s\alpha\beta$, can be used in approximate form (neglecting the last term) even in the absence of calorimetric data.

IV. EFFECT OF NATURE OF DISSOLVED IONS ON PROPERTIES OF SURFACE LAYER

In this Section we shall discuss results calculated by means of the above formulae for binary aqueous salt systems studied hitherto. Calculations have been made at one or more temperatures depending on the completeness and quality of the experimental data. The calculated thermodynamic characteristics of surface layers of various aqueous salt systems at the same temperature permit the systems to be compared and the effects of cations and anions on the structure and properties of the surface layer to be elucidated. The temperature 25 °C was chosen for this purpose. Most published surface-tension data relate to the range 10–30 °C, which permits interpolation for 25 °C. Furthermore, heats of mixing[49–51] as well as activity coefficients[52] are most often given for this temperature. Calculations at other temperatures are also important for revealing the temperature dependence of these properties of surface layers.

[References containing data on surface tension and activity coefficients for aqueous salt solutions.]

Salt	Surface tension	Activity coeff.	Salt	Surface tension	Activity coeff.
LiCl	9, 10, 55–57	58, 59	$NaNO_3$	3, 7, 60, 70, 75	52
NaCl	7, 14, 28, 60, 61	58, 59	KNO_3	3, 62, 70, 72, 75	52
KCl	9, 61, 62	52, 58, 59	$CsNO_3$	26	52
RbCl	48, 63, 86	52, 64	NH_4NO_3	3, 7, 19, 65, 75	52, 76
CsCl	48, 86	52	$AgNO_3$	9, 19, 77	52
NH_4Cl	55, 58	58, 59	$Ba(NO_3)_2$	7, 65	52
$MgCl_2$	68, 75	52	$Zn(NO_3)_2$	66, 68	52
$CaCl_2$	15, 56, 65–67	52	Na_2SO_4	7, 65 70, 75, 78	52
$SrCl_2$	59, 68, 69	52	K_2SO_4	7, 27, 62, 70	52
$BaCl_2$	27, 59	52	$(NH_4)_2SO_4$	3, 65, 75	52
$MnCl_2$	65, 68	52	$CuSO_4$	69, 70, 75	52
LiBr	3, 10, 56	52	$MgSO_4$	68, 72, 75, 79	52
NaBr	45, 65	58	$ZnSO_4$	59, 72, 75	52
KBr	3, 7, 10, 71, 72	52	$Al_2(SO_4)_3$	65, 80	52
LiI	3, 10	52	$K_3[Fe(CN)_6]$	58, 65	52
NaI	10, 36, 61	58, 59	Na_2CO_3	3, 8, 75, 81	52
KI	61, 62	58, 59	K_2CO_3	19, 70, 75	52
$LiNO_3$	3, 73, 74	52			

The Table summarises the published sources used. The second column gives references to determinations of surface tension, and the third column the sources of data on activity coefficients or vapour pressures. The molar entropies of the pure components have been taken from Refs. 53 and 54.

1. Dependence of Relative Adsorption on Energy of Hydration of Ions of Dissolved Salt

When calculating relative adsorptions in aqueous salt systems, we must bear in mind that the concentrations of hydroxide and hydrogen ions are far smaller than those of the ions of the dissolved salt. From the electrical neutrality of the surface layer (III, 3) we may then suppose that the condition of equivalent adsorption of cation and anion of the salt is a quite good approximation. Formulae (III, 9–11) have therefore been used to compute relative adsorptions.

The calculated adsorptions show (Figs. 2–15) that the relative adsorption of water $\Gamma_{2(1)}$ is positive in all the systems examined. The adsorption isotherms pass through an extremum in aqueous potassium, rubidium, and caesium chlorides, aqueous lithium and zinc nitrates, and aqueous ammonium sulphate (in potassium chloride solution it is perceptible only at 40 °C [61]). The relative adsorption of the salt $\Gamma_{1(2)}$ is negative, and in most cases increases numerically with concentration.

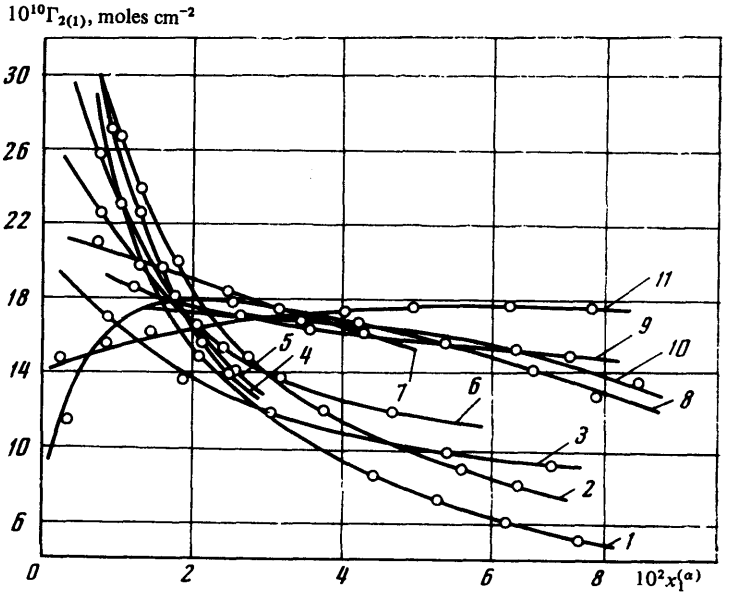

Figure 2. Relative adsorption of water at 25°C in aqueous solutions of: 1) $MgCl_2$; 2) $CaCl_2$; 3) LiCl; 4) $BaCl_2$; 5) $SrCl_2$; 6) $MnCl_2$; 7) CsCl; 8) RbCl; 9) KCl; 10) NaCl; 11) NH_4Cl.

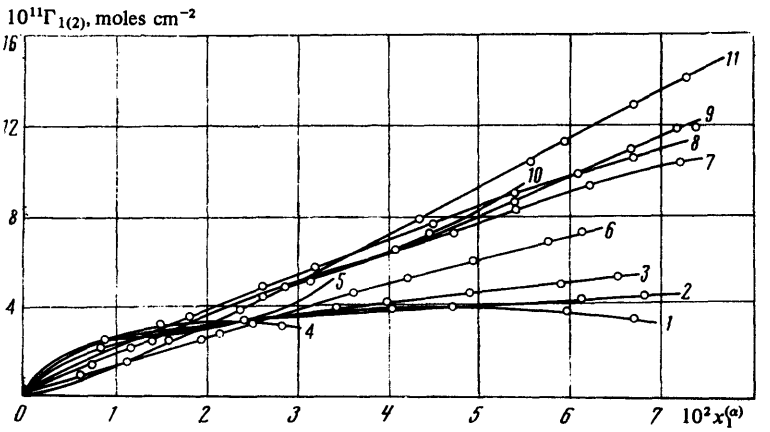

Figure 3. Relative adsorption of salt at 25°C in aqueous solutions of: 1) $MgCl_2$; 2) LiCl; 3) $CaCl_2$; 4) $BaCl_2$; 5) $SrCl_2$; 6) $MnCl_2$; 7) RbCl; 8) NaCl; 9) KCl; 10) CsCl; 11) NH_4Cl.

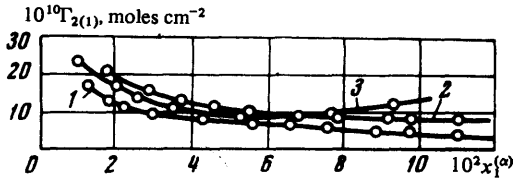

Figure 4. Relative adsorption of water at 25°C in aqueous solutions of: 1) LiBr; 2) NaBr; 3) KBr.

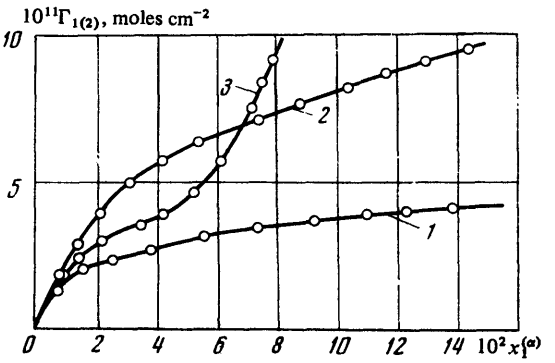

Figure 5. Relative adsorption of salt at 25°C in aqueous solutions of: 1) LiBr; 2) NaBr; 3) KBr.

In order to interpret the adsorption data we must consider the relation between the relative adsorption and the nature of the ions adsorbed. Consideration is usually given to published ionic hydration energies when adsorption isotherms for different salts are compared[82,83]. Indeed, the ability of an ion to pass from the bulk of the solution to the surface layer is largely determined by the strength of bonding of the ion with solvent molecules, i.e. by its hydration. However, data on the energy of hydration of individual ions generally relate to infinite dilution[49,84], so that the concentration dependence of this energy must be taken into account when discussing adsorption over a wide concentration range. Use for this purpose of Mishchenko's qualitative theory[49], which classifies solutions of electrolytes according to the form of isotherm for their integral heats of distribution, shows that substances whose dissolution becomes continuously less exothermic exhibit the most substantial change (weakening) of hydration with increase in solution concentration. Among the systems examined, aqueous solutions of lithium chloride, bromide, iodide, and nitrate, magnesium chloride and sulphate, calcium and barium chlorides, and zinc nitrate and sulphate belong to this group.

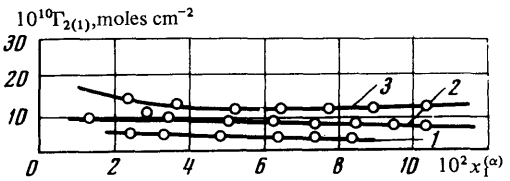

Figure 6. Relative adsorption of water at 25°C in aqueous solutions of: 1) LiI; 2) NaI; 3) KI.

A similar conclusion concerning the variation of hydration with concentration can be reached by comparing values of df/dc (where f is the mean activity coefficient and c the concentration). Positive values of df/dc indicate partial dehydration of the ions. Comparison of these derivatives for solutions of alkali-metal chlorides shows that, with increase in concentration, ionic dehydration is most significant with lithium chloride solution[20].

As example we shall examine in detail the series of solutions of alkali-metal chlorides. In infinitely dilute solutions the hydration energies $-\Delta H_0$ of the lithium, sodium, potassium, rubidium, caesium, and ammonium cations are respectively 127, 101, 81, 75, 67, and 78 kcal g-ion^{-1}.[49] However, the above discussion shows that bonding with water molecules becomes weaker with increase in concentration (energetic and coordinative dehydration) more noticeably with the lithium ion, which is most strongly hydrated at infinite dilution, than with the other cations, which facilitates transfer of these ions from the bulk of the solution to the surface layer. In sufficiently concentrated solutions the adsorption may thus become greater (numerically less) than that from solutions of the other chlorides.

The above considerations apply also to solutions of lithium bromide, iodide, and nitrate, magnesium chloride and sulphate, calcium and barium chlorides, and zinc nitrate and sulphate, and correspond to results obtained over a considerable concentration range. Fig. 3 shows that at concentrations $x_1^{(\alpha)} = 0.03$ and above the numerical value of the adsorption is significantly smaller from solutions of lithium, magnesium, and calcium chlorides than from solutions of other chlorides. Similarly, with the alkali-metal bromides (Fig. 5) adsorption from lithium bromide solution is greater (numerical value smaller) than from sodium and potassium bromide solutions beginning from $x_1^{(\alpha)} = 0.01$. The conclusions reached are supported also by the adsorption isotherms for solutions of iodides (Fig. 7), nitrates (Fig. 9), and sulphates (Fig. 11).

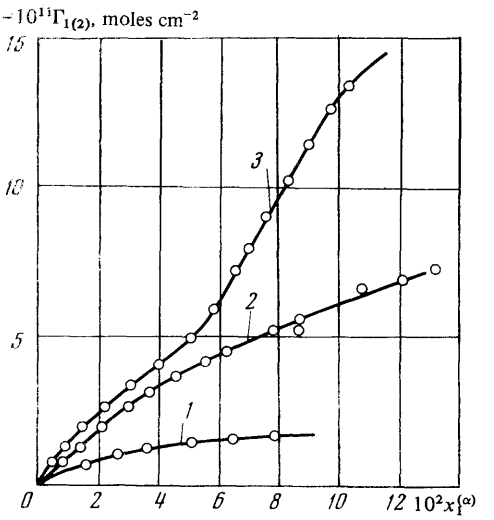

Figure 7. Relative adsorption of salt at 25°C in aqueous solutions of: 1) LiI; 2) NaI; 3) KI.

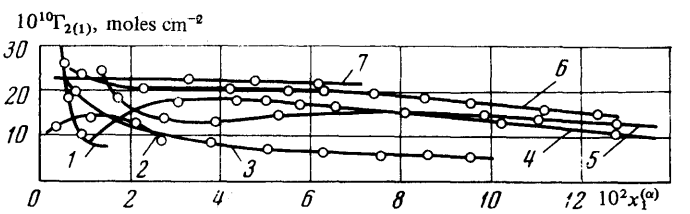

Figure 8. Relative adsorption of water at 25°C in aqueous solutions of: 1) $Ba(NO_3)_2$; 2) $LiNO_3$; 3) $Zn(NO_3)_2$; 4) $NaNO_3$; 5) NH_4NO_3; 6) $AgNO_3$; 7) KNO_3.

In very dilute solutions, however, it must be expected that the relative positions of the isotherms will correspond to the hydration energies for infinite dilution. The diagrams show, nevertheless, that the adsorption isotherms almost coalesce at low salt concentrations. Additional calculations were therefore made for the chlorides of various metals. With $x_1^{(\alpha)} = 0.004$ adsorption of the salt at 25°C (expressed as -10^{-11} mole cm^{-2}) is respectively 0.4, 0.6, 0.8, and 0.9 in aqueous rubidium, ammonium, lithium, and barium chlorides. Thus at such concentrations adsorption decreases with increase in the energy of hydration of the cation. In the above series it is

least with the barium ion, which is the most vigorously hydrated in infinitely dilute solution[49] ($-\Delta H_0$ = 320 kcal g-ion^{-1}).

For nitrate solutions calculations were made of the adsorption with $x_1^{(\alpha)}$ = 0.002 at 25°C. The values obtained for aqueous caesium, lithium, and zinc nitrates (respectively 0.3, 0.6, and 0.9 measured in -10^{-11} mole cm^{-2}) are also consistent with the energies of hydration of the cations at infinite dilution[49] ($-\Delta H_0$ = 67, 127, and 496 kcal g-ion^{-1}).

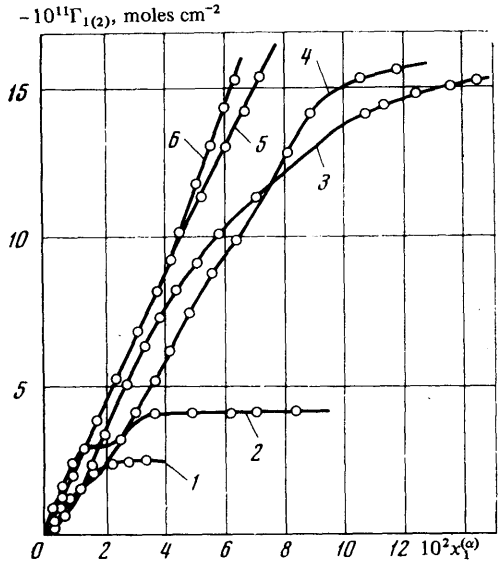

Figure 9. Relative adsorption of salt at 25°C in aqueous solutions of: 1) $LiNO_3$; 2) $Zn(NO_3)_2$; 3) $NaNO_3$; 4) NH_4NO_3; 5) $AgNO_3$; 6) KNO_3.

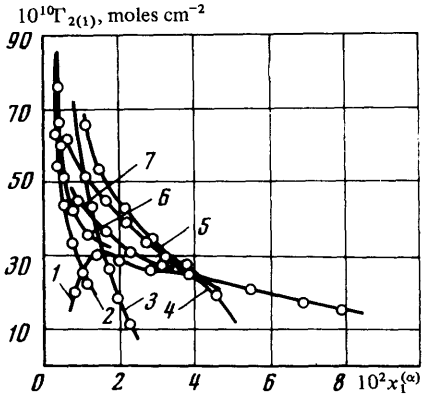

Figure 10. Relative adsorption of water at 25°C in aqueous solutions of: 1) $(NH_4)_2SO_4$; 2) $Al_2(SO_4)_3$; 3) $CuSO_4$; 4) $MgSO_4$; 5) $ZnSO_4$; 6) K_2SO_4; 7) Na_2SO_4.

In other cases (when the salts exhibit no marked difference in the concentration dependence of the hydration energy) the relative positions of the salt-adsorption isotherms correspond throughout the concentration range to the hydration energies at infinite dilution, e.g. for lithium, sodium, and potassium halides (Figs. 13–15). In conformity with Mishchenko's classification, solutions of lithium chloride, bromide, and iodide are of the same type according to the form of the isotherms for the integral heats of dissolution, while solutions of the sodium halides belong to another type, and those of the potassium halides to a third type. This means that the variation (increase or decrease) in the energy of hydration of the anions is roughly the same in each of the three cases. The relative positions of the adsorption isotherms should then correspond to these hydration energies at infinite dilution. For the chloride, bromide, and iodide ions we have[49] $-\Delta H_0$ = 84, 76, and 67 kcal g-ion^{-1}. The diagrams show that the numerical value of the adsorption diminishes in this sequence in all three cases.

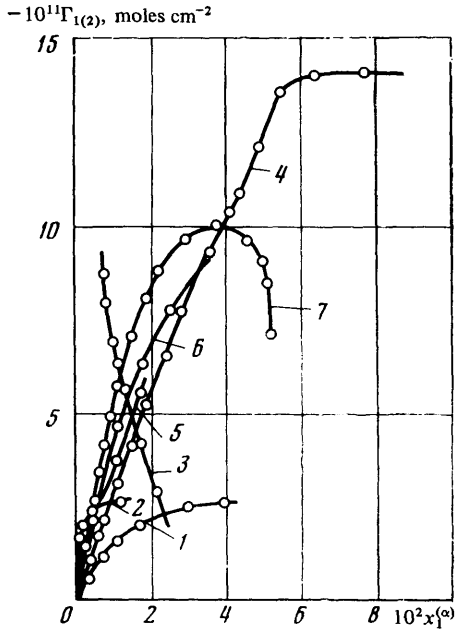

Figure 11. Relative adsorption of salt at 25°C in aqueous solutions of: 1) $ZnSO_4$; 2) K_2SO_4; 3) $CuSO_4$; 4) $(NH_4)_2SO_4$; 5) $Al_2(SO_4)_3$; 6) Na_2SO_4; 7) $MgSO_4$.

As already mentioned, calculations of adsorption have been made for several temperatures where suitable data on surface tension and activity coefficients were available. Comparison of results for 25° and 40°C indicates only a slight change (in most cases within the limits of error of the calculation) in the relative adsorption with temperature[43,61]. Only in aqueous ammonium chloride is a significant increase in $\Gamma_{1(2)}$ produced by raising the temperature from 25° to 40°C.[55] The evident reason is that the energy of hydration of the ammonium ion diminishes more rapidly with rise in temperature than do those of metal ions.

Increase in the numerical adsorption of surface-inactive non-volatile substances is accompanied by an increase in the surface tension of the solution (a direct consequence of the Gibbs adsorption equation). However, the surface

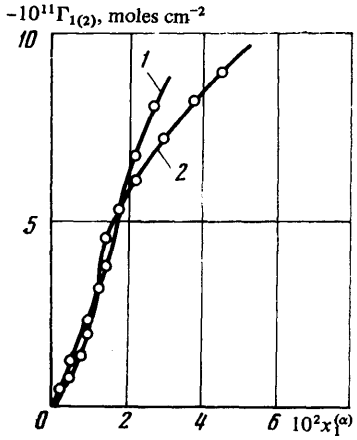

Figure 12. Relative adsorption of carbonates at 25°C from aqueous solutions of: 1) Na_2CO_3; 2) K_2CO_3.

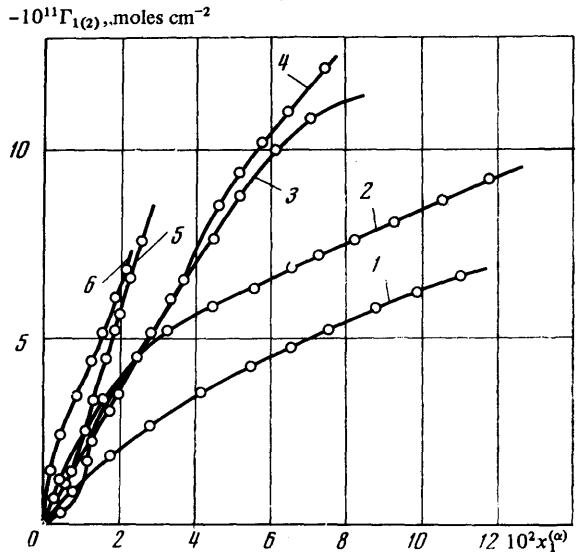

Figure 13. Relative adsorption of sodium salts at 25°C from aqueous solutions of: 1) NaI; 2) NaBr; 3) NaCl; 4) $NaNO_3$; 5) Na_2CO_3; 6) Na_2SO_4.

tension depends also on structural changes occurring in the solution under the influence of ions of the dissolved salt (this fact is reflected in the Gibbs equation by the activity coefficients). On the one hand, disruption of the structure of water by ions facilitates the transfer of water molecules to the surface layer and thus tends to diminish surface tension. On the other hand, the fields due to the ions, whose concentration in the solution may exceed considerably their concentration in the surface layer, promote the transfer of molecules into the interior of the solution and increase surface tension[20]. The presence of opposing tendencies provides an explanation for the fairly closely similar surface tensions exhibited by solutions of salts containing markedly different ions. For example, the presence of lithium ions structures a solution[85] and hinders the transfer of water molecules to the surface layer, which corresponds to an increase in surface tension relative both to pure water and to potassium chloride solution (potassium ions are known to loosen the structure of water[85]). But Fig. 3 shows that the adsorption of potassium chloride is numerically greater than that of lithium chloride. Hence on this basis the presence of potassium chloride in solution should produce a greater increase in surface tension. As a result, the surface-tension isotherms of these two solutions are quite close (Fig. 16).

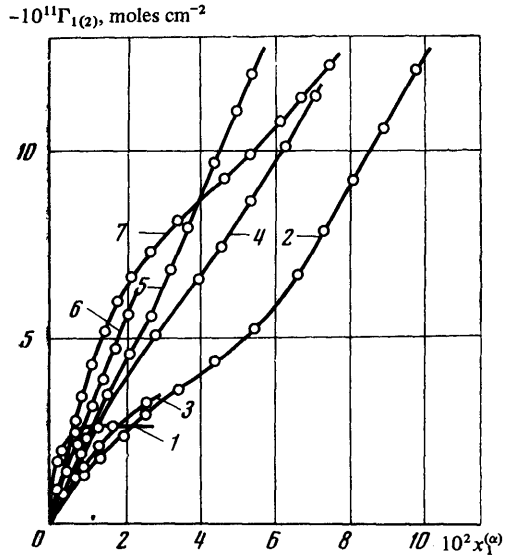

Figure 14. Relative adsorption of potassium salts at 25°C from aqueous solutions of: 1) K_2SO_4; 2) KI; 3) KBr; 4) KCl; 5) KNO_3; 6) $K_3[Fe(CN)_6]$; 7) K_2CO_3.

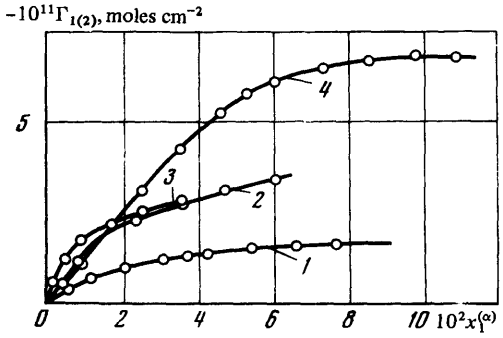

Figure 15. Relative adsorption of lithium salts at 25°C from aqueous solutions of: 1) LiI; 2) LiBr; 3) $LiNO_3$; 4) LiCl.

2. Composition and Minimum Possible Thickness of Surface Layer in Aqueous Salt Systems

A value of τ exceeding the minimum possible thickness must be specified in order to calculate the composition of the surface layer by means of formulae (III—16, 18, and 21), as in the calculation of its molar entropy. Thus the choice of thickness for the calculation entails estimation of its minimum possible value.

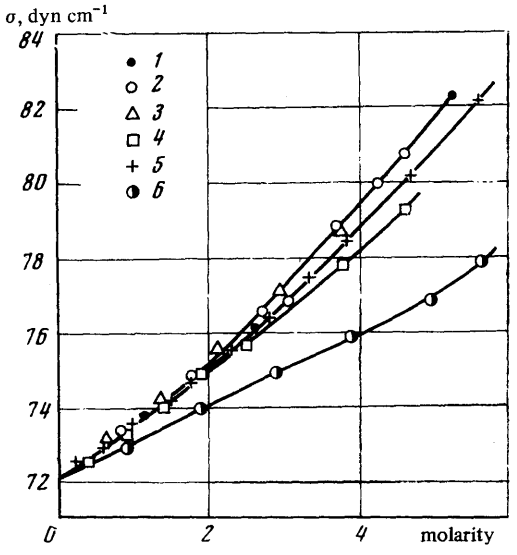

Figure 16. Surface tension at 25°C of solutions of ammonium and alkali-metal chlorides[48,55,61]: 1) LiCl; 2) NaCl; 3) KCl; 4) RbCl; 5) CsCl; 6) NH_4Cl.

The estimation has been based on the inequalities (III, 22 and 23). The larger of the two values of τ_{min} obtained from these inequalities are plotted against composition in Figs. 17–20. In most cases the minimum possible thickness decreases with increase in solution concentration. The diagrams show also that, with the exception of solutions of sulphates and carbonates, τ_{min} does not exceed 5 Å even at low salt concentrations. It is noticeable also that the minimum possible thickness falls more rapidly with concentration in solutions of sulphates.

The inequality (III, 23) can be used also to make the interesting estimation of the maximum possible thickness of a layer of pure water on the surface of the solution if such a layer can exist (an analogous method has already been applied to aqueous sodium chloride[14]). Another possibility for estimating the thickness of a film of water on the surface of a salt solution is to solve Eqns. (III, 18 and 21 [sic]) for τ with $x_1^{(\sigma)} = 0$. The hypothetical absence of salt in the surface layer implies a transition from a real surface layer to a model in which vapour and salt solution are separated by a film of water of thickness τ.

Calculations by different methods for solutions of lithium and sodium chlorides show (Fig. 21) that the film of water becomes thinner with increase in solution concentration, and that the water present on the surface of concentrated solutions is insufficient to form a monolayer. This implies that in these systems the ions of the salt enter a monolayer at the solution—vapour interface—a conclusion which is consistent with earlier results[8,9,15,16,45].

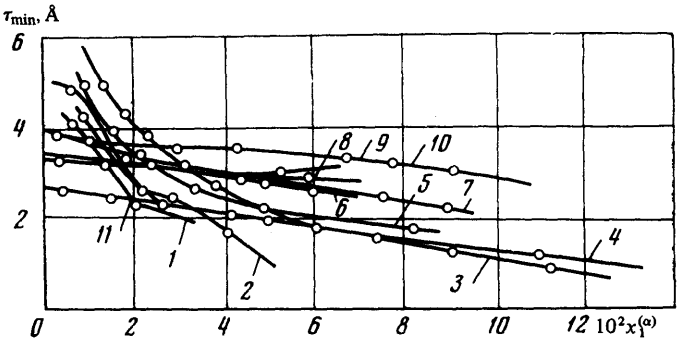

Figure 17. Concentration dependence of minimum possible thickness of surface layer at 25°C in aqueous solutions of chlorides: 1) $SrCl_2$; 2) $MgCl_2$; 3) $CaCl_2$; 4) LiCl; 5) $MnCl_2$; 6) RbCl; 7) NaCl; 8) KCl; 9) CsCl; 10) NH_4Cl; 11) $BaCl_2$.

Estimation of the minimum possible thickness was followed by calculation of the composition of the surface layer. In the case of carbonate and sulphate solutions the calculations were based on a layer 10 Å thick, and in the remaining cases 5 Å was chosen. These values are acceptable on purely thermodynamic grounds, since they deliberately exceed the minimum possible thickness.

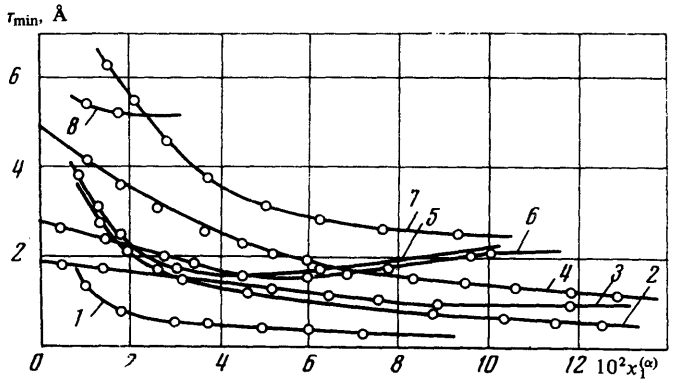

Figure 18. Concentration dependence of minimum possible thickness of surface layer at 25°C in aqueous solutions of alkali-metal halides and carbonates: 1) LiI; 2) LiBr; 3) NaI; 4) NaBr; 5) KBr; 6) KI; 7) Na_2CO_3; 8) K_2CO_3.

Choice of the same thickness (e.g. 5 or 10 Å) for the surface layers of several salt solutions helps to reveal several regularities indicating a relation between the nature of the ions and the properties of the surface layer.

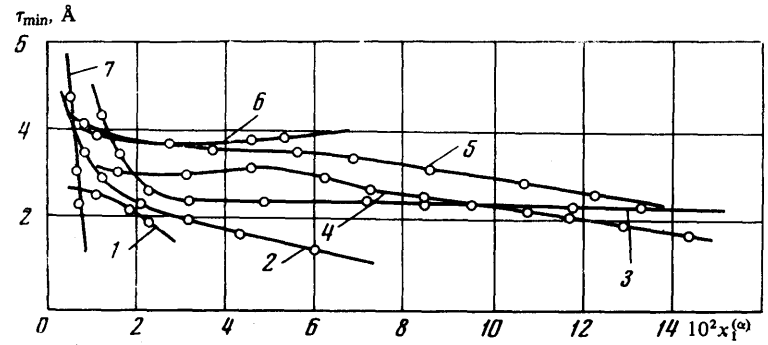

Figure 19. Concentration dependence of minimum possible thickness of surface layer at 25°C in aqueous solutions of nitrates: 1) $LiNO_3$; 2) $Zn(NO_3)_2$; 3) NH_4NO_3; 4) $NaNO_3$; 5) $AgNO_3$; 6) KNO_3; 7) $Ba(NO_3)_2$.

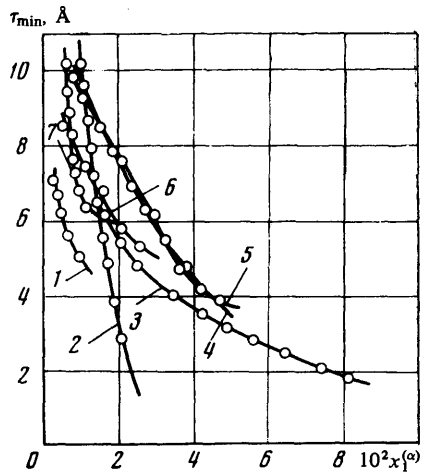

Figure 20. Concentration dependence of minimum possible thickness of surface layer at 25°C in aqueous solutions of sulphates: 1) K_2SO_4; 2) $CuSO_4$; 3) $(NH_4)_2SO_4$; 4) $MgSO_4$; 5) $ZnSO_4$; 6) Na_2SO_4; 7) $Al_2(SO_4)_3$.

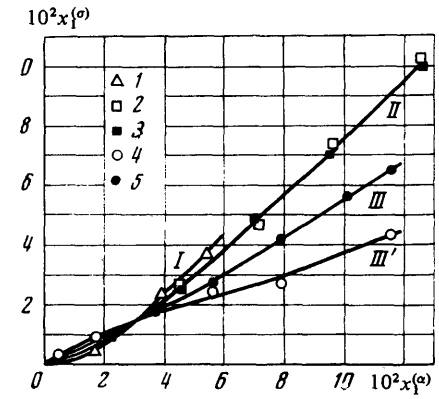

Figure 22. Composition of surface layer 5 Å thick in aqueous solutions of chlorides of: I) calcium; II) lithium; III, III′) ammonium at: 1,2,4) 25°C; 3,5) 40°C.

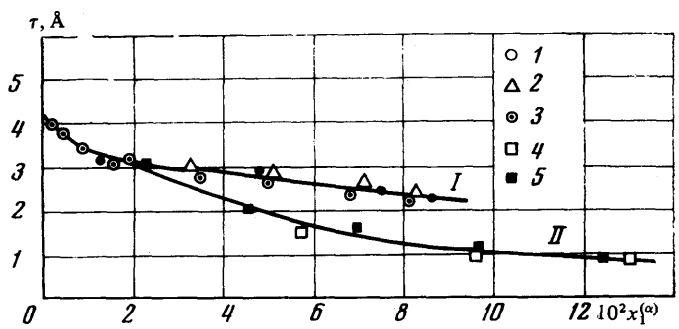

Figure 21. Thickness at 25°C of layer of water on surface of solutions of: I) sodium chloride; II) lithium chloride from: 1) formula (III, 17); 2) inequality (III, 22); 3) Ref. 14; 4) formula (III, 17); 5) inequality (III, 22).

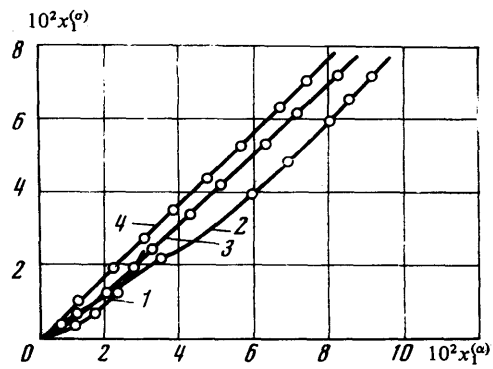

Figure 23. Composition of surface layer 5 Å thick in aqueous solutions at 25°C of lithium salts: 1) nitrate; 2) chloride; 3) bromide; 4) iodide.

Parallel calculations of composition by means of Eqns. (III–16, 18, and 21) for solutions of alkali-metal and ammonium chlorides showed good agreement [43,55,61], so that composition in the remaining systems was calculated only by means of (III, 16). Plots of the results show (Figs. 22–27) that the surface layer is in all cases depleted in salt relative to the solution, which corresponds to negative relative adsorption of the salt. This is a natural and necessary feature, since the parameters are directly related by formula (III, 16).

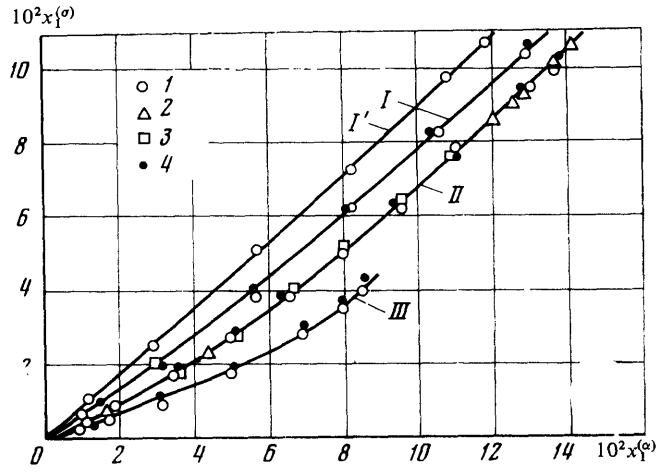

Figure 24. Composition of surface layer 5 Å thick in aqueous solutions of sodium halides: I) iodide; I') iodide (10 Å); II) bromide; III) chloride at: 1–3) 25°C; 4) 40°C.

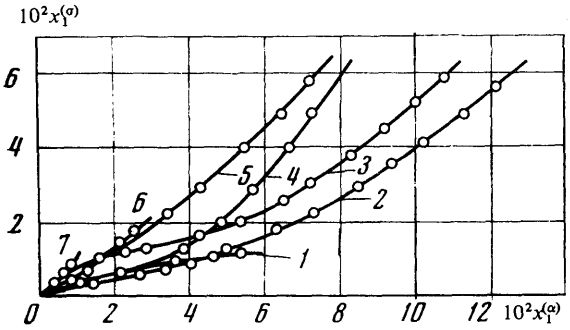

Figure 25. Composition of surface layer 5 Å thick at 25°C in aqueous solutions of nitrates: 1) KNO_3; 2) $AgNO_3$; 3) $NaNO_3$; 4) NH_4NO_3; 5) $Zn(NO_3)_2$; 6) $LiNO_3$; 7) $Ba(NO_3)_2$.

Comparison of the isotherms for the lithium halides shows (Fig. 23) that, for solutions of the same composition, the salt content of the surface layer diminishes in the sequence LiI > LiBr > LiCl throughout the concentration range. A similar pattern is exhibited by the halides of sodium (Fig. 24) and of potassium [55]. Thus the results obtained for adsorption and composition indicate that iodides penetrate into the surface layer more readily than do bromides and chlorides (and bromides in turn more readily than chlorides). As already mentioned, the increase in salt contents of lithium, sodium, and potassium halides in the sequence—chloride < bromide < < iodide—corresponds to the hydration energies of these ions.

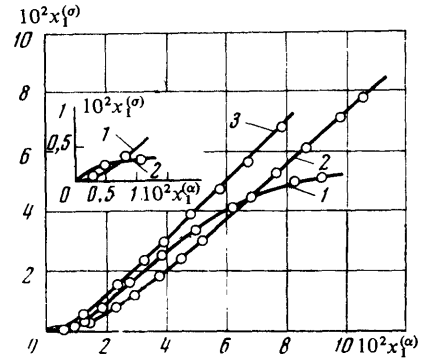

Figure 26. Composition of surface layer 5 Å thick at 25°C in aqueous solutions of alkali-metal bromides: 1) KBr; 2) NaBr; 3) LiBr.

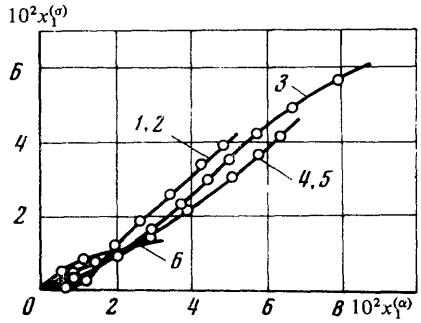

Figure 27. Composition of surface layer 10 Å thick at 25°C in aqueous solutions of sulphates and carbonates: 1) $CuSO_4$; 2) $ZnSO_4$; 3) K_2CO_3; 4) $(NH_4)_2SO_4$; 5) Na_2SO_4; 6) Na_2CO_3.

The isotherms for the composition of the surface layer in solutions of lithium, calcium, and ammonium chlorides show (Fig. 22) that at low concentrations ($x_1^{(\alpha)} < 0.03$) the quantity of salt in the surface layer diminishes in the sequence $NH_4Cl > LiCl > CaCl_2$, i.e. with increase in the energy of hydration of the cation at infinite dilution ($-\Delta H_0 = 78$, 127, and 386 kcal g-ion^{-1}). [49] The relative positions of the isotherms change in more concentrated solutions, which is explained by differences in the concentration dependence of the hydration energy for these ions [49].

A similar situation is observed with the surface layers of solutions of alkali-metal bromides and of sulphates (Figs. 26 and 27). The concentration of salts containing

the most strongly hydrated cations (lithium bromide and copper and zinc sulphates respectively) is lower in the surface layers of dilute solutions than are those of the other bromides and sulphates. For the above reasons the relative positions of the composition isotherms change with increase in concentration of the solution.

In conclusion we note that rise in temperature from 25° to 40°C has little effect on the composition of the surface layer in solutions of salts having a metal cation (Figs. 22 and 24).

3. Entropy of Surface Layers

Excess entropy

After the molar entropy of the solution $s^{(\alpha)}$ and the relative adsorption have been calculated, formulae (III, 26–28) can be used to estimate the excess entropies $\bar{s}_{(1)}$ and $\bar{s}_{(2)}$. The first calculations of excess entropy in binary systems were published by the Reviewers[43] (with unary systems excess entropy can be determined by means of the Gibbs adsorption equation).

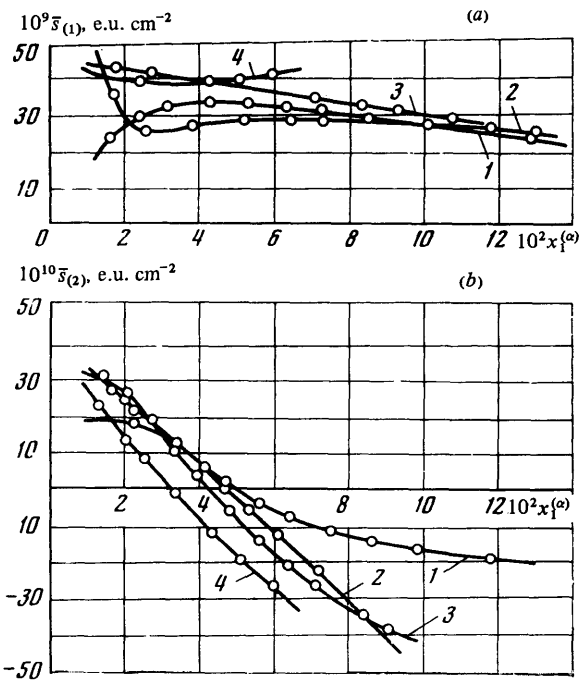

Figure 28. Excess entropies at 25°C in aqueous solutions of: 1) $NaNO_3$; 2) NH_4NO_3; 3) $AgNO_3$; 4) KNO_3.

The calculated results show that $\bar{s}_{(1)}$ is positive and in all cases exceeds $\bar{s}_{(2)}$ (e.g. Figs. 28 and 29 together with Refs. 43, 55, 61, and 68). Since $\bar{s}_{(1)}$ and $\bar{s}_{(2)}$ represent the excess entropies for the surfaces $\Gamma_1 = 0$ and $\Gamma_2 = 0$ respectively, the fact that $\bar{s}_{(1)} > \bar{s}_{(2)}$ implies that the dividing surface, for which $\Gamma_1 = 0$, is located below the surface corresponding to the condition $\Gamma_2 = 0$ (Fig. 1).

In all the systems examined the quantity $\bar{s}_{(2)}$ diminishes with increase in concentration, in some cases (e.g. nitrate solutions) becoming negative. Such a negative value (with $\bar{s}_{(1)} > 0$) does not necessarily mean that the molar entropy of the surface layer is smaller than the entropy of the solution. It may be due merely to variation in the position of the surface $\Gamma_2 = 0$ with concentration. Upward movement of this surface (increase in its coordinate z_S in Fig. 1) corresponds to a decrease in $\bar{s}_{(2)}$ down to negative values.

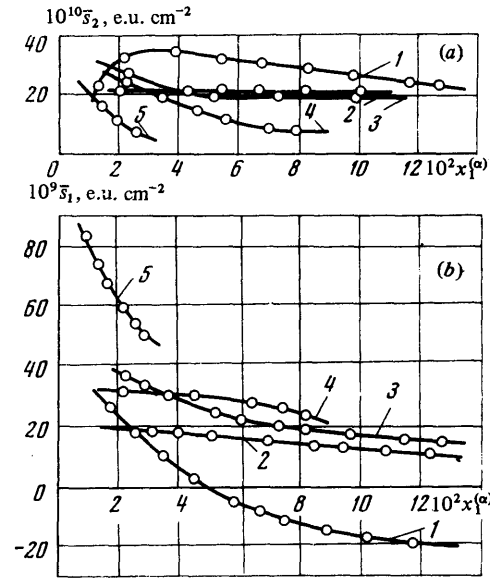

Figure 29. Excess entropies at 25°C in aqueous solutions of: 1) $NaNO_3$; 2) NaI; 3) NaBr; 4) NaCl; 5) Na_2SO_4.

Molar entropy of Surface layer

The molar entropy of a surface layer 5 Å thick was calculated by means of formulae (III—24, 32, and 35) for solutions of alkali-metal halides and ammonium chloride at 25° and 40°C (the calculation for aqueous sodium iodide was repeated with $\tau = 10$ Å); the results showed satisfactory agreement[43,45,55,61]. For the remaining systems Eqn. (III, 24) was used to calculate entropy at 25°C, since this method is the most accurate. Figs. 30–35 illustrate (*a*) the dependence of the entropy of the surface layer $s^{(\sigma)}$ on the composition of the layer and (*b*) the molar entropies of the solutions $s^{(\alpha)}$ as a function of solution composition.

The entropy of the solution is in all cases smaller than that of the coexisting surface layer: $s^{(\sigma)} > s^{(\alpha)}$. However, this difference is not entirely attributable to surface phenomena, since the solution shows a substantial difference in composition in bulk and at the surface. It is therefore of interest also to compare the entropy characteristics of solution and surface layer having the same salt concentration. Even in this case $s^{(\sigma)} > s^{(\alpha)}$. In aqueous lithium chloride with $x_1^{(\alpha)} = 0.045$, for example, $s^{(\alpha)} = 16.1$ e.u. mole^{-1}. With the same salt concentration in the surface layer, however, the entropy of the latter is $s^{(\sigma)} = 16.8$ e.u. mole^{-1}. In aqueous caesium chloride with $x_1^{(\alpha)} = 0.020$ we have similarly $s^{(\alpha)} = 17.5$ e.u. mole^{-1},

whereas with the same salt concentration in the surface layer $s^{(\sigma)} = 18.6$ e.u. mole^{-1}. Comparison of the entropies of surface layer and solution both containing 1 mole % of the salt gives for $s^{(\alpha)}$ and $s^{(\sigma)}$ the respective values 17.0 and 17.6 e.u. mole^{-1} (Figs. 30–34).

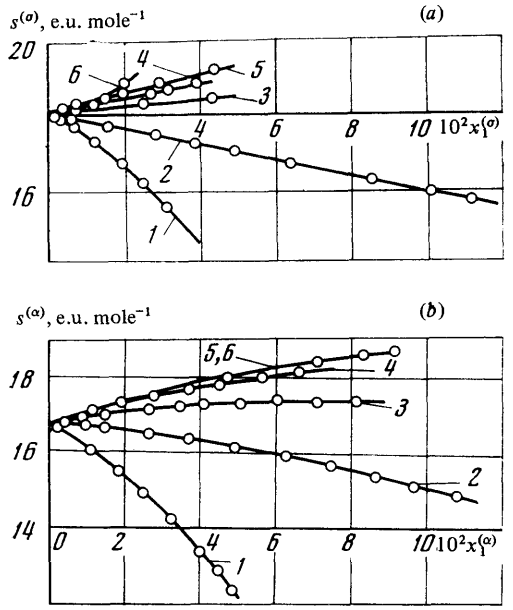

Figure 30. Composition dependence of molar entropy at 25°C in: *a*) surface layer 5 Å thick; *b*) solution for aqueous: 1) $MgCl_2$; 2) LiCl; 3) NaCl; 4) KCl; 5) RbCl; 6) CsCl.

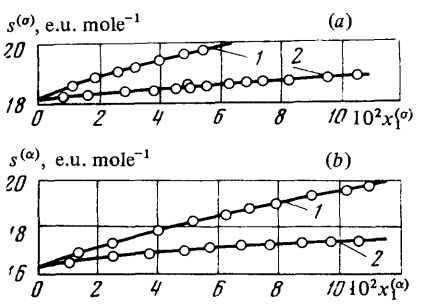

Figure 31. Composition dependence of molar entropy at 25°C in: *a*) surface layer 5 Å thick; *b*) solution for aqueous: 1) KI; 2) NaI.

The above examples show that the greater entropy of the surface layer is due not only to depletion with the salt but also to definite structural changes in the layer (with loosening of the surface structure on passing to the vapour). Nevertheless, a parallel variation in the entropies of solution and surface layer must be noted: increase in the salt concentration is accompanied by decreases in $s^{(\sigma)}$ and $s^{(\alpha)}$ in aqueous lithium chloride, magnesium chloride, and lithium nitrate, and by increases in the remaining cases. Such variation of entropy with concentration seems reasonable: increase in the content of the positively hydrated lithium and magnesium ions orders both the solution and the surface layer [85] with a consequent decrease in entropy; but accumulation of the large, weakly hydrated rubidium, caesium, and ammonium ions produces an increase in entropy.

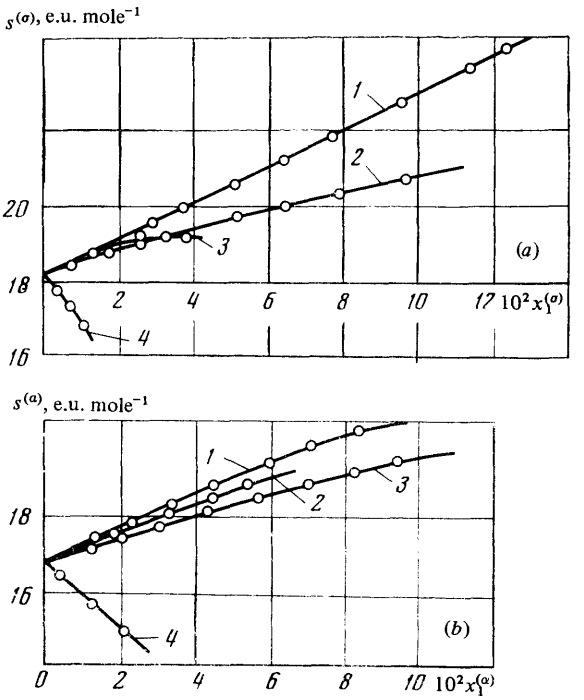

Figure 32. Composition dependence of molar entropy at 25°C in: *a*) surface layer 5 Å thick; *b*) solution for aqueous: 1) NH_4NO_3; 2) $NaNO_3$; 3) $AgNO_3$; 4) $LiNO_3$.

Comparison of the entropies of surface layers in different aqueous salt systems will reveal the effects of individual ions on the structure of the solution. Change in structure is due firstly to reorientation of water molecules by ion–dipole interaction. Among ions of the same valency the smallest will be the most effective. Secondly, the introduction of ions would tend to distort and disrupt the structure of water, and the more strongly the larger their size. Bonner [87] has concluded from ample experimental data that the combined effect of the above two factors would be minimal with sodium among singly charged ions. This conclusion is fully supported by the results obtained (Figs. 30 and 33). The entropy isotherm for the surface layer in aqueous sodium chloride is very nearly horizontal, which means little increase in entropy with the accumulation of salt in the surface layer: i.e. the introduction of sodium ions in fact causes minimal disruption of the structure on the surface layer.

Fig. 33(*a*) illustrates the molar entropies $s^{(\sigma)}$ as functions of composition of surface layer for aqueous solutions

of sodium chloride, bromide, iodide, and nitrate. At low salt concentrations the entropies are almost identical. But with increase in the salt content of the surface layer ($x_1^{(\sigma)} > 0.03$) the difference in behaviour among the halide ions affects the entropies of the surface layer (the chloride ion has less effect than have bromide and iodide ions on the structure of water [49]). Differences in the entropies of the solutions $s^{(\alpha)}$, however, are observed (Fig. 33*b*) at far higher concentrations ($x_1^{(\alpha)} > 0.08$). We reach the same conclusion from the molar entropies of solutions and surface layers in aqueous potassium chloride and iodide (Fig. 34).

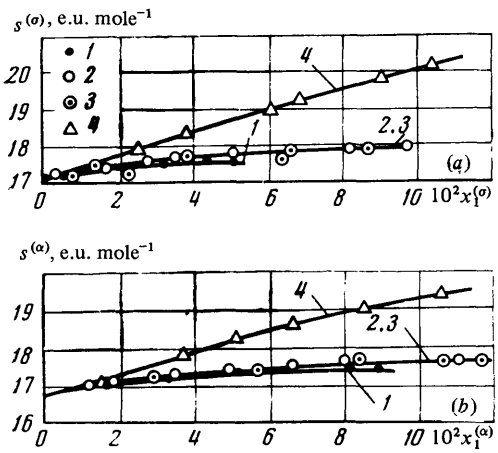

Figure 33. Composition dependence of molar entropy in: *a*) surface layer 5 Å thick; *b*) solution for aqueous: 1) NaCl; 2) NaBr; 3) NaI; 4) $NaNO_3$.

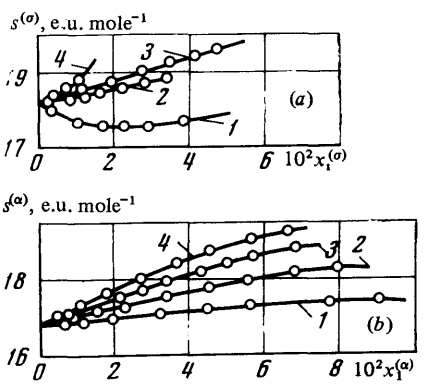

Figure 34. Composition dependence of molar entropy in: *a*) surface layer 5 Å thick; *b*) solution for aqueous: 1) KBr; 2) KCl; 3) KI; 4) KNO_3.

The entropy characteristics of solutions of rubidium and caesium chlorides (Fig. 35) are especially interesting. The isotherms of the molar entropies of the solutions coincide throughout the concentration range. Beyond the concentration $x_1^{(\sigma)} = 0.02$ the entropy of the surface layer increases more rapidly with the concentration of caesium chloride in the layer than with that of rubidium chloride.

The examples cited show that in several cases differences in behaviour among ions are more strongly developed in the surface layer than in the solution. The differences in the values of the corresponding thermodynamic functions of the systems therefore become appreciable sooner (at lower concentrations) in the surface layer than in the solution.

In conclusion we note that, among all the properties of surface layers, the entropy is most sensitive to variation in temperature, and increases appreciably on passing from 25° to 40°C. [43,45,55,61]

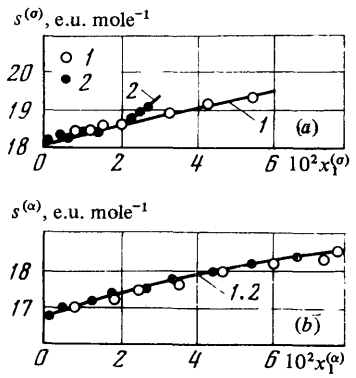

Figure 35. Composition dependence of molar entropy at 25°C in: *a*) surface layer 5 Å thick; *b*) solution for aqueous: 1) RbCl; 2) CsCl.

The Review has shown that thermodynamic calculations based on experimental data for surface tension and discussion of the thermodynamic characteristics obtained for surface layers are useful for studying the structure of aqueous salt systems and the effect of the nature of dissolved ions on the properties of solutions and surface layers.

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Advances in the Chemistry of Triptycene

V.R.Skvarchenko, V.K.Shalaev, and E.I.Klabunovskii

Information is presented on the preparation of triptycene, its homologues, and substituted derivatives. The spectroscopic, X-ray, optical, and other physical properties of these compounds are discussed. A systematic account is given of the behaviour of substituents located at a bridgehead, and of the differing reactivities of α- and β-positions in the aromatic rings on nucleophilic and electrophilic substitution. Reactions involving opening of the bridge system, the polarographic reduction of triptycenequinones, and the catalytic hydrogenation of triptycene are considered. The list of references contains 247 items.

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I. INTRODUCTION

Triptycene, which was first described in 1942,[1] has now become readily available thanks to the well known work of Wittig[2-9] on the preparation of dehydrobenzene and its interaction with anthracene.

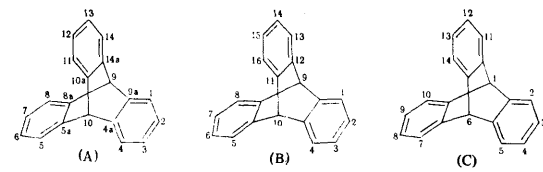
The specific properties of triptycene—the low mobility of bridge substituents, the difference in reactivity towards substitution between α- and β-positions in aromatic rings, steric peculiarities due to the rigidity of the molecule—attracted the attention of research workers. The large number of differently substituted isomeric compounds is due to the presence of three equivalent aromatic rings in the triptycene molecule. The bulky structure of the thermally stable triptycene suggests that certain polymers containing a triptycene fragment may possess valuable specific properties.

The chemistry of triptycene has been studied in comparative detail. A considerable quantity of interesting work of fundamental character has appeared during recent years, but only one review paper has hitherto been published on triptycene, which is small in scope and not readily accessible to a wide range of readers[10]. The present Review examines methods for constructing the triptycene system, together with the reactivity, spectral characteristics, and certain physicochemical properties of compounds of this series.

II. CONSTRUCTION OF TRIPTYCENE SYSTEM

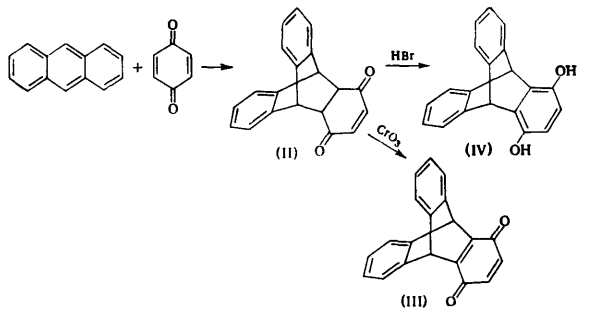
The most general method for building up the polycyclic triptycene system—9,10-*o*-benzo-9,10-dihydroanthracene† (I)—is diene synthesis between anthracene or a substituted derivative and a sufficiently active six-membered carbocyclic dienophile. Thus Clar[14] was the first to isolate the adduct (II) of anthracene with *p*-benzoquinone,

† A nomenclature which regards triptycene as a derivative of dihydroanthracene is now generally accepted[11,12], with the carbon atoms numbered as in (A) (used in the present Review) or (B):

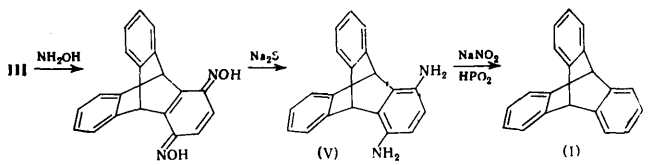


In some publications triptycene compounds have been regarded as substituted bicyclo[2,2,2]octanes, with the carbon atoms numbered as in (C).[1,13]

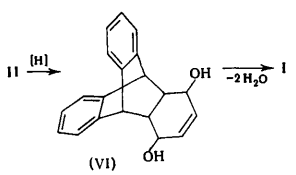
which he converted into triptycene derivatives—triptycenequinone (III) and triptycenequinol (IV):



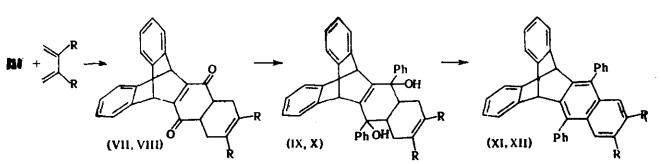
from which, however, he was unable to obtain triptycene. Bartlett et al.[1,15] extended Clar's scheme, and were the first to accomplish the multistage synthesis of triptycene:

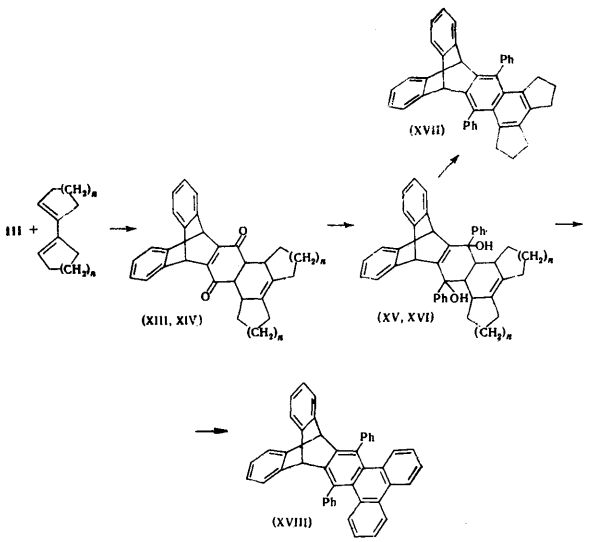


Triptycene was obtained also by dehydration of the dion (VI) (by boiling with alcoholic hydrogen chloride[16] or with a mixture of phosphorus trichloride and phosphoryl chloride), which is readily formed by direct reduction of the adduct (II) with lithium tetrahydroaluminate[16] or with aluminium isopropoxide in propan-2-ol:[11]

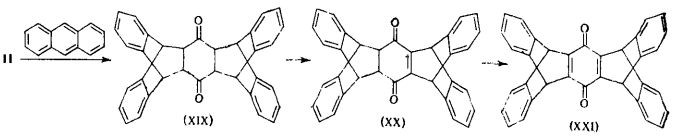


Triptycenequinone (III), which was used by Bartlett in the preparation of triptycene (I),[1,15] later served as the starting compound for the synthesis of several more complicated structures containing a triptycene fragment. Thus a detailed study was made of the dienophilic reactivity of triptycenequinone (III) with aliphatic dienes (butadiene, 2,3-dimethylbutadiene) and bicyclic dienes (1,1'-bicyclohexenyl, 1,1'-bicyclopentenyl) (an adduct of triptycenequinone (III) with acecyclone had been described earlier)[17]. The action of phenyl-lithium on the adducts obtained (VII, VIII, XIII, XIV) gave the corresponding diols (IX, X, XV, XVI), whose dehydration produced quantitative yields of 5,12-diphenyltetrahydro-6,11-benzonaphthacenes, which on subsequent dehydrogenation are converted into hydrocarbons of complicated structure—1,4-diphenyl-2,3-benzotriptycenes (XI, XII, XVII, XVIII):[18-20]



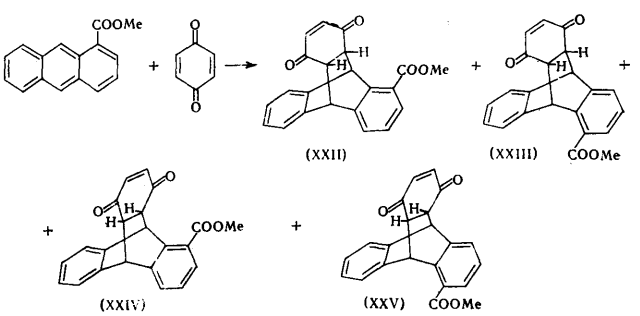


Other dienophiles which have been made to react with anthracene are derivatives of *p*-benzoquinone[21-27] and 1,4-naphthaquinone[28-31], 1,4-anthraquinone[32], quinones of the triptycene series[33-35] and bicyclo[2,2,1]heptadiene-2,3-dicarboxylic anhydride[36], but no attempts were made to obtain from these adducts the corresponding hydrocarbons having a triptycene structure. Depending on the conditions the reaction between anthracene and *p*-benzoquinone yields not only the adduct (II) but also other compounds. Thus with excess of anthracene the double adduct (XIX) is formed; at 140–165°C this is dehydrogenated first to the diketone (XX), and at 165°C to the quinone (XXI):[11]

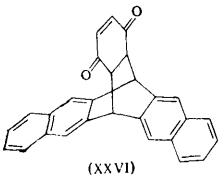


In the presence of aluminium chloride the adduct (II) is formed in high yield even at room temperature, and with excess of anthracene the double adduct (XIX).[37]

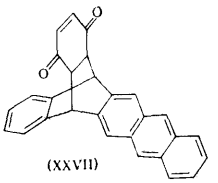
With substituted anthracenes *p*-benzoquinone forms isomeric compounds. Thus with methyl 1-anthroate adducts of *exo*- and *endo*-configuration are obtained, each of which in turn is a racemic mixture of stereoisomers (XXII–XXV):[13]



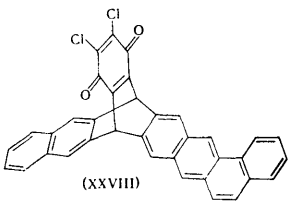
Other acenes react similarly to anthracene with *p*-benzoquinone. Thus pentacene undergoes diene synthesis with the formation of two adducts, of symmetrical (XXVI) and unsymmetrical (XXVII) structure[38].



(XXVI)



(XXVII)

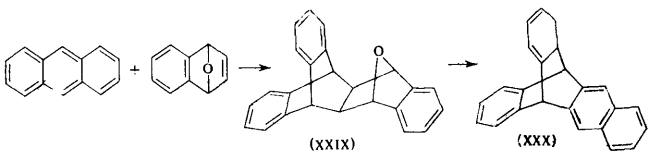


(XXVIII)

Pentacene reacts similarly with chloranil[14], and the latter has been reported to react with 7,14-dihydro-1,2-benzohexacene to yield the adduct (XXVIII).[39]

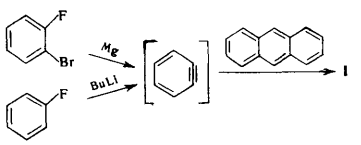
Hydrocarbons having a partly hydrogenated triptycene structure are obtained by diene synthesis between anthracene and cyclohexene[40], 1,4-dihydronaphthalene[28], 1,4-dihydro-1,4-methanonaphthalene[41], and bicyclo[2,2,1]-heptadiene[42,43].

An original route to 2,3-benzotriptycene (XXX) was suggested by Wittig et al.[41], who applied the Diels–Alder reaction to anthracene and 1,4-epoxy-1,4-dihydronaphthalene (in turn obtained by diene synthesis from furan and dehydrobenzene), and heated the resulting adduct (XXIX) in acetic acid[44]:



(XXIX) (XXX)

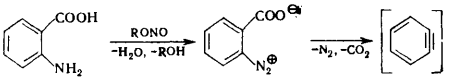
The direct method of preparing triptycene by diene synthesis from anthracene and dehydrobenzene, proposed by Wittig in 1956,[2] is at present time the simplest and the most convenient. Its development has made triptycene readily available as a subject for many interesting investigations. Various processes have been described for generating dehydrobenzene from numerous monosubstituted and *ortho*-disubstituted benzene derivatives‡, as well as procedures for conducting the diene synthesis. Triptycene is obtained in various yields depending on the method of producing dehydrobenzene and on the conditions of its reaction with anthracene. Thus Wittig et al. obtained a 30% yield by the action of magnesium on *o*-bromofluorobenzene (in oxolan or ether) in the presence of anthracene[2,3,6]; reaction of anthracene with dehydrobenzene generated by treating fluorobenzene with *n*-butyllithium in oxolan gave only a 10% yield of triptycene[5]:



‡ A special monograph[45] was devoted to dehydrobenzene and arynes.

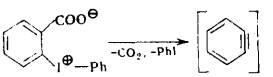
Triptycene has been obtained also from dehydrobenzene generated from fluorobenzene by the action of lithium hexaphenylantimonate[7], from halogenobenzenes by the action of potassium t-butoxide[46,47], by the decomposition of *N*-nitrosoacetanilides[47-52], by the oxidation of 1-aminobenzotriazole[53], by the decomposition of *N*-*o*-carboxyphenyl-*N'*-toluene-*p*-sulphonyldi-imide *N*-oxide[54], by heating benzo-1,2,2-thiadiazole dioxide in oxolan[8,9], and by decomposing *o*-diiodobenzene with zinc in the gas phase (at 550°C).[55]

The most convenient mode of generating dehydrobenzene for the preparation of triptycene is to decompose *o*-diazonium benzoate (a betaine obtained by diazotising anthranilic acid) by heating in an aprotic solvent[56,57]:



In the improved method of Friedman and Logullo[58,59] anthranilic acid dissolved in acetone (oxolan, butan-2-one, or diglyme) is added to a boiling solution of anthracene and pentyl (or butyl) nitrite in dichloromethane (chloroform or 1,2-dichloroethane). The yield of triptycene is 50–60%, but with simultaneous mixing of the reactants it sometimes falls to 10%; use of a molar excess of anthracene or anthranilic acid tends to raise the yield to 70–80%. With difficulty accessible substituted anthracenes it is sometimes better to use a modified method involving intermediate isolation of *o*-diazonium benzoate[60]. Dioxan[61] and *p*-xylene[62] have also been used as high-boiling solvents in the preparation of substituted triptycenes.

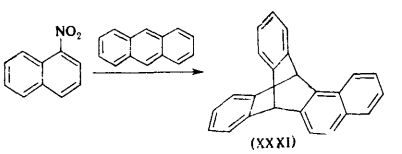
The use in certain cases of dehydrobenzene formed by the decomposition of iodonium *o*-benzoate (in boiling diglyme[63] or triglyme[64], sometimes in the presence of catalytic additions of iodine or copper sulphate or acetate[65])



has no significant advantages over the above method[58,59].

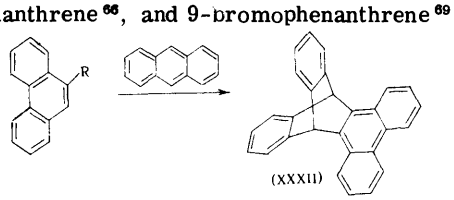
Not only dehydrobenzene and its substituted derivatives but also other arynes—2,3-dehydronaphthalene[58], 9,10-dehydrophenanthrene[66], 2,3-dehydro-9,10-anthraquinone[67], and dehydro[2,2]paracyclophane[68]—have been used in diene syntheses with anthracene.

Many reactions yielding benzotriptycenes (XXX–XXXII) also involve the intermediate formation of arynes—e.g. the reaction of anthracene (at 300°C) with 1-nitronaphthalene[28]



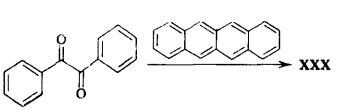
(XXXI)

9-nitrophenanthrene[66], and 9-bromophenanthrene[69]

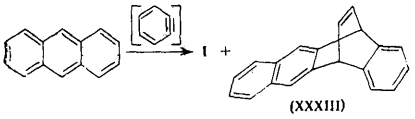


(XXXII)

and the pyrolysis of benzil in the presence of naphthacene[70].

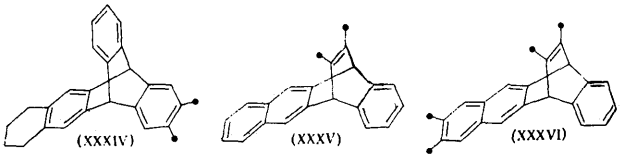


Dehydrobenzene adds to anthracene not only at the *meso*(9,10)-positions but also partly at the 1,4-positions, so that triptycene is accompanied by traces of 5,12-dihydro-5,12-ethenonaphthacene (XXXIII):[71]



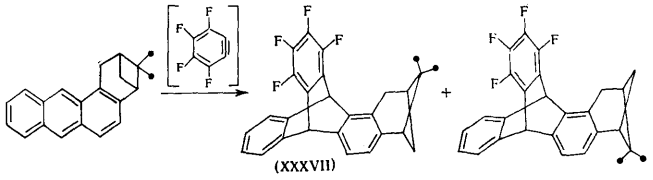
(XXXIII)

Substituted anthracenes react similarly, with the nature of the substituents and their positions in the anthracene molecule determining the proportions of isomeric adducts formed. Electron-accepting or sufficiently bulky substituents diminish appreciably the diene activity of the anthracene system towards dehydrobenzene and orient its addition predominantly to the unsubstituted rings[53,72]. Thus the presence of two *meso*-nitrile groups deactivates both the middle and the outer rings, so that isomeric adducts are obtained in equal quantities but with a very low total yield (4%).[71] The activity of 9,10-diphenylanthracene is only 20% of that of anthracene, while the ratio of products of addition at positions 9,10 and 1,4 falls to 8%.[53] Electron-donating substituents direct the addition of dehydrobenzene predominantly to the substituted ring, at the same time increasing the diene activity of the anthracene system[72]. Depending on the structure of the initial methylanthracenes the addition of dehydrobenzene takes place either solely at the 9,10-positions with formation of a triptycene compound (XXXIV from 1,2,3,4-tetrahydro-8,9-dimethylnaphthacene) or also at the 1,4-positions with the formation of substituted ethenonaphthacenes (XXXV and XXXVI from 2,3-di- and 2,3,6,7-tetra-methylanthracenes).



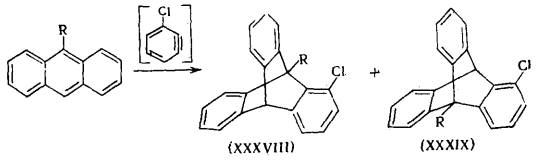
(XXXIV) (XXXV) (XXXVI)

Reaction between dehydrotetrafluorobenzene[74] and 1,2,3,4-tetrahydro-3,3-dimethyl-2,4-methanobenz[*a*]-anthracene yields a mixture of two isomeric compounds:



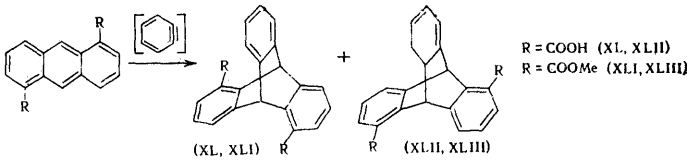
(XXXVII)

where the products (XXXVII) of addition on the sterically most hindered side of the initial anthracene molecule predominates[75]. Several substituted anthracenes form mixtures of *quasi-cis*- and *quasi-trans*-isomers (XXXVIII and XXXIX) by diene synthesis with substituted dehydrobenzenes:



(XXXVIII) (XXXIX)

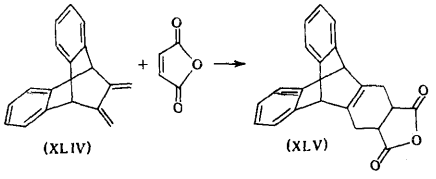
The reactions of 9-substituted anthracenes with 3-chloro-dehydrobenzene show that the ratio of the isomers formed depends mainly on the inductive effect of the substituent R, not on its size[76]. Anthracene derivatives substituted in the outer rings give with dehydrobenzene racemic mixtures of optical enantiomers. Thus stereoisomeric disubstituted triptycenes (XL–XLIII) have been obtained from 1,5-disubstituted anthracenes[77]:



(XL, XLI) (XLII, XLIII)

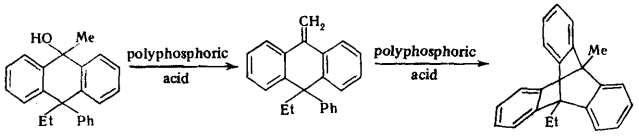
Other reactions of substituted dehydrobenzenes with substituted anthracenes have also been reported[78–80].

A specific method for building a partly hydrogenated triptycene system by diene synthesis is the action of maleic anhydride on the compound (XLIV), which gives 1,2,3,4-tetrahydrotriptycene-2,3-dicarboxylic anhydride (XLV):[81]



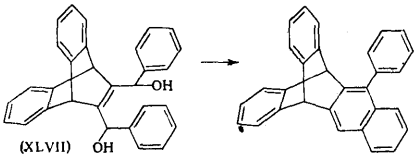
(XLIV) (XLV)

Cyclisation has been used to synthesise certain substituted triptycenes. For example, 9-ethyl-10-methyl-triptycene (XLVI) was obtained in theoretical yield by the action of polyphosphoric acid on 10-ethyl-9,10-dihydro-9-methyl-10-phenyl-9-anthrol:[82]



(XLVI)

1-Phenyl-2,3-benzotriptycene has been obtained by the cyclodehydration of (XLVII):[44]



(XLVII)

III. STRUCTURE AND PHYSICAL PROPERTIES OF TRIPTYCENE COMPOUNDS

Triptycene is a colourless substance, melting at 254.03°C when 99.999 mole % pure and readily soluble in the usual organic solvents[83]. It crystallises in the orthorhombic system with a unit cell belonging to the $P2_12_12_1$ space group and having the parameters 0.822, 2.064, and 0.816 nm, number of formula units $z = 4$, and volume 1.384 nm^3; the crystallographic density is 1.227 g cm^{-3}, and the symmetry of the molecule $\bar{6}m2$.[84,85]

Changes in the enthalpy of triptycene correspond to the integral of heat capacity with respect to temperature between 429° and 519°K, and the temperature dependence of heat obeys Debye's law. The large difference in heat

capacity between solid and liquid triptycene (11.48 cal deg^{-1} $mole^{-1}$) indicates strong bonding of the molecules in the crystal lattice; movement of the molecules is restricted at temperatures somewhat above the melting point. The heat capacity of triptycene is well approximated by that of a model in which three benzene rings are superposed on bicyclo[2,2,2]octane.[83]

The highly symmetrical structure of the triptycene molecule is confirmed by infrared, ultraviolet, and proton magnetic resonance spectroscopy. The infrared spectrum is characterised by absorption bands having wavenumbers (νmax, cm^{-1}) of 3040 (stretching vibrations of aromatic carbon–hydrogen bonds), 2960 (aliphatic carbon–hydrogen bonds of bridging methine groups), 1470 to 1450 (aromatic carbon–carbon bonds), and 755–740 (deformation vibrations of carbon–hydrogen bonds in *ortho*-disubstituted benzenes)[65,86,87]. The ultraviolet spectra of triptycene and its 9,10-substituted derivatives are characterised by bands having λmax (in nm) (and $\lg\epsilon$)—263 (3.25), 271 (3.56), and 278 (3.66)[87-92]—and can be interpreted[89] by the superposition of three benzene chromophores, which is supported by calculation of the intensities of the bands of longest wavelength for several chlorinated triptycenes[76] and benzo-derivatives[67]. The ultraviolet spectra reveal only an inductive effect of substituents in the bridges, since their conjugation with the aromatic rings is impossible[87].

The ^1H n.m.r. spectrum of triptycene contains a multiplet of aromatic protons (with its centre δ = 7.05 ppm) and a singlet of bridge protons (δ = 5.21 ppm).[93,94] The measured transition frequencies in the multiplet agree well with those calculated for the four-spin system AA'BB'.[93,95] A certain broadening of the AA' part of the spectrum is due to interaction between α-protons and bridge protons[95].

The ^1H n.m.r. spectra of triptycenes substituted in an aromatic ring differ markedly depending on the position of the substituent. Thus β-substituents have almost the same effect on the chemical shifts of the two bridge protons, since their signals appear in the spectrum as one singlet. Probably the only exception is provided by the nitro-group: the signal due to one bridge proton in 2-nitrotriptycene is displaced 3 Hz from that due to the other[96], and with 2,7-dinitrotriptycene the separation is 5 Hz.[97] The ^1H n.m.r. spectra of α-monosubstituted triptycenes always contain two singlets due to the bridge protons (because of the non-equivalence of the latter relative to the α-substituent)[44]. Analysis of the spectra has shown that the signal due to the bridge proton adjacent to the substituent is usually displaced down-field[44,62,76,96,98].

In the series—1-chloro-, 1,8-dichloro-, and 1,8,14-trichloro-triptycenes—the average increase in the difference between the chemical shifts of the signals due to the bridge protons is 0.43 ppm. This quantity is the sum of the contributions by magnetic anisotropy, the electrical field, and the van der Waals effect, among which the field effect makes the main contribution (0.29 ppm).[76] Triptycene derivatives are thus convenient compounds for the study of magnetic anisotropy[76].

In 1,4-diphenyltriptycene steric factors hinder a coplanar arrangement of the phenyl substituents, which is also apparent in their spectra[98].

The isomeric vinyltriptycenes have been the simplest convenient models for studying several structural features of differently substituted unsaturated triptycene derivatives. Thus the ^1H n.m.r. spectra indicate that the protons of a 2-vinyl group in triptycene are less shielded than are those of a vinyl group in position 1 and of course 9. The coplanarity of vinyl group and benzene ring in 1- and 2-vinyltriptycenes is confirmed by an analysis of spectroscopic results (ultraviolet and n.m.r.).[99]

The structure of triptycene has been reliably confirmed by X-ray diffraction[84,85,100-102]. The molecule possesses a threefold axis of symmetry and a plane of symmetry perpendicular to this axis. The aliphatic carbon–carbon bonds in the bicyclo[2,2,2]octane system and also the carbon–carbon bonds in the aromatic rings have the normal length, but the $C_{(4a)}-C_{(9a)}$ bond, which is common to the bicyclic system, is somewhat elongated. The presence of a strained bicyclic system is evident also in the variation in the bond angles. Thus the angles between the aliphatic carbon–carbon bonds are 105° (instead of 109°47′), and those between aliphatic and aromatic carbon–carbon bonds common to the bicyclic system are 113° (instead of the usual 120°). The distortion of the angles produces corresponding changes in hybridisation of the orbitals bonding atoms of the bicyclic system and the neighbouring atoms of the aromatic rings.

Certain distortions are observed in triptycene derivatives with substituents at positions 9 and 10. Thus internuclear distances are somewhat increased for atoms in the vicinity of the bridge substituents in 9-bromotriptycene[100] and 9-2′-chloroethyltriptycene[101]; the angles between the aliphatic carbon–carbon bonds in the former molecule are 107°. Rotation of the chloroethyl group in the latter molecule is retarded by the spatial proximity of α-hydrogen atoms of the aromatic rings, which in turn causes a general distortion of structure and non-equivalence of the aromatic rings[101]. Retarded rotation of a chloromethyl group attached to a bridging carbon atom is also definitely revealed in the ^1H n.m.r. spectra of 9-chloromethyl- and 9,10-bischloromethyl-triptycenes. The activation energy of rotation of such a chloromethyl group determined from the spectroscopic results (~16 kcal $mole^{-1}$) was about treble that for an ordinary σ-bond.[103]

The ^1H n.m.r. spectra of several other 9-substituted triptycenes have been studied[104]. The spectrum of the adduct of *p*-benzoquinone with 9,10-di-t-butylanthracene reveals the methyl protons as three separate singlets[105]. Stable rotational isomers may be formed in the presence of sufficiently bulky bridge substituents. Thus two conformers have been isolated and characterised in the reaction of dehydrobenzene with anthracene-9,10-bis-$\alpha\alpha$-dimethylacetonitrile; their equilibrium interconversion occurs at 200°C.[106]

Certain features of the chemical behaviour of 9-substituted triptycenes are due to the steric hindrance of substituents in this position. Examples are the stability of triptycen-9-yl iodoformate, the impossibility of obtaining ditriptycen-9-yl oxalate, the low reactivity of triptycen-9-ol towards alkali metals[107], and the difficulty of the formation of 9,9′-bitriptycenyl[15] (although ditriptycen-9-ylmercury has been obtained in good yield by the mercuration of triptycen-9-yl-lithium[108]). The low yield of α-nitrotriptycene obtained by the nitration of triptycene has been attributed[97] to steric hindrance of the α-positions in the aromatic rings. The difficulty of the solvolysis of compounds containing halogenomethyl bridge groups is also explained by peculiarities of the three-dimensional structure of the triptycene system[109,110].

The mass spectra of triptycene have been discussed in several papers[111-113], but the interpretation of the experimental results is ambiguous.

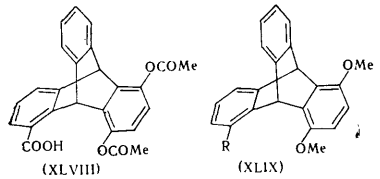
Studies have been made also of the electron spin resonance spectra of triptycene[12,114-121], its substituted derivatives[121-125], and semiquinones[126-130]. The absence

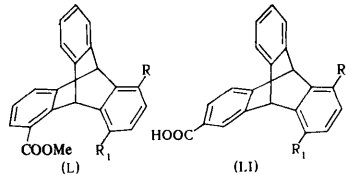
of fine structure from the e.s.r. spectrum in the last case indicates that the bridge carbon atoms completely interrupt conjugation of electrons between the benzene rings and the quinonoid portion of the molecule [129].

The hypothesis that transannular interactions may occur between the aromatic rings in the triptycene molecule, which appeared in several publications [88,95,98], was not subsequently confirmed [67,97,131].

Thus the factors responsible for the peculiarities of chemical behaviour are probably the strain in the bicyclic structural fragment and the three-dimensional structure of the triptycene system.

The molecule of a substituted triptycene having three non-equivalent rings is chiral, which leads to the appearance of optical isomers. Such a system is an ideal model for studying the effect of substituents on optical activity, since the rigid structure of the molecule excludes the possibility of interaction between its various parts, and conversions can be accomplished without racemisation or inversion of configuration [13].



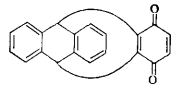
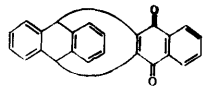
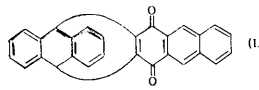
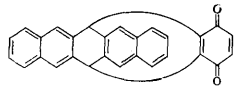
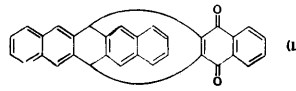
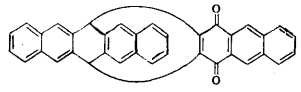
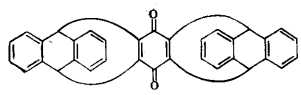
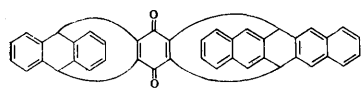


Optical activity in the triptycene series was first shown for 5,8-diacetoxytriptycene-1-carboxylic acid (XLVIII), obtained by conversion of the isomeric compounds (XXII–XXV) and resolved into enantiomers [13]. A series of 5-substituted (+)-1,4-dimethoxytriptycenes (XLIX) were obtained [77,132–134] from (+)-(XLVIII), and from these the the absolute configuration 9*R*, 10*S* was established for (+)-5-*NN*-dimethylamino-1,4-dimethoxytriptycene hydrobromide [XLIX: R = $N(CH_3)_2$.HBr] by X-ray structural analysis by Bijvoet's method [102]. This configuration is possessed by other members of the (XLIX) series, as well as by 5,8-disubstituted methyl triptycene-1-carboxylates (L), [135] for which the optical rotatory dispersion was also studied [132]. The structure of the isomeric methyl 5-hydroxy-8-methoxy- and 8-hydroxy-5-methoxytriptycene-1-carboxylates was established from the measured dipole moments [136]; in the latter ester infrared spectroscopy reveals an intramolecular hydrogen bond between the spatially contiguous methoxycarbonyl and hydroxyl groups.

Other optically active triptycene derivatives have been obtained from enantiomeric 5- and 8-substituted triptycene-1-carboxylic acids [137]. The absolute configuration of the chiral centres (9*R*, 10*R*) has been determined by chemical correlation with (+)-(XLIX) in (+)-5-methoxytriptycene-1-carboxylic acid, and confirmed by comparison of the circular dichroic spectrum with that of (+)-methyl 5-acetoxy-8-methoxytriptycene-1-carboxylate (L). The absolute configuration of (−)-5-methoxytriptycene-1-carboxylic acid (9*S*, 10*S*) was established by X-ray structural analysis and chemical correlation; the configuration of (+)-5-chlorotriptycene-1-carboxylic acid was also determined. The chiral 5,8-disubstituted triptycene-2-carboxylic acids (LI) and esters have been studied; the absolute configuration (9*R*, 10*S*) has been determined by chemical correlation for the dextrorotatory enantiomers [138]. Chiral 1,5- and 1,8-disubstituted triptycenes have also been obtained. Chemical correlation has established the absolute configuration 9*R*, 10*R* for the dextrorotatory enantiomer of 8-methoxytriptycene-1-carboxylic acid, and the inverse configuration for the laevorotatory enantiomer [77,139].

Determination of the absolute configuration of 1,5-disubstituted triptycenes by means of circular dichroism gave results [140] directly opposite to those obtained earlier by X-ray and chemical methods. However, these conclusions [140] were revised a little later [141].

Polorgraphic characteristics of quinones of the triptycene series (in 0.1 *N* KNO_3 in dimethylformamide).

Quinone	First wave K'	First wave $-E'_{1/2}$, mV	Second wave K''	Second wave $-E''_{1/2}$, mV	$\overline{E}$, mV	E^0, mV	$\lg K_{sq}$
 (III)	1.55	644	1.34	1248	946	666	10.237
 (LII)	1.62	877	1.33	1473	1175	437	10.169
 (LIII)	1.53	944	1.28	1400	1172	440	7.728
 (LIV)	1.09	673	1.14	1280	977	635	10.305
 (LV)	1.11	806	0.92	1352	1079	533	9.254
 (LVI)	1.06	819	0.91	1350	1085	527	8.983
 (XXI)	1.57	665	1.56	1342	1004	608	11.592
 (LVII)	1.42	633	1.31	1260	947	667	10.644

A study has been made of the polarographic reduction of triptycenequinone (III) and benzotriptycenequinones (XXI and LII–LVII) containing different numbers of annelated benzene rings in the quinonoid and triptycene moieties [32,34,142–148]. Quinones are characterised by two one-electron polarographic waves on reduction in dimethylformamide. Reduction occurs reversibly, with

intermediate formation of the semiquinone to yield the dianion of the quinol (or the quinol itself at sufficient hydrogen-ion concentrations):

$$Q + e^- \overset{K_{sqn}}{\rightleftarrows} S; \quad S + e^- \rightleftarrows Q^{-2} .$$

The Table[148] illustrates the effect of annelation on the redox potentials of the quinones E°, the constants of the diffusion currents K, the half-wave potentials, and the effective formation constants of the semiquinone

$$K_{sqn} = \left[10^{\frac{0.5(E'_{1/2}-E''_{1/2})F}{RT}} - 3 \cdot 10^{-\frac{0.5(E'_{1/2}-E''_{1/2})F}{RT}} \right]^2,$$

where $E'_{1/2}$ and $E''_{1/2}$ are the first and second half-wave potentials. The constant of the diffusion current seemed to vary little for the triptycenequinones (III, LII, LIII) and also for the dibenzotriptycenequinones (LIV–LVI). The ratio of these constants K''/K' is about 0.85 for all quinones, indicating partial protonation of the semiquinone, which is further reduced at the same potential. On annelation in the quinonoid part of the molecule the negative potentials $E'_{1/2}$ and $E''_{1/2}$ increase in all these compounds, while Ksqn decreases and reduction is hindered only at the first stage. Annelation in the hydrocarbon part of the quinone molecules produces negative shifts in $E'_{1/2}$, $E''_{1/2}$, and $1/2(E'_{1/2} - E''_{1/2})$, accompanied by increase in Ksqn and in the hindrance to catalytic hydrogenation (cf. quinones III and LIV). With the quinones (LII) and (LV), as well as with (LIII) and (LVI), annelation displaces $E'_{1/2}$ and $E''_{1/2}$ to more positive potentials; the former pair of quinones show a decrease in Ksqn with increase in annelation, whereas the latter pair shown an increase. With the quinones (XXI) and (LVII) annelation makes the half-wave potentials more positive and diminishes both the constant of the diffusion current and Ksqn: i.e. in this case reduction occurs more easily as the structure becomes more complicated. Comparison of quinones (III) and (XXI), however, shows that reduction becomes more difficult with complication of the structure. This effect is almost completely absent with the quinones (III) and (LVII).

IV. REACTIVITY OF BRIDGE ATOMS

The early work on the chemistry of triptycene showed that the halogen at the bridgehead in 9-halogenated triptycenes is inert towards various nucleophilic reagents. Thus Bartlett and his coworkers were unable to make 9-bromotriptycene[88,149] or 9-iodotriptycene[15] react with sodium ethoxide, tin(II) chloride, sodium sulphide, or silver nitrite even under severe conditions. Nucleophilic substitution at a bridging carbon atom in the triptycene molecule is difficult for structural reasons. Reactions having an S_N1 mechanism are improbable, since intermediate formation of a carbonium cation would have required transition of the bridging carbon to an sp^2-hybridised state and a coplanar arrangement of the aliphatic carbon–carbon bonds§ in the already strained bicyclic fragment of triptycene; furthermore, such a carbonium ion could not have been stabilised by conjugation with the aromatic rings but, on the contrary, would have been destabilised by the negative inductive effect of the three *o*-phenylene substituents[88,152]. An unsuccessful attempt to generate a bridging carbonium ion from triptycen-9-yl iodoformate by the action of silver tetrafluoroborate has been reported[107]: only triptycen-9-yl fluoroformate was isolated from the reaction products.

Reactions occurring by an S_N2 mechanism are also impossible, since carbon atoms at a bridgehead are shielded from attack by nucleophilic reagents[88,152]. This confirmed the S_N2 rule, according to which substitution by an S_N2 mechanism always involves inversion of configuration[153].

As already remarked above[84–86], distortion of the tetrahedral angle at a bridging carbon atom in the triptycene molecule produces a change in hybridisation of the corresponding orbitals, and the carbon–carbon bonds acquire a greater p-character, while the bridge carbon–hydrogen bond is enriched with the s-component, approximating in character to bonds having sp^2-hybridisation of the carbon orbitals. This is accompanied by an increase in electronegativity of the bridging carbon atom, while the hydrogen atom becomes the positive pole of the dipole of the carbon–hydrogen bond, thereby becoming more acidic (in comparison with the methine hydrogen atoms in alkanes[86]). These structural peculiarities of triptycene find confirmation in its infrared spectrum[86,87]: the frequency of the absorption band due to the bridge carbon–hydrogen bond approaches that of a carbon–hydrogen bond in an alkene (3000 cm^{-1}). X-Ray examination shows that the bridge carbon atom has $sp^{2.26}$-hybridisation (the $J_{^{13}C-H}$ interaction constant gives $sp^{2.45}$-hybridisation). The smaller hybridisation calculated from crystallographic data was attributed[154] to curvature of the aliphatic carbon–carbon bonds in the triptycene molecule.

Nevertheless, halogenated triptycenes react with organometallic compounds under conditions under which nucleophilic attack at a bridging carbon atom is impossible. For example, 9-bromotriptycene reacts with n-butyllithium to give triptycen-9-yl-lithium[4,108,155]; 9-bromo- and 9,10-dibromo-2,3-benzotriptycenes react similarly[41]. The transition state leading to triptycen-9-yl-lithium may be four-membered with little carbanion character, and the lithium compound itself largely covalent[152]. Triptycen-9-yl-lithium undergoes substitution with intermediate formation of a carbanion bridge, and reacts in the usual way with carbon dioxide, benzophenone, triphenylboron, benzenediazonium tetrafluoroborate, mercury(II) chloride, and selenium chloride; it can be hydrolysed to triptycene[108].

Formation of a tetrahedral carbanion bridge, in contrast to a carbonium ion bridge, does not obstruct the structural peculiarities of the triptycene molecule. The straining of the bond angles at the carbon bridge should destabilise the carbanion, but this effect may be balanced by increase in the electronegativity of the bridging carbon atom. The stability of the carbanions would also be increased by the $-I$ effect of the three *o*-phenylene groups (although stabilisation by conjugation is excluded).

The comparatively ready formation of a bridging carbanion in triptycene is confirmed by a study of the kinetic acidity of the attached hydrogen atom[154,156]. Triptycene is similar to aromatic hydrocarbons in its ability to split off a bridge proton: the acidity of the hydrogen atom is closely similar to that of an *o*-hydrogen in toluene, and

§ The adamantyl cation with a tertiary carbonium atom at the bridgehead, for which a planar configuration is also impossible because of the three-dimensional structure, nevertheless is formed and exists in SbF_5-SO_2 solution[150]. In this case stabilisation is attributed to polarisation of the electrons of the carbon–hydrogen bonds of the tertiary carbon atoms (at positions 3, 5, and 7), which are attracted to the cationoid centre inside the adamantane skeleton[151].

far higher than in cyclohexane. According to Streitwieser and Ziegler [154] the enhanced acidity of the bridge hydrogen in triptycene is two-thirds due to the $-I$ effect of the three *o*-phenylene groups and only one-third due to strengthening of the *s*-character of the bridge carbon–hydrogen bond. This conclusion is consistent with the kinetic acidities of the bridge hydrogen atoms in triptycene and in 2,3-benzotriptycene [157]. Furthermore, the acidity of the 9-hydrogen atom in 2-methyltriptycene, in which the bicyclic part of the molecule has remained unchanged, is one-half, and that of the 10-hydrogen one-third, of the acidity of the hydrogen atoms in triptycene [154].

9-Bromotriptycene reacts with magnesium in ether [88] or oxolan [158], but the triptycen-9-ylmagnesium bromide formed, which can be hydrolysed to triptycene, cannot be carbonylated [88]. 9-Bromotriptycene is unaffected by sodium in boiling toluene, but reacts with the metal when heated in mineral oil to 140°C (even in an atmosphere of carbon dioxide), being converted almost quantitatively into triptycene [88]. This reaction probably involves intermediate formation of the triptycen-9-yl radical.

Barlett et al. showed [15] that the thermal decomposition of triptycen-9-ylcarbonyl peroxide was about two-thirds due to homolytic rupture of the oxygen–oxygen bond. Free-radical breakdown was accompanied by inversion of the carboxyl, yielding on subsequent hydrolysis triptycen-9-ol and triptycene-9-carboxylic acid:

$$\mathrm{Tr{-}COO{-}OOC{-}Tr \rightarrow 2\,Tr{-}COO\cdot;\ Tr{-}COO\cdot \rightarrow Tr\cdot + CO_2;}$$

$$\mathrm{2\,Tr\cdot \rightarrow Tr{-}Tr;\ Tr\cdot + C_6H_6 \rightarrow TrH + Ph\cdot;\ 2\,Ph\cdot \rightarrow Ph{-}Ph;}$$

$$\mathrm{Tr{-}CO{-}O{-}O{-}CO{-}Tr \rightarrow Tr{-}CO{-}O{-}CO{-}O{-}Tr \rightarrow TrOH + TrCOOH + CO_2.}$$

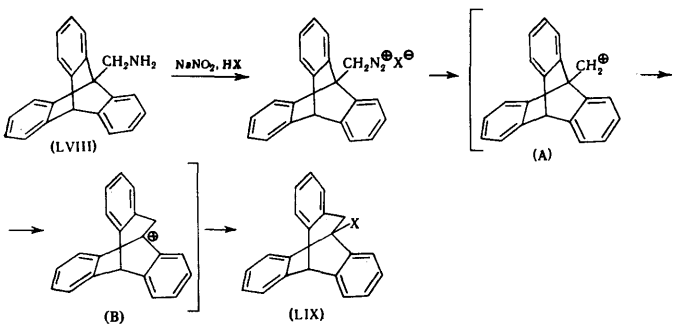
The free radical formed by decomposition of the peroxide possessed great affinity for hydrogen and iodine. The formation of triptycene in the reactions of triptycen-9-yllithium with halides of transition metals (silver, copper, cobalt, nickel) and of 9-bromotriptycene with metallic silver probably involves the triptycen-9-yl radical as an intermediate stage [108]. A small yield of a substance of high melting point, regarded as 9,9′-bitriptycenyl in view of its infrared spectrum, was isolated on decomposition of the peroxide. (9,9′-Bitriptycenyl obtained by addition of dehydrobenzene to 9,9′-bianthryl melted at 577°C and had a similar infrared spectrum [159].) In other reactions in which the radical occurred as an intermediate stage formation of a dimer was not observed (e.g. in the decomposition of ditriptycen-9-ylmercury of ditriptycen-9-yl diselenide in the presence of metallic silver or copper) [108].

Thermal decomposition of t-butyl triptycene-9-peroxycarboxylate gave triptycene in the high yield of 92%, attributable to the fact that the t-butyl groups in the original ester and in the decomposition products of the t-butoxyl radical are active donors of hydrogen. Decomposition of the same ester in chlorobenzene gave an 80% yield of triptycene (with traces of triptycene-9-carboxylic acid) [160].

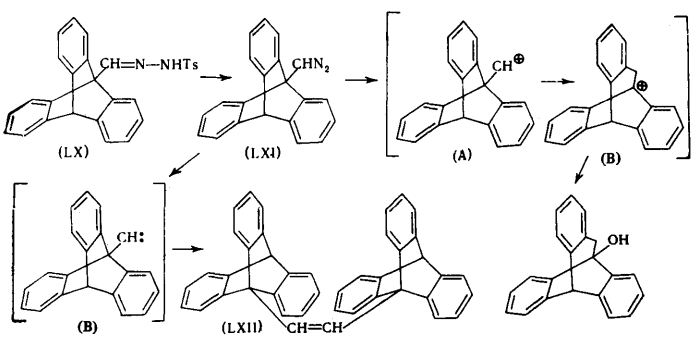
Decomposition of triptycen-9-al in the presence of t-butyl peroxide in carbon tetrachloride led to the isolation, after treatment with methanol, of 9-chlorotriptycene and methyl triptycene-9-carboxylate [160]. The results established that detachment of a chlorine atom from the solvent greatly predominated over decarbonylation. The thermal decomposition of triptycen-9-yl iodoformate to give 9-iodotriptycene (in 52% yield) is a peculiar substitution of the bridge oxygen function by homolysis of the carbon–oxygen bond [107]. 9-Iodotriptycene has been obtained also by irradiation of triptycene-9-carboxylic acid in the presence of iodine and lead tetra-acetate [155].

The ability of the bridge positions in triptycene to undergo radical substitution is thus a well established fact. The radical formed obviously has a tetrahedral configuration and is not stabilised by conjugation with the aromatic rings. Triptycen-9-yl is closely similar to the 1-norbornyl radical in stability [160], which supports Bartlett's suggested analogy [15] in the properties of the bicyclo[2,2,1]-heptane and triptycene bicyclic systems, which exhibit closely similar angular strains. It is also obvious that destabilisation of the triptycenyl radical due to the negative inductive effect of the three aromatic rings is slight [150].

The enhanced acidity of hydrogen atoms and the reactivity of halogen atoms at a bridgehead in the triptycene molecule make the bridging carbon atoms like aromatic carbon atoms. Among other reactions of 9-substituted triptycenes several transformations have been reported of the 9-nitro, [161] 9-nitroso, [161,162] and 9-bromo [163–165] derivatives, as well as reactions of 9-aminotriptycene-1,4-quinone [166], triptycene-9-carboxylic acid [167], and triptycen-9-ylmethylamine [168]. Diazotisation of this amine (LVIII) yields derivatives of a homologue of triptycene—homotriptycene (tribenzobicyclo[3,2,2]nonatriene (LIX)—formed by a Dem'yanov rearrangement involving expansion of the ring [168]:



Studies have been made [169] of the reactions of 9-diazomethyltriptycene (LXI), obtained by treating triptycen-9-al toluene-*p*-sulphonylhydrazone (LX) with sodium methoxide in pyridine. Decomposition of the hydrazone (LX) at 80° to 90°C involved intermediate formation of the carbonium ions (A) and (B) together with the carbene (C); decomposition of the dry sodium derivative of the hydrazone in a vacuum at 170–200°C involved preferential formation of the carbene (C), which was converted into a high yield of the hydrocarbon (LXII):



Unsuccessful attempts have been made to prepare a bridge iodonium salt of triptycene [155] and also to solvolyse a chloromethyl group located at a bridgehead in triptycene [109]. The bromine atom in 9-bromomethyltriptycene is also unreactive [110].

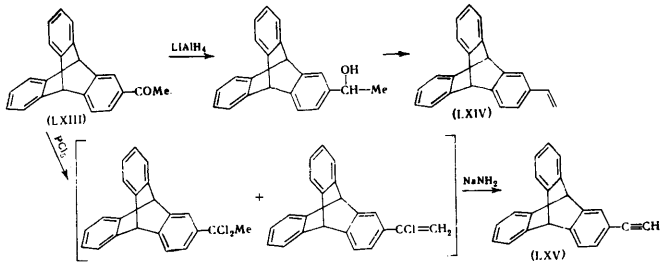
Functional substituents distant two or more methylene units from the bridging carbon atoms develop their normal reactivity [61].

Results obtained for the dissociation constants of several 10-substituted triptycene-9-carboxylic acids and for their esterification with diazodiphenylmethane were analysed by means of the linear free-energy equation. As was to be expected, the acidity and the rate of esterification of these acids are determined mainly by the inductive effect of the substituent [170].

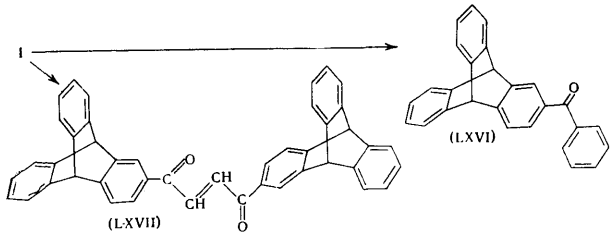
9-Vinyltriptycene [99,171] and 9-ethynyltriptycene [172] have been prepared, and their properties studied. Many 9- and 9,10-substituted triptycenes have been obtained with the aim of studying their physiological activity [61,173,174]. Certain amines of this series possess anti-inflammatory activity [61]; triptycene itself binds nucleosides weakly [175]. Several 9,10-disubstituted triptycenes have been subjected to polycondensation; the resulting polyesters were thermostable, in several cases also plastic, and could be processed into films and fibres [42,43,60]. A film based on a polyamide containing triptycene fragments enables hydrogen and helium to be separated from methane [176].

V. REACTIVITY OF AROMATIC RINGS

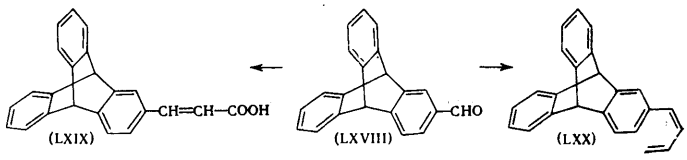
Electrophilic substitution usually occurs preferentially at the β-position in the aromatic rings of triptycene. Thus treatment of triptycene with acetyl chloride in the presence of aluminium chloride (at $-20°C$) gives a high yield of 2-acetyltriptycene (LXIII). [96] This compound has been used as a readily accessible starting material for the preparation of unsaturated hydrocarbons of the triptycene series—the 2-vinyl (LXIV) [99] and 2-ethynyl (LXV) [177] derivatives:



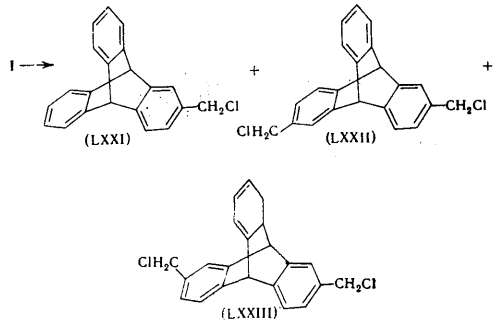
Triptycene is acylated by benzoyl and fumaroyl chlorides also exclusively at position 2 to form the corresponding ketones (LXVI and LXVII): [178]



The direct formylation of triptycene with excess of dichloromethyl methyl ether in the presence of aluminium chloride (at $-20°C$) gives a 51% yield of triptycen-2-al (LXVIII). [179] This aldehyde had previously been obtained from 2-acetyltriptycene (LXIII) in several stages [180]. Triptycen-2-al (LXVIII) has been used for the preparation of 2-butadienyltriptycene (LXX) [179] and β-triptycen-2-ylacrylic acid (LXIX): [180]



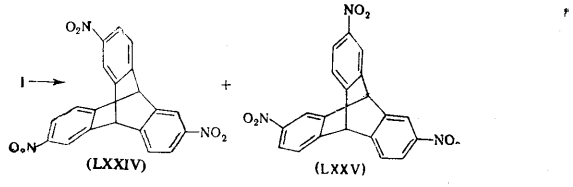
Triptycene undergoes chloromethylation under comparatively severe conditions with the formation of three products—the 2-chloromethyl (LXXI, 15%), 2,6-bis-chloromethyl (LXXII, 52%), and 2,7-bischloromethyl (LXXIII, 16%) [181] derivatives:



Treatment of triptycene with concentrated nitric acid in acetic anhydride led to isolation of the 2-nitro (44%), 2,6- and 2,7-dinitro, and traces of the 1-nitro (2.3%, identified from the ^{1}H n.m.r. spectrum) compounds [97].

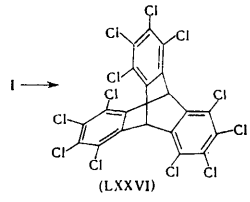
The formation of isomeric dinitro- and bischloromethyl-triptycenes and the presence of unchanged triptycene in the reaction mixture indicate that a substituent in one aromatic ring has little effect on the reactivity of unsubstituted rings towards sufficiently active electrophilic reagents.

A mixture of isomeric 2,6,12- and 2,7,13-trinitrotriptycenes (LXXIV and LXXV) containing no α-substituted isomers is formed when triptycene is treated with fuming nitric acid [182]:



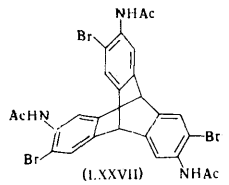
Preparation of a hexanitrotriptycene of undetermined structure has been reported in the patent literature [183].

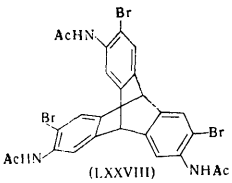
The action of a combined chlorinating agent (sulphuryl chloride in the presence of sulphur monochloride and aluminium chloride) gave dodecachlorotriptycene (LXXXVI) in high yield [184]:



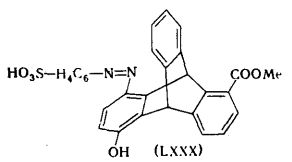
Among other compounds of the series 9,10-dimethyltriptycene has been most thoroughly studied in relation to

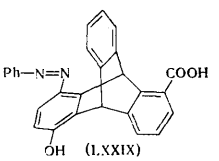
electrophilic substitution[185]; β-monosubstituted derivatives are obtained on bromination, acylation, and nitration[186]. Monosubstituted derivatives of undetermined structure were obtained by the nitration and acylation of 1,2-benzotriptycene, but this hydrocarbon could not be brominated[28]. The chloromethylation of 2-chloromethyltriptycene (**LXXI**) gives the 2,6-bischloromethyl derivative (**LXXII**) in theoretical yield[181]. The bromination of isomeric triacetamidotriptycenes (obtained by reducing a mixture of trinitrotriptycenes in acetic acid) gives a mixture of isomeric triacetamidotribromotriptycenes


(LXXVII)


(LXXVIII)

in high yield[182]. The reaction of 5-hydroxytriptycene-1-carboxylic acid with benzenediazonium chloride and that of its methyl ester with diazotised sulphanilic acid yield the corresponding azo-compounds (**LXXIX** and **LXXX**).[137]


(LXXX)


(LXXIX)

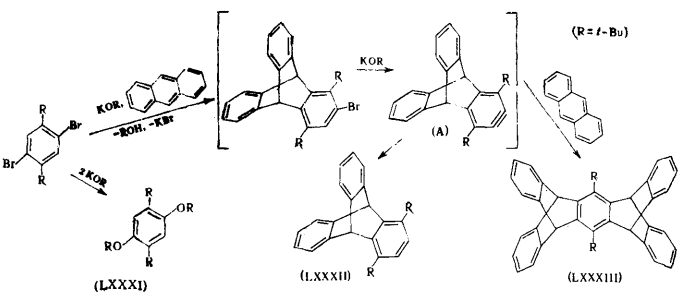
The reactivity of α- and β-positions in the aromatic rings of the triptycene molecule towards electrophilic and nucleophilic reagents has been studied quantitatively by deuterium exchange in the presence of trifluoroacetic acid[187,188] and caesium cyclohexylamide[188] respectively. In the former case exchange of a hydrogen atom was more rapid in the β- than in the α-position by factors of 7–8; but isotopic exchange in the presence of the amide was more rapid in the α- than in the β-position by factors of 7.3–7.5. Under conditions of electrophilic isotope exchange a hydrogen atom in either position was less mobile than in *o*-xylene or 9,10-dihydroanthracene[187]; but under conditions of nucleophilic isotope exchange it was more mobile than in benzene[154].

Differences in reactivity between α- and β-positions in the aromatic rings of the triptycene molecule are attributed to strain in the bicyclo[2,2,2]octane system[188], which distorts the angles between aromatic and aliphatic carbon–carbon bonds[84,85]. This results in changes in the hybridisation of the orbitals and the lengths of the carbon–carbon bonds in the aromatic ring. The bond common to the bicyclic system and the aromatic ring acquires an enhanced *p*-character like an aliphatic carbon–carbon bond, and the remaining orbitals of the bounding carbon atoms acquires a greater *s*-character, while becoming more electronegative. Therefore the α-carbon atom attached by the electronegative orbital is less reactive towards electrophilic substitution than is the β-carbon atom (which remains unaffected by the strained ring); as a consequence the α-hydrogen atom develops enhanced acidity.

An attempt was made to explain the preferential β-substitution on electrophilic attack also by the Mills–Nixon effect[189]—by the fixation of multiple bonds at the 1–9a, 2–3, and 4–4a positions in the aromatic rings of triptycene because of the strain in the bicyclic system—indirect support for which was obtained by comparing the oxidation potential of triptycenequinone with those of other *p*-quinones[38]. Dynamic factors may also determine the final results of electrophilic substitution and the differently strained σ-complexes formed on α- and β-substitution[190].

Nucleophilic substitution in an activated aromatic ring in triptycene has been accomplished with 2,3-dichlorotriptycene-1,4-quinone, which is analogous to 2,3-dichloro-1,4-naphthaquinone in chemical behaviour. This triptycene derivative reacted with amines to form quinonoid compounds, but the latter did not dye cellulose acetate fibre, probably owing to non-coplanarity of the structure[191,192].

Nucleophilic substitution in an unactivated aromatic ring of triptycene involves intermediate formation of 1,2-dehydrotriptycene, indicated by the reactions of 2-bromotriptycene with potassamide and lithium piperidide, as well as that of 1-chlorotriptycene with the latter, which yield mixtures (~1 : 3) of 1- and 2-substituted triptycenes. Phenyl-lithium reacts similarly with 2-fluoro- and 2-chloro-triptycenes, but with 2-bromotriptycene under these conditions the bromine atom is exchanged for lithium[193]¶. The intermediate formation of 1,2-dehydrotriptycene appears at first glance to be inconsistent with the distribution of bond lengths in the aromatic ring[84,85], since it should have been more strained than 2,3-dehydrotriptycene. For this reason, however, 1,2-dehydrotriptycene is obviously the more reactive, which probably explains the composition of the reaction products[193]. Formation of an sp-hybridised $C_{(2)}-C_{(3)}$ bond in triptycene compounds (2,3-dehydrotriptycene, A) has been postulated[47] only for the action of potassium t-butoxide on 1,4-dibromo-2,5-di-t-butylbenzene in the presence of anthracene, when 1,4-di-t-butoxy-2,5-di-t-butylbenzene in the presence of anthracene, when 1,4-di-t-butoxy-2,5-di-t-butylbenzene (**LXXXI**), 1,4-di-t-butyltriptycene (**LXXXII**), and the adduct (**LXXXIII**) were isolated, which suggested the reaction scheme.



Homolytic substitution in an aromatic ring of triptycene has not been studied. A substance containing a little chlorine and of undetermined structure was isolated from the products of the radical chlorination of triptycene[1].

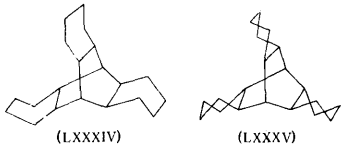
Triptycene derivatives containing functional substituents in the aromatic rings exhibit no significant difference in properties from other aromatic compounds[1,96,99,133,135,137,139,178–182,193–195]. Thus 2-chloromethyltriptycene (**LXXI**) is comparable in reactivity with benzyl chloride: it undergoes nucleophilic substitution (solvolysis, cyanolysis) and reduction and also forms an organomagnesium compound, under the same conditions as benzyl chloride.

¶ Triptycen-2-yl-lithium was formed also by the reaction of 2-bromotriptycene with n-butyl-lithium[96]. Triptycene was obtained on hydrolysis of this compound[193], but treatment with acetonitrile gave 2-acetyltriptycene[96].

The hydrolysis rate constant of 2-chloromethyltriptycene (LXXI) (in 40% aqueous acetone) exceeds that of benzyl chloride by a factor of 2.73, which indicates that the dihydroanthrylene fragment of triptycene exerts a positive inductive effect [109].

More severe conditions are required for the nucleophilic substitution of 1-chloromethyltriptycene. Its hydrolysis rate constant is smaller than that of 2-chloromethyltriptycene by a factor of 5.8. [194] Isomeric α- and β-carboxylic acids differ in acidity: triptycene-1-carboxylic acid is stronger than the 2-isomer, which is weaker than benzoic acid (as established by potentiometric titration in non-aqueous solvents—acetonitrile and dimethylformamide) [196]. This is also consistent with the general rule that substituents in α- and β-positions in the aromatic rings of triptycene differ in behaviour and with the change in hybridisation of the orbitals of the corresponding carbon atoms.

Triptycene is hydrogenated over palladium or ruthenium on carbon (under 30–100 atm at 100–200°C), either partly or completely depending on the conditions [197]. Exhaustive hydrogenation gives iso-*cis*-perhydrotriptycene (LXXXIV) rapidly and iso-*trans*-perhydrotriptycene (LXXXV) far more slowly (in 60% yield after 1 month).



(LXXXIV) (LXXXV)

In triptycenequinol (IV) either the substituted or an unsubstituted ring is reduced depending on the conditions [1]. Variously annelated quinones of the triptycene series undergo very rapid catalytic hydrogenation by an electronic mechanism [198–205]. Steric factors have a slight effect on the rate of hydrogenation. The rate usually increases with the degree of annelation of the quinones. Comparison of results for the catalytic hydrogenation of quinones over nickel and palladium on carbon with those for polarographic reduction (see Table in Section III) revealed the linear relation $\lg k_1 - \lg k_2 = \chi(E_1^\circ - E_2^\circ)$, where k_1 and k_2 are the hydrogenation rate constants for two members of the series, E_1° and E_2° are their standard potentials, and it was found that $\chi = 1.7\ V^{-1}$. The rate of catalytic hydrogenation should thus increase as the standard potential of the quinone falls (as a result of the diminished stability of the intermediate semiquinone). On hydrogenation over nickel, furthermore, the first-order rate constant increases with the activation energy owing to an increase in the entropy factor.

The hydrogenation of adducts of anthracene and pentacene with *p*-benzoquinone was investigated on the basis of the multiplet theory of catalysis [206–214]. Since successive complication of the structure of the non-reacting part of the molecule (II, XXVI, XXVII) has no significant effect on the rate or the extent of the process, it was deduced that the catalyst (nickel) surface contained projecting active centres, on which the indicial group of the reactant molecule was superposed (hydrogenation of the $C_{(2)}-C_{(3)}$ bond). The results enabled a model of the active complex to be constructed and permitted determination of the number of active centres (1.20^{20} [sic] g^{-1} Ni) and their optimum dimensions (height not exceeding 3.9 Å).

Hydroaromatic compounds of the triptycene series are dehydrogenated by sulphur or palladium on carbon with the formation of substituted triptycenes [18,19,28,215].

A high-melting complex of triptycene with tricarbonylchromium was obtained and found to be soluble in organic solvents and to decompose on fusion, sublimation, or illumination. Its proton magnetic resonance spectrum indicated that the chromium atom was coordinated with one of the aromatic rings [216].

Several substituted triptycenes readily form clathrates [30,34,35,38,98,139]. For example, 1,4-diphenyltriptycene gives with carbon tetrachloride and cyclohexane stable clathrates containing one solvent molecule per two hydrocarbon molecules [98].

It has been reported that quinols of the triptycene series can be used as photographic developers [217,218] and stabilisers for synthetic elastomers [219,220]. The reactivity of 2-vinyltriptycene (LXIV) is close to that of styrene under conditions of radical homo- and co-polymerisation, whereas 9-vinyltriptycene, in which the vinyl group is sterically hindered and is not conjugated with the ring system, is inert under these conditions and does not polymerise. Polymerisation of 2-vinyltriptycene (LXIV) occurs at the vinyl bond to give a linear polymer containing the triptycene fragment in the side-chain, which is less thermostable than polymers containing a triptycene residue in the main chain [220].

VI. REACTIONS INVOLVING OPENING OF THE BRIDGE SYSTEM

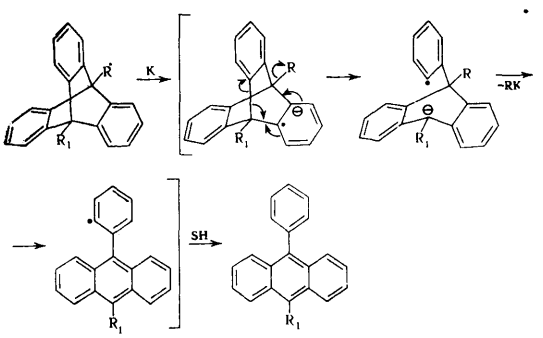
Triptycene is comparatively readily oxidised by strong oxidants such as chromium trioxide or potassium permanganate in acetic acid with the formation of anthraquinone, which resists further oxidation under these conditions [1]. Formally oxidation involves cleavage of the bicyclic system, but initial attack by the oxidant on one of the aromatic rings is not excluded. Intermediate oxidation products could not be isolated (probably because of their enhanced activity under the reaction conditions).

Triptycenequinone (III) is also oxidised to anthraquinone [14]. The latter compound and 1,4-diphenylanthraquinone (2 : 1) have been isolated from the oxidation of 1,4-diphenyltriptycene, the ratio of the products being obviously determined not only by statistical factors (otherwise the inverse ratio would have been obtained) [98]. The oxidation of 1,2-benzotriptycene [28] and 9,10-dibromo-2,3-benzotriptycene [41] also yielded anthraquinone, and no other reaction products could be identified. Thus derivatives of anthraquinone are the most usual oxidation products of compounds of the triptycene series. Nevertheless, the oxidation of substituted triptycenequinones with ammonium persulphate leads to cleavage of the quinonoid ring with the formation of substituted 9,10-dihydro-9,10-ethenoanthracenes [134].

Under milder conditions functional groups can be oxidised while the triptycene structure is preserved. Thus triptycenequinol (IV) can be oxidised to triptycenequinone (III), [1] 9,10-bishydroxymethyltriptycene to triptycene-9,10-dicarboxylic acid [60], 2-acetyltriptycene (LXIII) to triptycene-2-carboxylic acid [178], and triptycen-2-ylmethanol to triptycen-2-al (LXVIII). [180] Triptycene compounds with substituents containing multiple bonds can be ozonised without affecting the triptycene structure [178,222].

The bridging system of triptycene is opened up by reduction under severe conditions. Thus triptycene-1,4-quinol (IV) and triptycenequinone (III) give 9,10-dihydroanthracene when distilled with zinc dust [14]; 1,2-benzotriptycene breaks down into naphthalene and 9,10-dihydroanthracene [28].

Triptycene hydrocarbons undergo an interesting cleavage reaction under the influence of potassium in oxolan [223] or a potassium–sodium alloy in ether [224]. The electron spin resonance spectra of the reaction products indicate intermediate formation of a radical-anion of anthracene. Study of the effect of a substituent group on the stability of the intermediate radical-anion suggested the reaction mechanism. [223]



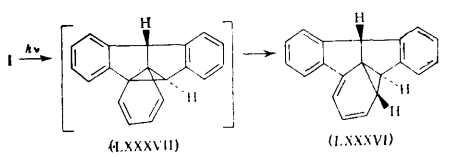
The detachment of 9,10-substituents accelerates in the sequence

$$CH_3 > C_6H_5 < H, C_6H_5CH_2$$

which confirms that one of the substituents leaves as an anion. Metallic sodium has a slight effect on the cleavage of 9-phenyltriptycene, and does not interact at all with other hydrocarbons of the series [223].

The previously mentioned diazotisation of triptycen-9-ylmethylamine (LVIII) [168] and decomposition of 9-diazomethyltriptycene (LXI) [169] also involve cleavage of the bicyclic system.

The product of the photochemical isomerisation of triptycene, in contrast to the related barrelene and benzobarrelene (which are converted into a mixture of semibullvalenes and cyclo-octatetraenes) [225], is the hydrocarbon (LXXXVI), which has been regarded [226] as formed by the sigmatropic rearrangement of the intermediate semibullvalene (LXXXVII):



(LXXXVII) (LXXXVI)

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Papers have appeared recently on the chemistry of triptycene. Thus it has been synthesised from dehydrobenzene generated from 1,1-dimethyl-3-phenyltriazen in the presence of sodium trichloroacetate and trichloroacetic acid [227], and the preparation of deuterotriptycene has been reported [228]. The enthalpy of formation and the energy of strain of triptycene have been determined [229]. The high-resolution ^1H n.m.r. spectrum of triptycen-2-amine exhibits signals due to non-equivalent bridge protons [230]. The electron spin resonance and optical spectra of the radical-ions of certain derivatives have been studied [231]. Hindered rotation of the methyl group has been detected in tetra- and octa-chloro-9-methyltriptycenes [232,233]. The optical activity of 5-substituted 1,4-dimethoxytriptycenes has been investigated [234]. 9-Butadienyltriptycene has been prepared [235], and several reactions of 9-bromo- and 9,10-dibromo-triptycenes have been accomplished [236]. β-Substituted mono-, di-, and tri-nitrotriptycenes are formed by the action of acetyl nitrate [237], and the bromination of triptycen-2-amine gives 3-bromotriptycen-2-amine [238].

Tetrahydrodi-*o*-benzopentacene has been obtained by the reaction of 2-bromo-3-fluorotriptycene with magnesium in the presence of anthracene in oxolan, which indicates the intermediate formation of 2,3-dehydrotriptycene [238]. The photoisomerisation of triptycene in methanol involves an intermediate carbene stage [239]. Other publications have also appeared [240–247].

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Advances in and Problems of Solid-phase Peptide Synthesis

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The present state of the solid-phase method of peptide synthesis is considered, its advantages and disadvantages are analysed, and the trends in and prospects of its further development are described. Attention has been concentrated on problems of improving polymeric carriers, of obtaining aminoacyl polymers, and also the problem of the formation of erroneous sequences in solid-phase peptide synthesis.
The bibliography includes 376 references.

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I. INTRODUCTION

In 1973 ten years elapsed since the publication of Merrifield's report [1] of the synthesis of peptides on an insoluble polymeric carrier. The method proposed, called the solid-phase method, has been widely used in the synthesis not only of peptides but also of a number of compounds of other classes. About 500 papers have already been published on the solid-phase synthesis of peptides, among them several reviews, the most complete of which are those of Merrifield [2] and Losse and Neubert [3] as well as the monograph of Stewart and Young [4], which has been translated into Russian.

The above reviews [2-4] cover the literature until the beginning of 1969, representing a survey of approximately 150 experimental papers. It is useful to review the literature from 1969 to the beginning of 1972. The available reviews of Marglin and Merrifield [5], Geiger [6], Wünsch [7], Waki and Izumiya [8], Kishida and Sakakibara [9,10], and Losse [11] deal only with separate aspects of solid-phase peptide synthesis. There is only one review in Russian, that of Vesa, which was published in 1968. Later investigations are described in the monograph of Stewart and Young [4] and the reviews of Merrifield [2] and Losse and Neubert [3]. We regard the present publication as a continuation of these reviews.

Abbreviations Adopted

The abbreviations used for the names of aminoacids are those recommended by the IUPAC–IUP Commission on Nomenclature [Biochemistry, 5, 2485 (1966)].

AOC	= t-amyloxycarbonyl †;
BOC	= t-butyloxycarbonyl;
BMV	= *N*-(2-benzoyl-1-methylvinyl);
DVB	= *p*-divinylbenzene;
BPOC	= 2-(*p*-biphenylyl)isopropyloxycarbonyl;
DMSO	= dimethyl sulphoxide;
DME	= dimethylformamide;
DNP	= 2,4-dinitrophenyl;
DCHA	= dicyclohexylamine (or dicyclohexylammonium);
DCC	= *NN'*-dicyclohexylcarbodi-imide;
Z	= benzyloxycarbonyl;
CDI	= *NN'*-carbonyldi-imidazole;
MBZH	= di-(4-methoxyphenyl)methoxy-(4,4'-dimethoxybenzhydryl);
MZ	= *p*-methoxybenzyloxycarbonyl;
NPS	= *o*-nitrophenylsulphenyl;
THF	= tetrahydrofuran;
TFA	= trifluoroacetyl;
FOC	= furfuryloxycarbonyl;
Pht	= phthalyl;
P	= polymeric carrier.

†POC = cyclopentyloxycarbonyl is quoted in the IUPAC–IUB Report (Ed. of Translation).

II. POLYMERIC CARRIER

The polymeric carrier is the main component in solid-phase peptide synthesis. Clearly the selection of the carrier is extremely important for the success of the process.

The copolymer of styrene and 1–2% DVB proposed by Merrifield[1] is completely insoluble in the usual solvents but swells satisfactorily in methylene chloride, DMF, dioxan, and chloroform. This is extremely important, since it makes it possible to employ virtually the entire bulk of the polymeric bead for the reactions[13].

The above carrier[1,14] is still most frequently used. The same may be said of the "anchor" group with the aid of which the first aminoacid is added to the polymeric carrier: as can be seen from the data quoted in Table 1, the chloromethyl group clearly predominates.

Although in the vast majority of studies[15–227] the authors used the chloromethylated copolymer of styrene and 1–2% DVB, a considerable proportion of studies on solid-phase peptide synthesis in fact dealt with the modification of the "anchor" group. This is due to a number of difficulties involved in the preparation of the aminoacyl polymer by Merrifield's method (see the next section of the present review).

Table 1. Polymeric carriers.

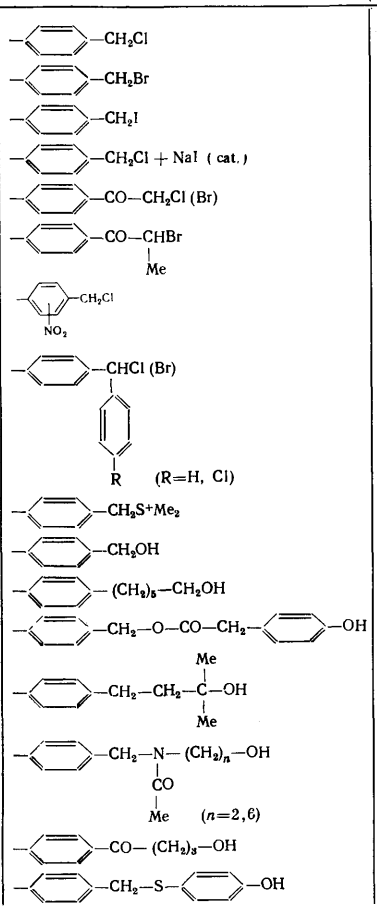
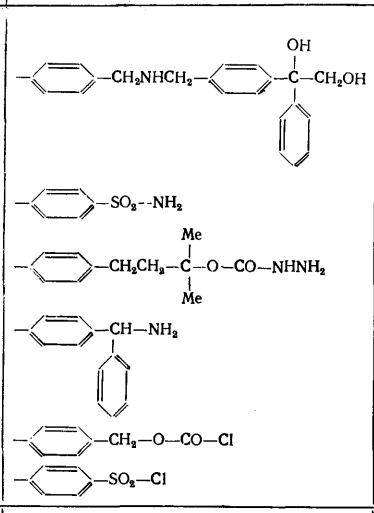
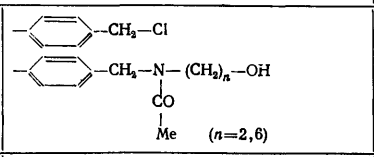
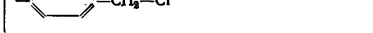
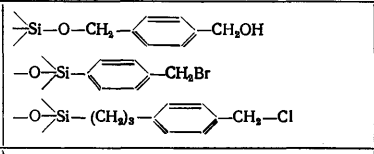
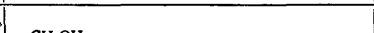
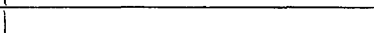
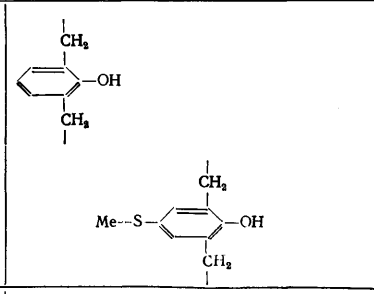
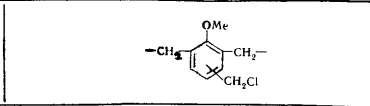
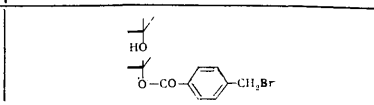
Type of polymer	Functional group	References
Gel copolymer of styrene and 1-2% DVB		13–105, 106[a], 107–227 143, 228, 230–233 228, 229 229, 234–238 239–245 240–241 1, 246–248 249–251 218, 252, 253 65, 209, 233, 254–260 261 262 263 264–266 264, 267 268, 269

Table 1 (continued).

Type of polymer	Functional group	References
Gel copolymer of styrene and 1-2% DVB		270 271 263, 272 273–282 283[b], 284–287 288, 289
Macroporous highly cross-linked styrene-DVB (up to 12%) copolymer		173, 199, 294–297 296
Glass beads coated with a layer of polystyrene		53, 173, 199, 298, 299
Pellicular carrier		62, 300–302 302, 303 304
Polystyrene, mol.wt. 200000		305–309
Poly(ethylene glycol), mol. wt. 10000–20000		310–312
Graft copolymer of polychlorotrifluoroethylene and chloromethylstyrene		313
Polyphenol		314, 315 269
Resitol		93, 115, 316
Sephadex LH-20 and G-25		317, 318 317, 318

[a] Copolymer of styrene and 5% DVB.
[b] "Popcorn" type of copolymer of styrene and 0.5 DVB.

Attempts have been made to employ bromomethylated and iodomethylated styrene–DVB copolymers. However, such carriers can be prepared only in two stages‡. Thus Tilak[228] initially condensed the chloromethylated polymer with a carboxylic acid and then decomposed the resulting ester linkages with a solution of hydrogen bromide or iodide in acetic acid. The comparatively rare employment of such carriers, particularly of the iodomethylated polymer[143,229–233], is probably in fact due to the difficulties in their preparation. Therefore the method of the intermediate formation of iodomethylpolystyrenes by the reaction of chloromethylated derivatives of *N*-protected aminoacids in the presence of sodium iodide as the catalyst[234] is extremely attractive. Subsequently this method was successfully applied in a number of other laboratories[229,235–238].

Weygand[239] and, independently, Mizoguchi[240,241] suggested that a halogenoacetyl polymer be used. It improves the conditions governing the addition of the first aminoacid to the polymeric carrier but precludes the employment of acid reagents for the separation of the peptide from the carrier. The alkaline reagents used for this purpose[239–243] increase the risk of racemisation of the peptide. For this reason, halogenoacetyl polymers are usually employed to synthesise amides, hydrazides, and esters of protected peptides[240,241,244,245]. The same may be said also of the α-bromopropionyl polymer proposed by Mizoguchi and coworkers[240,241].

The polymeric carriers examined suffer from the same disadvantages as the chloromethylated Merrifield copolymer nitrated in the aromatic rings[1]. The enhanced resistance of the ester linkage of the peptide to acid reagents makes the nitrated carrier more suitable for the synthesis of protected amides and hydrazides of peptides[246]. Thus, using ammonia or amines for the separation of peptides from the polymeric carrier, Takashima et al.[247,248] obtained a number of oxytocin analogues.

The benzhydryl polymer proposed by Southard and coworkers[249–251] permits the employment of mild acid reagents for the separation of the peptide from the carrier but requires the use in the synthesis of extremely acid-labile protective groups, which also involves certain difficulties.

An interesting version of the synthesis of aminoacyl polymers without using condensing agents and tertiary amines was proposed by Dorman and coworkers[252]. The dimethyl(arylmethyl)sulphonium polymer employed by these workers was subsequently used to synthesise a number of biologically active peptides[218,253].

The polymeric carriers in which a hydroxyl forms part of the "anchor" group are of undoubted interest. This is primarily the hydroxymethylated polymer of styrene proposed by Bodanszky and Sheehan[254], which has been frequently used in solid-phase peptide synthesis despite a number of important disadvantages[65,209,233,250–260]. The hydroxyhexamethylene polymer proposed by Bayer et al.[261], the *p*-hydroxyphenylacetoxy polymer investigated by Blake and Li[262], and the t-hydroxyalkyl polymer of Wang and Merrifield[263] belong to the same group of carriers. The hydroxyalkylamino-polymer, developed by Tilak and Hollinden[264], is also suitable; it can be used successfully in combination with the Z-protected α-amino groups of aminoacids. The hydroxybutyryl polymer has similar properties[264,267]. The impossibility of using acid reagents in the stage involving the removal of the peptide from the carrier must be regarded as a disadvantage of these carriers.

Many of the hydroxyl-containing carriers make it possible to convert the peptidyl polymer into a polymeric activated peptide ester at the end of the synthesis, which leads to many possibilities in its subsequent use (see Section VII). This is primarily the polymer with hydroxyphenyl sulphide groups proposed by Marshall and Liener[268] and independently by Flannigan and Marshall (G.R. Marshall)[269]. The oxidation of the sulphide group to the corresponding sulphone leads to the formation of an activated peptide ester. A carrier with analogous properties was obtained by Wieland et al.[270] by the reaction of 4′-aminomethyl-2,2-diphenylmethanediol with a chloromethylated carrier. It can be converted by dehydration into an activated vinyl ester of the peptide. The polymeric carrier containing the sulphonamide group has similar properties[271]. *N*-Alkylation of the sulphonamide group facilitates the alkaline hydrolysis, ammonolysis, and hydryzinolysis of the "anchor" linkage.

Special carriers whose "anchor" sections already contain the appropriate functional groups are used to synthesise the amides and hydrazides of peptides under the conditions of the acid cleavage of peptidyl polymers. These are the t-alkyloxycarbonylhydrazide polymer of Wang and Merrifield[263,272] and the benzhydrylamino-polymer proposed by Pietta and Marshall[273]. Monahan, Rivier, and coworkers[274–279] as well as other investigators[280–282] frequently used the benzhydrylamino-polymer to obtain a number of biologically active peptide amides.

Together with polymeric carriers whose functional groups are capable of interacting with the carboxyl of the combined aminoacid, carriers permitting the synthesis of peptides from the terminal NH_2 group are sometimes used. Thus Letsinger and Kornet[283] proposed a carrier of the alkyloxycarbonyl chloride type capable of interacting with the α-amino-group of an aminoacid. However, the suggested approach has not been widely used in solid-phase synthesis owing to the risk of racemisation in the activation of the carboxy-group of the peptide. Nevertheless a carrier of the alkyloxycarbonyl chloride type has been used effectively to add to a polymeric carrier peptides containing ω-amino-groups in diaminoacid residues[284–286]. The peptidyl polymers thus obtained can be cyclised directly on the carrier[284,285].

A novel method for solid-phase peptide synthesis from the terminal NH_2 group was developed by Felix and Merrifield[287], who suggested that aminoacid BOC-hydrazides can be used for the synthesis. The activation of the carboxyl of the peptide being synthesised by the azide method virtually rules out the possibility of racemisation in the peptide formation stage. Dahlmans and coworkers[288,289] also suggested that a polymeric carrier containing sulphonyl chloride groups be used for the synthesis of peptides from the terminal NH_2 group, the aminoacid residues being introduced into the chain in the form of their t-butyl esters. However, like the entire approach of this kind, this method has not so far become widely used.

‡There exists a little known but extremely simple method of synthesising iodomethylated styrene polymers and copolymers by treating the chloromethylated polymer with NaI [see V. V. Korshak, S. V. Rogozhin, and V. A. Davankov, Izv. Akad. Nauk SSSR, Ser. Khim., 1912 (1965); Vysokomol. Soed., 8, 1686 (1966)] (Ed. of Translation).

Not only the anchor group of the carrier but also the physicochemical properties of the polymeric matrix itself are important for the solid-phase synthesis. The polymeric carrier proposed by Merrifield ensures the diffusion of the dissolved reactants within the grains as a result of swelling in many organic solvents, which permits the employment of the entire bulk of the polymeric bead and at the same time its mechanical strength is fairly high. On the other hand, it is not free from many disadvantages. Studies of the structure of styrene–DVB copolymers are being continued [290–293]. The variation of the swelling of the gel polymeric carrier as a function of the chemical nature of the solvent and also the inadequate dimensions of the cells of the polymeric network complicate the diffusion process. To improve the diffusion of the solutes into the polymeric grain and to stabilise the polymer structure, some investigators suggest the employment of macroporous rigidly cross-linked carriers based on polystyrene. The advantages of the latter were noted a long time ago [294], but their practical application began later [173,199,295–297]. A comparative assessment of different carriers [173] suggests that macroporous carriers are extremely promising.

A higher rate of diffusion of solutions into the carrier beads can be achieved by employing fine-mesh polymers, but such carriers are inconvenient to handle. Therefore Bayer et al. [53] suggested that glass beads coated by a thin layer of polymers be used as the carrier. The possibility of employing such hybrid carriers was also demonstrated by other investigators [173,199,298,299]. The disadvantages of these carriers are their low specific capacity and the possibility of the gradual disruption of the outer organic layer, which leads to an appreciable loss of the peptide synthesised. The latter disadvantage is to a large extent eliminated when the anchor organic molecules are fixed on the glass beads by covalent bonds [60,300–304]. According to the authors, such pellicular carriers can be used for column solid-phase peptide synthesis.

The effectiveness of the interaction of the polymeric carrier with reactant solutions is low owing to the presence of a heterogeneous system. Here the advantages of the solid phase synthesis give rise to a significant disadvantage. A way out of this difficulty can be found by combining the possibilities of the solid-phase synthetic method with the synthesis of peptides in solution. For this purpose, Shemyakin, Ovchinnikov et al. [305] developed a method of peptide synthesis on a soluble polymeric carrier. It was suggested that polystyrene ($M = 2 \times 10^5$), soluble in organic solvents and insoluble in water, be employed. This makes it possible to carry out the peptide synthesis in a homogeneous medium and the peptidyl polymer can be purified in a heterogeneous medium. However, under these conditions there are losses of the peptidyl polymer in its precipitation from solution and also certain other complications. Nevertheless a number of biologically active peptides, including gramicidin S could be synthesised by this method [306–309].

The proposed approach is now being developed by the group of Bayer and coworkers [310–312] using poly(ethylene glycol) ($M = 1 \times 10^4$–2×10^4) as the carrier. The authors use ultracentrifugation and ultrafiltration through membranes to purify the intermediates.

Apart from poly(ethylene glycol), which differs in its nature from the traditional carriers based on polystyrene, attempts have been made to use other polymers in the solid-phase synthesis, in particular graft polychlorotrifluoroethylene, chloromethylated polystyrene [313], various polyphenols [269,314,315], and also resitol methylated in the phenolic hydroxyl and chloromethylated in the aromatic ring [93,115,316]. Polymers based on dextrans [2], for example Sephadex LH-20 and G-25, were also tried for this purpose [317,318].

III. THE ADDITION OF THE FIRST AMINOACID TO THE POLYMERIC CARRIER

The method of adding *N*-protected aminoacid to the chloromethylated polymeric carrier in organic solvents in the presence of tertiary amines is most commonly used. To reduce the possibility of the formation of ionogenic groups on the carrier as a result of the interaction of the tertiary amine with the chloromethyl polymer via the mechanism

$$Et_3N + Cl{-}CH_2{-}\textcircled{P} \longrightarrow Cl^- \cdot Et_3N^+{-}CH_2{-}\textcircled{P},$$

it is suggested that triethylamine be replaced by other bases, for example by ethyldi-isopropylamine [23]. An even greater effect is achieved when quaternary tetramethylammonium bases, proposed for this purpose by Loffet [133,152], are used. A definite effect is also observed on changing the solvent in which the ester is formed. t-Butyl alcohol is most promising for this purpose [207,208].

The standard methods of preparation of aminoacyl polymers presuppose interaction between the components at high temperatures (50–80°C), which is not always acceptable. Thus Marglin [176] observed a number of side effects under these conditions and suggested that they can be eliminated by synthesising aminoacyl polymers in DMF with triethylamine in the course of 24 h at 25°C. The results were somewhat unexpected, since hitherto DMF could be used at this stage only at 50–75°C. [23,220]

Since the nature and conditions of the interaction of the *N*-protected aminoacid with the polymeric carrier are determined primarily by the nature of the "anchor" group of the latter, clearly all the above considerations are applicable also to all other carriers containing the chloroethyl group in the aromatic ring.

N-Protected aminoacids add to bromo- and iodomethylated carriers under milder conditions. The reaction is usually carried out with triethylamine in DMF at 20 to 30°C in the course of 36–72 h. [228,230–233] Dicyclohexylamine is sometimes used instead of triethylamine [231,232]. A *C*-terminal aminoacid is added to a chloromethylated carrier in the presence of sodium iodide as the catalyst under still milder conditions [234,236–238].

Analogous conditions are required for addition also in the case of halogenoacetylated carriers. Ethyl acetate, methylene chloride, or DMF are usually employed as solvents [239–245] and the bases are normally triethylamine or ethyldi-isopropylamine [239,242].

In conjunction with the benzhydryl polymer, Southard and coworkers [249,250] used DCHA salts of BMV-aminoacids and other *N*-protected aminoacids for the preparation of aminoacyl polymers. The reaction was carried out by refluxing in chloroform for 12 h [249] or in methylene chloride at 20°C for 4 days [250].

Using a dimethyl(arylmethylene)sulphonium polymer, an aminoacyl polymer was obtained under very mild conditions without a tertiary amine [252]:

$$Me_2S + Cl{-}CH_2{-}\textcircled{P} \longrightarrow Cl^- \cdot Me_2S^+{-}CH_2{-}\textcircled{P} \xrightarrow{HCO_3^-}$$

$$\longrightarrow HCO_3^- \cdot Me_2S^+{-}CH_2{-}\textcircled{P} \xrightarrow[2.\ \text{drying}\ 3.\ \text{heating}]{1.\ \text{BOC-aminoacid}}$$

$$\longrightarrow BOC{-}NH{-}CHR{-}COO{-}CH_2{-}\textcircled{P} + CO_2 + Me_2S\ .$$

The yield of reaction product is then 87–96%, [218,253] while with chloromethylated carriers it does not as a rule exceed 25–30%.

Condensing agents such as CDI and DCC are used for the addition of the first aminoacid to carriers whose "anchor" group incorporates a hydroxyl. It is then necessary to block the remaining free hydroxy-groups when condensing agents are used in the peptide formation stage, which is not always very convenient.

Toluene-*p*-sulphonyl chloride is sometimes used as the condensing agent in the stage involving the formation of the aminoacyl polymer [263,265,266].

Condensing agents are also employed for the addition of the first aminoacid to carriers whose "anchor" groups contain an amino- or a hydrazino-group. DCC is most frequently used for this purpose [263,273–282]. The corresponding 2,4,5-trichlorophenyl esters of aminoacids have been used with the sulphonamide carrier [271].

In the synthesis of peptides from the terminal NH_2 group different aminoacids are added to the polymeric carrier in the form of an ester, amide, or another involving the carboxy-group in the presence of trimethylamine [283–289].

An interesting modification of the addition of the aminoacid to the carrier involves a functional side group. Thus Glass et al. [226] used the imadazole ring of histidine for the interaction with a fluorodinitrophenyl group of the polymeric carrier.

In those cases where the carrier pore size changes in the course of the synthesis, the aminoacids can add to sections of the polymer which subsequently become appreciably inaccessible to chemical attack by other reagents [13]. As a result of screening by the carrier, these aminoacids do not enter into peptide formation reactions, which leads to the appearance of erroneous sequences. The amount of such inaccessible residues can reach 40%. [319]

One of the ways of overcoming these disadvantages is the addition to the polymeric carrier of short peptides, incapable of passing into the very small carrier pores, instead of the individual aminoacids. Attempts were made to employ for this purpose polymers with modified functional groups, in particular halogenoacetyl [239,242] and bromomethyl [230–232]. It proved possible to use a chloromethylated carrier only in the reaction with depsipeptides on refluxing in ethyl acetate [320,331] or with the simple dipeptide BOC-Gly-Gly-OH. [227] We believe that the employment of sodium iodide in conjunction with a chloromethyl polymer is very promising. It is then possible to add to the carrier di-, tetra-, and penta-peptides in amounts of the order of 0.12–0.32 millimole g^{-1}. [237,238]

IV. PROTECTION AND DEBLOCKING OF α-AMINO-GROUPS

The benzyloxycarbonyl protecting group, employed initially by Merrifield [1], proved to be relatively unsuitable under the conditions of solid-phase synthesis [4]. Therefore its application is limited if one disregards studies where Z-aminoacids were used to introduce the *N*-terminal residue of the peptide being synthesised. Under there conditions, the benzyloxycarbonyl group is removed in the acid separation of the peptide from the carrier or leads to more stable derivatives when the peptidyl polymer is subjected to ammonolysis, hydrazinolysis, or transesterification.

Z-Aminoacids can be used in combination with a hydroxyalkylamino-polymer [264–266,296] and a hydroxybutyryl polymer [264,267]. The benzyloxycarbonyl group is then removed with a 30% solution of hydrogen bromide in acetic acid without loss of peptide and carrier. Z-Aminoacids are also suitable for peptide synthesis on a polymer of the sulphonamide type [271]. The polymeric carrier based on poly(ethylene glycol) [310,312] has an interesting property, i.e. the benzyloxycarbonyl group can be removed by hydrogenation, which could not be done when insoluble carriers were used.

Nevertheless the main substituent used to protect the α-amino group in the synthesis of peptides on a polymeric carrier continues to be the BOC group (Table 2). The availability and stability of BOC-aminoacids, the possibility of removing the BOC group by mild acid reagents, and many other advantages make it virtually irreplaceable at the present stage of development of solid-phase peptide synthesis.

The BOC-group is usually removed with a 1 *N* solution of hydrogen chloride in acetic acid [14], despite the possible risk of acetylation of the peptide amino-groups by trace amounts of acetic acid in the last stage of peptide formation. However, careful neutralisation and washing reduce this risk to a minimum.

A 4 *N* solution of hydrogen chloride in dioxan, proposed for the first time by Stewart and Woolley [322], is beginning to be increasingly employed for the elimination of the BOC group. Dioxan promotes the swelling of the polymer, which improves the efficiency of the deblocking. This is important, since the incomplete removal of the *N*-protecting group can be one of the causes of the omission of aminoacid residues from the chain [169].

Trifluoroacetic acid [242,323] or its 50% solution in ethylene chloride were proposed in 1966–1967 for the removal of the BOC group. The methyl chloride solution was used by Gutte and Merrifield [324] in the synthesis of ribonuclease A. In addition trifluoroacetic acid prevents the formation of the pyroglutamic acid residue from the BOC-glutamine residue at the instant of the removal of the BOC group, which happens when a 1 N hydrogen chloride solution in acetic acid is employed [325]. A 4 *N* solution of hydrogen chloride in dioxan can also be used for this purpose. The present authors successfully applied this procedure in the solid-phase synthesis of a number of fragments of the insulin A-chain [126].

A mixture of standard reagents with mercaptoethanol is used to remove the BOC-group from the tryptophan residue. The possibility of employing for this purpose a 20% solution of mercaptoethanesulphonic acid in acetic acid [162] and also of a 0.1 *N* solution of hydrogen chloride in formic acid [221] has been demonstrated.

Special studies have been made on problems of the removal of the BOC group [60,97]. The possibility of employing at this stage hydrogen chloride solutions in propionic acid [97], in a methylene chloride–DMSO mixture [134], and in methanol [206] was investigated. Chou et al. [134] obtained interesting results demonstrating the dependence of the degree of removal of the BOC group on the chain length of the peptide synthesised, the nature of the deblocked aminoacid residue, and its location in the peptide chain, which the authors believe to be the most important factor.

The AOC group, whose chemical properties are similar to those of the BOC group, was employed in the solid-phase synthesis for the first time by Inukai et al. [314]. It will probably be used on a wider scale with increase in the manufacture of AOC-aminoacids.

The NPS group, which is readily removed by solutions of hydrogen chloride in an inert solvent [328] and also by thioacetamide in a mixture of acetic acid and methanol [327], was introduced almost simultaneously into the solid-phase

Table 2. N^{α}-protecting groups and methods for their removal in solid-phase peptide synthesis.

Protecting group	Methods of deblocking	References
Z	30% HBr in AcOH	264–267,271,296
	Hydrogenation over Pd/C	310,312
BOC	1 *N* HCl in AcOH, 30 min	16,17,19,22,29,32–34,38,39,43,44,47,48,52–55,57,59,60,62–64,67,70–72,74,75[a],76,78,81–83,86,89,90,94,95,97,98,100,102,104,106,108,111,112,116–119,122[b],123–125,127,131,132,137–145,153,155,156,159,161,165,166,170,172,174,177,178,184,188,195,198,201–203,205,214–217,220,221,224,225,233,235,247,248,253,255,257,261,269,273,297,300,301,308
	1,2–1.5 *N* HCl in AcOH, 30 min	80,96,107,135,175,240,241,312
	4 *N* HCl in dioxan, 30 min	24,30,31,36,37,41,42,45,49,51,60,65,66,73,79,85,87,92,105,110,113,129,126,146,147,157,160,179,180,182,200,212,222,236,238,280,299[c],310,311,313
	1 *N* HCl in dioxan, 30–45 min	21[d],88,161,231
	2 *N* HCl in dioxan, 20–30 min	284–286
	5.6 *N* HCl in dioxan	134
	30% HCl in dioxan, 20 min	50
	CF_3COOH, 30–40 min	46,74,226,242,253,271,278,317,318
	50% CF_3COOH in CH_2Cl_2, 15–30 min	42,60,84,97,128,129,134,148,157,165,167,168,190,191,193,194[e],196,197,202,209[f],211,213[g],218,223,233,258–260,262,268,275–277,281,282
	50% CF_3COOH in chloroform	101,103,183[h]
	0.8 *N* HCl in EtCOOH	97
	5.35 *N* HCl in 1:1 DMSO–CH_2Cl_2 mixture	134
	1 *N* HCl in MeOH, 30–40 min	206
BOC in the presence of Trp residue	20% $HSCH_2CH_2SO_3H$ in AcOH, 30 min	162
	0.1 *N* HCl in HCOOH	221
AOC	10% HCl in MeOH or dioxan, 1–2 h	241,245,315
	1 *N* HCl in AcOH, 40 min	28,241,244
	50% CF_3COOH in CH_2Cl_2	121
NPS	0.1–1 *N* HCl in organic solvent, 10–20 min	71,99,131,222,235,284,285
BPOC	0.5–1.5% CF_3COOH in CH_2Cl_2, 10–15 min	42,263,272
	0.05–0.1 *N* HCl in chloroform, 5–10 min	191,197,262
	Glacial AcOH, 8 h	156,159
BMV	Aqueous 0.4 *N* HCl in THF, 30 min	249
	1 *N* toluene-*p*-sulphonic acid in THF	250
FOC	1 *N* HCl in AcOH or dioxan	115,330
MZ	1 *N* HCl in AcOH, 30 min	149
	50% CF_3COOH in CH_2Cl_2, 30 min	232
Pht	N_2H_4.AcOH in DMF, 24 h	263
Me_3Si	1% AcOH in ethanol	309

[a] 0.5 *N* HCl in AcOH.
[b] 15 min instead of 30 min.
[c] 78 s instead of 30 min.
[d] 1:1 dioxan–CH_2Cl_2 mixture.
[e] 12.5–25% CF_3COOH in CH_2Cl_2.
[f] 75 min instead of 15–30 min.
[g] 4:1 CF_3COOH–CH_2Cl_2 mixture.
[h] 25% CF_3COOH in chloroform.

synthesis in three laboratories[326–328]. The group is extremely useful in many special cases owing to its high lability[71,99,131,222,235,284,285].

The BPOC group, proposed by Sieber and Iselin[329], is even more labile. It is two thousand times more sensitive than the BOC group to acid cleavage and can be removed with 75% trichloroacetic acid in 1.5 h,[329] with 0.5–1.5% solution of trifluoroacetic acid in methylene chloride[42,263,272], with 0.05–0.1 *N* hydrogen chloride solution in chloroform in 8–10 min,[191,197,262] and also with glacial acetic acid in 8 h.[156,159]

Mention should also be made of the BMV group, proposed by Southard and coworkers[249,250] in conjunction with a benzhydryl polymer. It can be removed with 0.4 *N* aqueous hydrogen chloride solution in THF or with 1 *N* solution of toluene-*p*-sulphonic acid in the same solvent. The FOC group[115,330] and MZ group[149,232], whose stabilities are similar to those of the BOC group, are also used in solid-phase peptide synthesis. The employment of the Pht group in conjunction with the hydroxy-t-alkylpolymer[263] and also of the trimethylsylyl group[309], which is suitable for the synthesis of peptides using aminoacid-*N*-carboxy-anhydrides, has been reported.

In selecting the N^{α}-protecting group, investigators devoted special attention to the deblocking stage[99].

V. PROTECTION AND DEBLOCKING OF THE FUNCTIONAL GROUPS IN THE SIDE CHAINS OF TRIFUNCTIONAL AMINOACIDS

Fairly convenient protecting groups, satisfying the requirements of the solid-phase method, which in general are the same as the requirements of the classical method for the synthesis of peptides, are now available for all trifunctional aminoacids.

Arginine. Nitroarginine[18,22,24,36,37,42,44,51,52,54,59,69,88,95,120,124,128,129,131,139,140,142,144,145,148,160,161,165,168,175,186,191,193,200,201,206,211,215,216,218,220,223,225,233,250,263,268,275–278,280,281] is usually employed with subsequent hydrogenation of the peptide when separated from the carrier. When the peptidyl polymer is treated with anhydrous hydrogen fluoride, this stage can be eliminated. For peptides containing cysteine and methionine, N^{G}-tosylarginine is usually employed[70,71,76,92,107,121,172,179,191,194,197,212,262].

Aspartic and glutamic acids. The ω-carboxy-groups of these aminoacids are successfully protected by the formation of benzyl esters[19–21,24,27,32,36,37,42,44,51,55,57,59,76,78,88,94,124,127–129,142,143,145,148,161,167,172,175,188,190,197,198,206,220,231,233,250,263,268,282], which are readily cleaved on treatment of the peptidyl polymer with acid. t-Butyl esters, which are more labile in an acid medium but are resistant to hydrazinolysis, are sometimes used[95,100,102,151,156,159,205,209,238,262]. In order to keep the ω-carboxy-group protected even after the separation of the peptide from the polymeric carrier by acid treatment, nitrobenzyl esters of the aminoacids are employed[90,113,126,194].

Asparagine and glutamine. The *p*-nitrophenyl esters of the BOC derivatives of asparagine and glutamine are usually employed to introduce their residues into the peptide, since the use of DCHA leads to the formation of the corresponding nitriles. On the other hand, if DCHA has to be used, the amide groups of asparagine and glutamine must be protected, for example by the MBZH group, which can be removed by refluxing with trifluoroacetic acid[131].

Histidine. The N^{Im}-benzyl group is most often used to protect the histidine imidazole ring. It can be removed either by catalytic dehydrogenation or by sodium in liquid ammonia[21,33,37,44,59,76,80,81,82,95,96,100,102,117,120,121,137,139,140,142,157,161,169,172,175,188,190,192,194,198,201,211,212,215,216,225,233,262,263]. The N^{Im}-group of histidine can be deblocked simultaneously with the separation of the peptide from the polymeric carrier when N^{Im}-tosylhistidine is employed[183,186,200,277,278].

The DNP group, which can be removed by treatment with thiols at pH 8 and room temperature, must be regarded as the most convenient protecting group for the histidine side chain[47,63,124,146,153,165,181,196,206,281,282,332]. The possibility of removing this group under the conditions of alkaline hydrolysis, aminolysis, and hydrazinolysis of peptidyl polymers has also been demonstrated[181]. The choice of the protecting group for the histidine imidazole ring has been the subject of a special examination by Losse[331,332].

Lysine. The benzyloxycarbonyl group, which can be readily removed by the acid cleavage of the peptidyl polymer but is entirely stable in combination with the N^{α}-BOC protecting group, is usually employed to protect the N^{ϵ}-amino-group of lysine[16,29-31,33,44,47,49,50,63,76,87,88,102,124,127,128,129,144,145,148,151,153,155,156,159,161,172,176,182,188,194,196,197,206,220,221,231,253,275,280,282]. There are, however, data demonstrating the partial elimination of the N^{ϵ}-Z group when the N^{α}-BOC group is removed. In this respect the *p*-Br-Z protecting group is more reliable[213]. The tosyl group[40,92,114,117,179,194,203,262], which can be removed by treatment with sodium in liquid ammonia, and also the TMA group[24,36,37,45,51,296], which is eliminated by treatment with 1 *N* piperidine solution, are sometimes used to protect the lysine side chain.

Methionine. Methionine is usually used without protecting the functional group in the side chain, but special protecting agents must be used in the stage involving the separation of the peptide from the carrier (which is not always successful). For this reason BOC-Met(O)-OH is sometimes employed to synthesise methionine-containing peptides[124,128,145].

Ornithine. As in the case of lysine, the amino-group of ornithine in the side chain is protected by the benzyloxycarbonyl[275,284,285] or tosyl[93] group; MZ-Orn(p-NO_2-Z)-OH has also been used[149].

Serine and threonine. Simple benzyl esters[21,24,33,36-38,51,52,76,92,94,104,112,124,128,129,132,143-145,148,151,153,156,159,161,168,172,174,176,186-188,193,194,196-198,200,206,212,213,215,216,220,223,241,253,262,268,276-287,282], which are cleaved under the conditions of the acid treatment of the peptidyl polymers, are normally used to protect the hydroxy-groups of serine and threonine. When activated esters are used in the peptide formation stage, serine and threonine are introduced into the peptide chain without protecting the hydroxyl. The employment of Weygand's protecting group (1-benzyloxycarbonylamino-2,2,2-trifluoroethyl) for the serine and threonine side chains has been reported[38].

Tyrosine. The tyrosine hydroxy-group is usually protected in the form of the benzyl ether[20,24,32,33,36,39-41,43,44,47,48,51,57,59,63,74,76,80,92,104,110,112,114,120,121,124,126,128,137-140,142,143-145,155,156,159,167,170,172,174,175,181,186,188,193,197,200,203,205-208,210,212,213,233,235,237,238,240,241,243,247,248,262,263,275-278,282]. The latter is readily cleaved by hydrogen bromide in trifluoroacetic acid or by hydrogenation, but, in contrast to the analogous serine and threonine derivatives, it is relatively stable in anhydrous hydrogen fluoride, which is not very convenient. It is suggested that the *p*-methoxybenzyl and *m*-bromobenzyl groups are more suitable in this respect[213].

Cysteine. In most cases the benzyl group, which can be removed from the cysteine residue only with sodium in liquid ammonia under rigorously controlled conditions (owing to the possibility of side reactions), is used to protect the SH functional group of cysteine[33,39,41,43,44,48,70,71,74,76,79,81,104,107,110,112,128,129,131,138,143,155,167,170,172,174,184,194,196,203,236-238,247,248,255].

The employment of anhydrous hydrogen fluoride can also be made difficult by N → S acyl migration. It has been suggested that *S*-*p*-methoxybenzylcysteine be used to prevent this[69,81,145,151,220,282].

Sometimes the SH group of cysteine is protected with the trityl[15,81] and benzyloxycarbonyl[235] groups, but at the present time two approaches are of greatest interest for the synthesis of crysteine peptides. These are in the first place the employment of different protecting alkylthio-groups (for example, the ethylthio-group), proposed by Weber and coworkers[20,32,57,150]. These groups are removed by sulphitolysis. The second approach to the solution of the problem is based on the suggestion of Lunkenheimer and Zahn[61,111] that bis-BOC-cysteine be used for the peptide synthesis, which eliminates the need for special protection of the SH group. Both approaches still require further investigation, like the problem of the protection of the SH group as a whole.

The studies of Zahn and coworkers[81] and of Weber and coworkers[144,150] have been devoted to these problems.

VI. METHODS FOR THE FORMATION OF THE PEPTIDE BOND

The peptide formation stage is of key importance in peptide synthesis, which is particularly true of the solid-phase method. The absence of intermediate stages involving the purification of the peptide synthesised necessitates the attainment of 100% yield in this stage.

DCC remains the most common condensing agent (Table 3). All the protein aminoacids (except asparagine and glutamine) can be successfully introduced with the aid of this agent into the peptide chain joined to the polymeric carrier. Difficulties are sometimes encountered in the introduction of valine and isoleucine residues into the peptide chain[167] owing to their steric structure. The structure of the polymeric carrier also has a definite influence on the degree of the peptide formation reaction[199].

The nature of the solvent is likewise very important; it must be of relatively low polarity. Therefore methylene chloride, sometimes with small amounts of added DMF, is usually employed in the condensation stage. Under these conditions, a 2.5-3-fold excess of the reactants is used, the reaction being carried out in the course of 2-4 h with stirring in a minimal volume of the solvent. Sometimes the condensation with DCC is performed in other organic solvents, in particular in chloroform[101,103,160,250] or THF.[30,31,49,50,87] The method of activated esters has been frequently attempted in the solid-phase synthesis, but without success. Thus Bodanszky and Sheehan[246,254] investigated the employment of *p*-nitrophenyl esters of aminoacids. However, despite a number of advantages compared with the carbodi-imide method, this procedure is as a whole more laborious, since it requires a longer

condensation time and the preliminary synthesis of amino-acid derivatives. Nevertheless many important peptides, including the insulin A-chain and its analogues, have been obtained using *p*-nitrophenyl esters[333,334]. Beyerman et al.[335] investigated the catalytic effect of 1,2,4-triazole when activated esters are used. This approach was employed also by a number of other investigators[116,117,161,215,216], despite the claim of Ragnarsson et al.[136] that 1,2,4-triazole has no catalytic effect.

Table 3. Methods for peptide formation in solid phase synthesis.

Method	Condensation conditions	References
Dicyclohexylcarbodi-imide	CH_2Cl_2, 25°C, 2-4 h	17,19,21,24,25,28,29,32—48,51,53—55,57,59—61,63,65,69—71,73,74,76—83,85,86,88—94,96,97,99,104,107,108,110,112,114—118,120—124,126—129,131,132,135,137—146,148,149,153—157,159,161,163,164,166,167,169,171,172,174,175,177—179,182—184,186,188,190—193,196—201,205—207,209—216,218,220,222,223,225,227,233,235,236,238,240,247—249,253,255—257,259—263,268,269,272,273,275—277,280—282,286,289,296,297,299—301,303,304,312,313
	CH_2Cl_2-DMF, 25°, 2-4 h	97,111,113,244
	DMF, 25°, 12-14 h	16,95,96,100,102,105[a],119,127,147,231[b],245,278,308
	$CHCl_3$, 25°, 2 h	101,103,160,250[c]
	THF, 20° (before swelling), 20° (12 h)	30,31,49,50,87
Activated *p*-nitro-phenylesters	DMF, 25°, 8-24 h	54,84,107,118,127,156,159,167,172,180,235,300,301,308[d],317,318
	with 1,2,4-triazole in DMF, 25°, 12-24 h	116,117,136,161,203[e],215,216,255
N-hydroxysuccinimide esters		44,70,106,107,192,317,318
	with 1,2,4-triazole	116
	N-hydroxysuccinimide + DCHA in DMF, 25°, 8-12 h	78,117,127,242,284,285
Pentachlorophenylesters	DMF, 25°, 12 h	52,56,95,100,102
	with *N*-methylmorpholine in DMF, 25°, 20 h	226
Trichlorophenylesters	DMF-CH_2Cl_2	67,69,111
	with 1,2,4-triazole in DMF, 25°, 20-65 h	157
	with 2,6-lutidine in DMF, 25°, 24 h	271
2-Pyridyl esters	CH_2Cl_2, 25°, 12 h	170
Mixed anhydrides with isobutyl chloro-carbonate	DMF	27,310—312
With *N*-ethoxycarbonyl-2-ethoxy-1,2-dihydro-quinoline	CH_2Cl_2, 25°, 2-12 h	168
Symmetrical anhydrides	CH_2Cl_2, 25°, 2 h	158,207
N-Carboxyanhydrides	DMF, 25°, 24 h	16
	$CHCl_3$, 25°, 1.5 h	309
Water-soluble carbo-di-imide	H_2O	310

[a] 5 h. [b] 72 h. [c] 12 h. [d] $CHCl_3$ instead of DMF. [e] 1-Hydroxybenzotriazole instead of 1,2,4-triazole.

N-Hydroxysuccinimide esters, used for the first time by Shemyakin, Ovchinnikov, and coworkers[305] in combination with a soluble carrier, are being increasingly applied in the peptide formation stage. This method has proved suitable also for insoluble polymers[44,70,106,107,116,192,318]. The esters are frequently obtained directly at the instant of condensation, using *N*-hydroxysuccinimide and DCC.[78,117,127,242,284,285]

Instances where trichloro- and pentachloro-phenyl esters were employed (Table 3), sometimes with added 1,2,4-triazole[157], *N*-methylmorpholine[226], and 2,6-lutidine[271], are also known. The use of 2-pyridyl esters has also been reported[170]. Some of the methods enumerated above have been compared by Bodanszky and Bath[56].

Among other procedures for the formation of the peptide bond, mention should be made of the method of mixed anhydrides with isobutyl chlorocarbonate, which has been used for the synthesis both from the *N*-end[283] and from the *C*-end[27,310-312]. The employment of the mixed anhydride of *N*-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline and a BOC-aminoacid has also been reported[168]. The possibility of employing symmetrical anhydrides of BOC-aminoacids[158,207] and aminoacid *N*-carboxyanhydrides is likewise possible[16]. Admittedly in this case it is still impossible to control exactly the number of combined aminoacid residues, which limits the applicability of this method. The possibility of the interaction of *N*-carboxyanhydrides with *N*-trimethylsilyl derivatives of aminoacids joined to a non-cross-linked polystyrene has been demonstrated[309].

When poly(ethylene glycol) is used in the solid-phase synthesis, the peptide chain may be grown using the water-soluble carbodi-imide[310].

VII. THE PROBLEM OF THE FORMATION OF ERRONEOUS SEQUENCES IN SOLID-PHASE PEPTIDE SYNTHESIS

It is noteworthy that none of the methods of peptide formation discussed above can guarantee 100% condensation. The situation is increasingly complicated with increasing growth of the chain being synthesised. To ensure an adequate degree of condensation, it is necessary to employ an increasing excess of the aminoacids. Thus in the synthesis of the 104-member analogue of the apoprotein of cytochrome c from horse heart, a 30–70-fold excess of BOC-aminoacids was used in the last stages[44,88]. The yields are somewhat improved, but the fundamental difficulties are not eliminated, by repeated condensations[104,112,121,148,169,198,207,209,211,233,259,260]. All this leads to the omission of individual aminoacid residues from the chain. Bayer, Hagenmaier, and coworkers[53,62,86] devoted much attention to the problem of the formation of erroneous sequences associated with the omission of aminoacid residues due to the incomplete occurrence of the deblocking and peptide formation stages. They estimated not only qualitatively but also quantitatively the possible related peptide impurities and suggested a number of methods for detecting such side reactions, in particular methods based on mass spectroscopy and ^{19}F NMR[132,302,312]. Baas et al.[336] actually proposed a special formula for the quantitative estimation of possible impurities, taking into account the yield at each peptide formation stage.

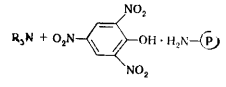
The foregoing considerations obviously demonstrate the importance of increasing the yield in the condensation stage and the necessity for careful and clear-cut monitoring of this stage as well as the stage involving the removal of N^{α}-protecting groups. There are a number of methods for following these processes. The most traditional are quantitative hydrolysis of the peptidyl polymers with subsequent aminoacid analysis[1], the separation of the intermediate peptides from the polymeric carrier and analysis of their homogeneity by various procedures, and spectrophotometric determination of any one reaction

product whose amount is proportional to the yield at the condensation or deblocking stages. For example, it is possible to determine the *p*-nitrophenol formed when one uses *p*-nitrophenyl esters of aminoacids[254,308,333], *o*-nitrophenylsulphenyl chloride, where NPS-aminoacids are employed[284,285], or benzoylacetone when the BMV protecting group is used[250].

The dansylation or dinitrophenylation method is sometimes employed to determine free amino-groups[73,185,215,216,312], but these procedures are laborious, which hinders their wide-scale employment.

The extent of the condensation reaction has also been analysed by determining the chloride ions in the triethylamine hydrochloride formed in the stage involving the neutralisation of the aminopeptidyl polymer (Table 4). However, it is then impossible to establish whether the reduced content of chloride ions is due to the incomplete condensation reaction or whether it is due to the incomplete deblocking of the α-amino-groups.

Table 4. Methods for the determination of free amino-groups in solid-phase peptide synthesis.

Reagent	References
Dansyl chloride or DNP chloride + H_2N–Ⓟ	73,185,215,216,312
Et_3N + HCl · H_2N–Ⓟ	29,38,70,81,90,94,107,108,111,113,142,159,253,284,285
Et_3N + HX · H_2N–Ⓟ (HX from Py.HX) (X = Cl or Br)	35,62,67,78,86,132,151,164,198,199,253
R_3N + 	258–260
2-Hydroxy-1-naphthaldehyde + H_2N–Ⓟ	60,77,84,99,129,191,257
2-Amino-1-naphthaldehyde + H_2N–Ⓟ	223
Ninhydrin + H_2N–Ⓟ	78,134,168,169,200,203,211,226,277,278,280–282,310,312,313
Bromocresol Purple (indicator)	337
Potentiometric titration with $HClO_4$ + AcOH	58,68,195,214

Dorman's method[35], in which the reaction mixture is treated with pyridine hydrohalide after the peptide formation stage in order to form the hydrohalides of the amino-groups which failed to condense, is more convenient in this respect. (The BOC group of the aminoacid introduced remains unaffected under these conditions.) The resulting salt of the aminoacyl polymer is treated with triethylamine, washed, and the filtrates are analysed for chloride ions[62,67,78,86,132,151,164,198,199,253]. Instead of pyridine hydrohalide, one can use, for example, picric acid[258–260]. The picrate formed is decomposed by a suitable amine and the solution is analysed spectrophotometrically for picric acid.

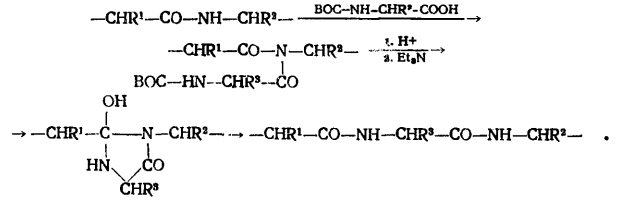
There are a number of other qualitative and quantitative methods whereby free amino-groups can be estimated. These include the use of 2-hydroxy-1-naphthaldehyde[60,77,84,99,129,191,257], 2-amino-1-naphthaldehyde[223], the Bromocresol Purple indicator[337], and also ninhydrin (Table 4).

Some of the methods quoted for estimating free amino-groups have been assessed in special investigations[164,338]. We believe that the procedure which is fastest, most accurate, and, what is most important, susceptible to automation is that proposed by Brunfeldt and coworkers[58,68,195,214], involving the potentiometric titration of the free amino-groups with perchloric acid in the presence of acetic acid.

Together with the problem of determining the extent of the condensation reaction, the problem of the blocking of the amino-groups which failed to enter into the peptide formation reaction merits examination. Thus, after each condensation stage, Merrifield[1] acetylated with acetic anhydride the amino-groups which failed to react, a procedure which is frequently employed also at the present time[62,86,91,92,116,117,139,148,179,197,198,212,215,216,260,281,313]. *N*-Acetylimidazole is also used for this purpose[91,282].

In order to create large differences between the acid–base properties of the required peptide and the side products, it is convenient to employ 3-nitrophthalic[55,177,203,207] and 3-sulphopropionic[131] anhydrides as blocking agents. The derivatives of shorter peptides formed under these conditions contain an additional acid group which facilitates their separation from the desired peptide.

Whereas the problem of monitoring the solid phase synthesis has to some extent been solved, that of increasing the yield of the peptide formation stage still remains entirely open. The duplication of the condensation stages and the employment of a large excess of *N*-protecting aminoacids do not provide a solution. Moreover, a large excess of BOC-aminoacids can lead to an additional number of erroneous sequences owing to the incorporation of the aminoacid residues within the peptide chain being synthesised[46], in accordance with the following mechanism:



It is inconvenient to employ an excess of *N*-acylated aminoacids also for purely economical reasons, since their regeneration is relatively ineffective and requires further development[339].

From this point of view, the most interesting method of economical solid-phase peptide synthesis is that of Esko and Karlsson[77], which is based on the sorption of the BOC-aminoacid by the aminoacyl polymer. The amount of sorbed reactant is sufficient to carry out the peptide formation stage and the excess BOC-aminoacid can be removed from the reaction vessel even before adding the condensing agent. The sorption phenomenon was used by Elliott et al.[218] in the synthesis of bradykinin analogues.

The low efficiency of the condensation reaction is probably related to the fact that, as the chain being synthesised grows in length, there is a possibility that it may roll up on the carrier into a disordered coil, which leads to the screening of the *N*-terminal amino-group. Hydrogen bonds can play a significant role in this process. This hypothesis is confirmed by the fact that the addition of urea, which dissociates hydrogen bonds, to the reaction mixture results in an increase of the rate and degree of deblocking of the BOC groups[134] and also in an increase of the yield in the peptide formation stage[97,148,282].

We believe that one of the possible methods of preventing the coiling of the peptide chain may be the additional (segmental) fixation of the individual sections of the growing peptide chain on the carrier as a result of the interaction with the latter of the functional side groups of the peptide [236].

Nevertheless the problem of the solid-phase synthesis of long peptide chains remains open. At the present stage the most rational procedure in this respect involves a combination of the possibilities of the solid-phase method (the synthesis of short chains) and the classical procedure for joining them together in solution. This approach has been called the solid phase-fragment method.

Furthermore, one should bear in mind the possibility of the block version of peptide synthesis on a carrier. This method was investigated for the first time by Weygand and Ragnarsson [340] and in greater detail by Omenn and Anfinsen [341]. Subsequently block synthesis in different versions was used also in other laboratories [96,102,117,127,147,215,227,231,232,257,297]. However, block condensation on a polymeric carrier involves a number of specific difficulties which so far restrict the application of this method in practice.

VIII. METHODS FOR THE SEPARATION OF PEPTIDES FROM THE POLYMERIC CARRIER

The commonest method for the separation of peptides from the polymeric carrier involves the use of hydrogen bromide in trifluoroacetic acid (Table 5). A number of protecting groups, other than the *S*- and N^{Im}-benzyl, N^{G}-nitro-, tosyl, and *O*-*p*-nitrobenzyl groups, are removed at the same time. A 1:1 mixture of trifluoroacetic acid and methylene chloride has been used recently fairly frequently as a solvent in this process [65,77,128,168,176,179,188,194], which increases the swellability of the polymer.

When the peptide does not contain serine and threonine residues, it is possible to separate it from the carrier by treatment with hydrogen bromide in acetic acid [116,260,284,285,301]. To protect the residues of certain other amino-acids (cysteine, methionine, and tyrosine) from the alkylating action of the benzyl bromide formed in the reaction, protecting agents such as anisole, ethyl methyl sulphide, or methionine are added to the reaction mixture.

Peptides are being increasingly separated from the polymeric carrier by treatment with anhydrous hydrogen fluoride, which was used for this purpose for the first time by Lenard and Robinson [342]. All protecting groups, other than the N^{Im}-benzyl group, are also removed at the same time.

Among other acid agents, one must mention the use of a 50% solution of trifluoroacetic acid in methylene chloride and a solution of boron trifluoride in ether, which are used in special cases (Table 5). The employment of hydrogen bromide in trifluoroacetic acid for a long period (more than 1h) can lead to partial degradation of the peptide, particularly when the chain contains proline residues [116,343,344].

Alkaline agents, for example a solution of sodium hydroxide in aqueous alcohols, are also used in the stage involving the cleavage of the peptidyl polymer [1,30,31,49,50,87]. Water–dioxan or water–alcohol–dioxan solutions of sodium hydroxide are likewise employed [25,171,238,240,241,310–312]. The use of sodium methoxide [312] and sodium thiophenoxide [241,242] has been described.

In order to obtain peptide amides, peptidyl polymers are treated with ammonia under different conditions

Table 5. Methods for the separation of peptides from the polymeric carrier.

Reagent	Reaction conditions	References
Acid reagents		
HBr in CF_3COOH	25°, 60–90 min	17,19,21,27[a],32,34,35,37,38,40,45—47, 52—55,57,59,63,74,76,79—83,86,90,91, 93—95,100,102,106,111,114—117,119,120, 122,126,130,132,135,137,139—143,148, 153,154,158,161,166,170,172,175,176,180, 190,196,201,207,208,210,211,215,216, 218[b],224,225,227,233,235,238,241,253, 256,257,260,286,287,299,301,303,304
HBr in 1:1 CF_3COOH–CH_2Cl_2 mixture	20–25°, 60–90 min	65,77,128,168,176,179,188,194
HBr in AcOH (40–60% soln.)	20–25°, 20–60 min	116,260,284,285,301
HF (liq.)	0°, 30–60 min	24,28,36,37,42,44[c],51,71,77,85,88,98, 113,121,124,127—129,145,154,160,167, 169,176,182,183,186,191,194,197,198, 206,213[c],216,220,221,223,231, 232[c], 273—282,297, 313
50% CF_3COOH in CH_2Cl_2 or $CHCl_3$	25°, 30 min	249,250,263,272
0.03 *N* BF_3 in ether + AcOH–$CHCl_3$	—	250
Alkaline reagents		
1–2 *N* NaOH in ROH (R = Me or Et)	25°, 30–60 min	30,31,40,49,50,87,114,116[d],243,296,315
0.5 *N* NaOH in dioxan	25°, 6 h	240,241
2–4 *N* NaOH in dioxan	20–25°, ~1 h	238,261
2 *N* NaOH in dioxan–ethanol mixture	—	25,171
Aqueous 0.05 *N* NaOH	—	310—312
1 M MeONa in MeOH	—	312
~10% PhSNa in DMF	20–25°, 5–10 h	241,242
Ammonolysis		
Sat. NH_3 in ROH (R = Me or Et)	0–4°, 12–24 h	29,39,43,48,69,71,73[e],104[f],112[f],123[g], 138,144,146[h],147h,155[f],176,178,184, 194,240,241,244,245,248,255
NH_3(liq.)	—	29
NH_3(liq.) in DMF	~20°, 5–10 days in sealed tube	156,159,174,205,209,261
Sat. NH_3 in 1:1 DMF–ROH mixture (R = Me or Et)	~20°, 24–72 h	41,105,107,110,192,193,200[i]
$MeNH_2$ or Me_2NH in MeOH	0–4°, 20–24 h	203,247
Hydrazinolysis		
N_2H_4 or $N_2H_4.H_2O$ in ROH (R = Me or Et)	20–25°, 3–15 h	42,118[j],240,241
N_2H_4 or $N_2H_4.H_2O$ in DMF	20–25°, 1–3 days	118,126,149,212,221
Transesterification		
MeOH–Et_3N or other tertiary amine	20–25°, 16–48 h	18,64[k],132,157,163,170,177,222,241,255
MeOH–Et_3N or other tertiary amine in DMF	~20°, 18–48 h	92[l],107,159
MeOH–anion exchanger	20–25°, 2 h	33,64

[a] 3–6 min. [b] At 5°C. [c] 1.5 h. [d] 1% NaOH. [e] Sat. at −20°, 48 h at 5°C. [f] 2.5 h at −10°C, 18 h at 22°C. [g] 70 h. [h] Sat. at 0°C, 48 h at 20°C. [i] 20°, 4:1 dioxan–MeOH mixture. [j] 48 h. [k] MeOH, EtOH, i-PrOH + various tertiary amines. [l] 22 h at 42°C.

(Table 5). The possibility of interchain aminolysis, which may lead to the occurrence of erroneous sequences, has been reported [227]. Intrachain aminolysis is sometimes also observed, particularly in the dipeptide stage, with formation of dioxopiperazines. This process is facilitated when the *C*-terminal aminoacid is proline or an *N*-methylated aminoacid [202,214,233,259,260].

Hydrazine or hydrazine hydrate is frequently used to separate the peptide from the carrier, particularly in the synthesis of fragments for subsequent azide block condensation in solution (Table 5).

The transesterification method in the presence of tertiary amines or a strongly basic anion-exchange resin has been applied quite recently in the stage involving the cleavage of the peptidyl polymer (Table 5). In this connection there is a risk of partial loss of the peptide from the polymeric carrier when the peptidyl polymer is washed with alcohol after the neutralisation stage [64] and also of the conversion of ω-benzyl esters into ethyl or methyl esters [345].

A comparative assessment of the various methods for the separation of peptides from the polymeric carrier has been carried out [346] and the effect of various solvents on the extent of separation of the peptide has been investigated [98].

Hydrogen bromide in trifluoroacetic acid in the case of a polymer of the alkyloxycarbonyl chloride type [287] and alkaline agents or a 36% solution of hydrogen bromide in acetic acid in the case of a polymer treated with sulphonyl chloride [289] are used to separate peptides attached to the carrier via the *N*-terminal amino-group.

Peptides joined to the carrier via a side chain amino-group are separated under similar conditions [284-286].

As already mentioned in Section II, there are many carriers whereby the peptidyl polymer can be converted at the end of the synthesis into an activated polymeric ester [268-271]. This ester can react with any amino-component, for example with the ester of the *C*-terminal aminoacid [268] or with the deblocked α-amino-group of the peptide synthesised (cyclisation on the carrier) [269]. A similar situation arises also when the hydrazides and 4-carboxyphenylhydrazides are used in the stage involving the formation of the aminoacyl polymer [108]. The above derivatives can be activated also at the end of the synthesis.

IX. AUTOMATION OF SOLID PHASE PEPTIDE SYNTHESIS

The absence of non-standard operations in the solid-phase synthesis makes it possible to mechanise and automate the entire process. The first automatic synthesisers were reported as early as 1965–1966. [347,348] A discussion of the design characteristics of such automatic apparatus can probably serve as the subject of a separate review and therefore we shall confine ourselves here to the examination of the principal trends in the construction of apparatus of this kind.

An interesting version of an automatic synthesiser with a perforated tape programming unit was proposed by Brunfeldt and coworkers [349-351], who also suggested a special apparatus whereby one can monitor automatically the synthesis by potentiometric titration [68,214]. A number of studies have been made on the development and improvement of individual units of the automatic device. Thus, a fundamentally new design for the reaction vessel was developed by Birr and Lechinger [166,352]. They made the reactor in the form of a rotor with porous walls, which made it possible to separate the solvent from the carrier by centrifugal filtration. The systems for the metering and supply of solutions, the methods of stirring the reaction components in the vessel, etc. are also being improved [211,219,353-356].

It is still difficult to specify the optimal version of the automatic synthesiser. However, it is already clear that such apparatus will become available to many investigators in the immediate future.

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Summarising the foregoing one can conclude that solid-phase peptide synthesis is in a state of intense development. While having many important advantages over classical methods of synthesis, it is not free from disadvantages which limit its practical applications. In assessing its present state and the prospects for its development, both undue enthusiasm and excessive skepticism would be inappropriate. A sorber, critical approach to this problem is particularly necessary. However, the data examined above show that many imperfections of the solid-phase method are typical growing pains, which are normally cured eventually. This is shown particularly by the recent publications on the improvement of the conditions for peptide formation [357], on the development of new protecting groups for trifunctional aminoacid residues [358], and on the application of modified polymeric carriers [359]. The methods for the addition of the first aminoacid to the polymeric carrier are also being improved [360,361] and the solid-phase-fragment method of synthesising peptides is being successfully developed [362].

The above trends have been reflected also in certain very recent publications [363-376] which appeared during the preparation of this review for the press.

All this leads to the hope that the existing versions of solid-phase peptide synthesis will be rapidly improved and that the serious disadvantages from which the method still suffers will be overcome.

On the whole, the solid-phase method can be regarded as an extremely promising procedure for peptide synthesis.

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Aminoalkyl Organophosphorus Compounds

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Data on the methods of preparation of aminoalkyl compounds of phosphorus (by transformation of functional groups and by aminoalkylation of tervalent phosphorus compounds) and their physical and chemical properties are presented and the practical applications of substances of this type are briefly described.
The bibliography includes 528 references.

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I. INTRODUCTION

Aminoalkyl organophosphorus compounds are used as complex-forming agents with chelating properties, extractants, herbicides, insecticides, wetting agents, pharmaceutical preparations, ion exchangers, etc. A number of novel methods have now been proposed for their synthesis. However, there are no reviews dealing with compounds of this class either in Soviet or foreign literature. These considerations and also the potential practical and theoretical value of these compounds led to the publication of this review.

II. METHODS OF SYNTHESIS

A wide variety of numerous methods of synthesis have been proposed for amino-substituted organophosphorus compounds, some of which are simple and can be used to prepare such compounds in large amounts. The methods of synthesis can be usefully divided into two groups in terms of the starting materials and the mode of introduction of the amino-group. The first group includes methods analogous to those used for the introduction of the amino-group into any organic compounds. They are based on the transformation of various functional groups in organophosphorus compounds into amino-groups, these reactions are classified as amination of organophosphorus compounds without the formation of new phosphorus–carbon bonds.

The second group includes methods specific to organophosphorus compounds, leading to the formation of phosphorus–carbon bonds. These are classified as aminoalkylation of phosphorus compounds with formation of phosphorus–carbon bonds.

1. Amination of Organophosphorus Compounds without the Formation of New Phosphorus–Carbon bonds

The method of conversion of carboxy- and carbonyl groups into the amino-group (the Curtius, Hofmann, Lossen, and Beckmann reactions) has been frequently used to synthesise amino-substituted organophosphorus compounds. By treating phosphonocarboxylic acid esters in succession with hydrazine and nitrous acid, one obtains azides, which are converted into aminophosphonic acids after the Curtius rearrangement, alcoholysis, and hydrolysis [1,2]:

$$\begin{aligned} &R{-}\underset{\underset{COOEt}{|}}{CH}{-}P(O)(OEt)_2 \xrightarrow{N_2H_4} R{-}\underset{\underset{CONHNH_2}{|}}{CH}{-}P(O)(OEt)_2 \xrightarrow{HNO_2} \\ &\rightarrow R{-}\underset{\underset{CON_3}{|}}{CH}{-}P(O)(OEt)_2 \xrightarrow{H_2O,H^+} R{-}\underset{\underset{NCO}{|}}{CH}{-}P(O)(OEt)_2 \xrightarrow{EtOH} \\ &\rightarrow R{-}\underset{\underset{NHCOOEt}{|}}{CH}{-}P(O)(OEt)_2 \xrightarrow{HCl,H_2O} R{-}\underset{\underset{NH_2}{|}}{CH}{-}PO_3H_2 , \end{aligned} \quad (1)$$

where R = H, Me, $PhCH_2$, or $Me(CH_2)n$ and n = 9–15. The yields of the desired products in this procedure are 31–83%. [1-4]

The Schmidt rearrangement, which is of a similar type, has been used to synthesise ω-aminodecylphosphonic acid [5]:

$$HO_2C(CH_2)_{10}PO_3H_2 \xrightarrow{HN_3} H_2N(CH_2)_{10}PO_3H_2 + CO_2 + N_2 . \quad (2)$$

The synthesis of diethyl α-aminobenzylphosphonate by the Hofmann degradation of α-(*OO*-diethylphosphono)phenylacetamide has been described [6]:

$$\underset{\underset{CONH_2}{|}}{PhCHP}(O)(OEt)_2 \xrightarrow{NaBrO} \underset{\underset{NH_2}{|}}{PhCHP}(O)(OEt)_2 . \quad (3)$$

This method is applicable also to the synthesis of β-aminoalkylphosphonates and phosphonic acids [7,8]. For example, 2-aminoethylphosphonic acid has been obtained by this method in 71% yield.

NN'-Bisdiphenylphosphinylmethylurea and *N*-diphenylphosphinylmethylurethane were obtained by the Lossen reaction, which has a mechanism similar to those described above, in 20 and 29% yields respectively [9]:

$$\begin{aligned} &Ph_2P(O)CH_2C(O)NHOH \xrightarrow{(EtO)_3CH} Ph_2P(O)CH_2NCO \rightarrow \\ &\xrightarrow{EtOH,H_2O} [Ph_2P(O)CH_2NH]_2CO + Ph_2P(O)CH_2NHCOOEt . \end{aligned} \quad (4)$$

The Beckmann rearrangement has been used to synthesise *N*-acyl-$\alpha\alpha$-dimethyl-β-aminoethyldiphenylphosphine oxides [10,11]:

$$R{-}\underset{\underset{NOH}{\diagdown}}{C}{-}CH_2CMeP(O)Ph_2 \xrightarrow{\text{polyphosphoric acid or } PCl_5} R{-}CONHCH_2CMe_2P(O)Ph_2 , \quad (5)$$

where R = Me, or $Ph_2P(O)CMe_2CH_2$.

Other methods of synthesis of the substances under consideration are based on the reduction of nitrogen-containing organic compounds of phosphorus. Thus α-aminobenzylphosphonic acid has been obtained[12,13] in yields up to 50% by the reduction of the *p*-nitrophenylhydrazone of diethyl benzoylphosphonate with sodium sulphide or, better, with aluminium amalgam and subsequent hydrolysis:

$$p\text{-}NO_2C_6H_4NH-N=\underset{\underset{Ph}{|}}{C}-P(O)(OEt)_2 \xrightarrow[2)\ HCl,H_2O]{1)\ Na_2S\ or\ Al/Hg} H_2NCHPO_3H_2 \cdot \quad (6)$$
$$\qquad\qquad\qquad

have been introduced into the reaction with potassium phthalimide in dimethylformamide:

$$\longrightarrow (H_2NCH_2)_nP(O)Ph_{3-n}\cdot \qquad (13)$$

(n = 2, 3; X = Cl; n = 1, X = OTs)

The corresponding phthalimidomethylphosphine oxides, which are formed in 46–81% yields, can be readily converted by treatment with hydrazine into aminomethylphosphine oxides in 70–95%.

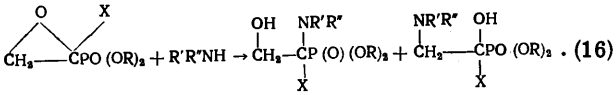
Phosphonoethylation of the sodium derivative of diethyl β-acetamidomalonate led after hydrolysis to γ-amino-γ-carboxypropylphosphonic acid in 46% yield [1]:

$$BrCH_2CH_2P(O)(OEt)_2 + Na^+C^-(COOEt)_2NHCOMe \rightarrow$$
$$\rightarrow (EtO)_2P(O)CH_2CH_2C(NHCOMe)(COOEt)_2 \xrightarrow{H^+,H_2O} H_2O_3PCH_2CH_2CH(CO_2H)NH_2 . \qquad (14)$$

The addition of amines to vinylphosphonates constitutes a specific method for the synthesis of β-aminoalkylphosphonates [57,61,63,74–79]. Thus the corresponding diethyl β-aminoethylphosphonates have been obtained in 53–83% yields by the reaction of diethyl vinylphosphonate with a number of amines in the presence of sodium ethoxide as the catalyst or in its absence on heating [74,76]:

$$CH_2{=}CH{-}P(O)(OEt)_2 \xrightarrow{HNR_2} R_2NCH_2CH_2P(O)(OEt)_2 , \qquad (15)$$

where R = H or Me and $R_2 = (CH_2)_2$ or $(CH_2)_5$. The esters of vinylphosphonothioic acid [80], the amides of vinylphosphonic and vinylphosphonothioic acids [81], acid esters of vinylphosphonous acid, vinylphosphonites [82], vinylphosphinates, vinylphosphines [82–84], vinylphosphine oxides [83–86], and trialkyl(aryl)vinylphosphonium salts [87–89] have also been used in this reaction. In all cases, the amino-group adds to the β-carbon atom of the vinyl group and an increase of the electron-donating properties of the substituents at the phosphorous atom significantly reduces the rate of reaction. The addition of lithium amides to diphenylvinyl- and diphenylallyl-phosphines, 1-phenylphosphorin-3-ene and 3,4-dimethyl-1-phenyl-3-phospholene also leads after hydrolysis to β-aminoalkylphosphines [90]. Epoxyethylphosphonates and the corresponding diphosphonates readily react with amines to form mixtures of 1-amino-2-hydroxy- and 2-amino-1-hydroxy-isomers [91,92]:



(X=H, P(O)(OR)$_2$)

Phosphonates with an active methylene group readily add to azomethines in the presence of acid or basic catalysts with formation of β-aminoalkylphosphonates [93–98]. The yields obtained by this method [93,94], which resembles the first stage of the addition of olefins to the P–O group, amount to 32–88%:

$$RCH_2P(O)(OR')_2 + PhCH{=}NAr \xrightarrow{R_2NNa} ArNHCH(Ph)CH(R)P(O)(OR')_2 . \qquad (17)$$

(R=Ph, COOEt CN; R'=Et, *i*-Pr; Ar=Ph, C_6H_4Cl-*p*,*m*, C_6H_4OMe-*p*, *m*)

Diphenylbenzylphosphine oxide reacts similarly with Schiff bases [99]. Alkylation of benzylphosphonate carbanions with dialkyl-2-chloroethylamines yielded the corresponding α-(γ'-aminopropyl)-α-phenylphosphonates [100]:

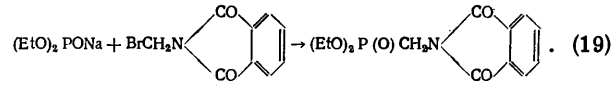
$$PhCH_2P(O)(OEt)_2 \xrightarrow[2.\ R_2N(CH_2)_2Cl]{1.\ NaNH_2} PhCH(C_2H_4NR_2)P(O)(OEt)_2 . \qquad (18)$$

2. Aminoalkylation of Phosphorus Compounds with Formation of Phosphorus–Carbon Bonds

A common feature of this group of methods for the formation of aminoalkyl organophosphorus compounds is the employment of phosphorus(III) compounds, including tautomeric P–H acids, as one of the reactants. The mechanisms of these reactions probably resemble those of Michaelis–Becker and Arbuzov reactions and the addition of phosphorus(III) compounds to systems with multiple bonds, which are widely used in phosphorus chemistry.

The Michaelis–Becker and Arbuzov Reactions

The reactions of dialkyl phosphites and sodium or potassium phosphites with ω-halogenoalkylamines and the corresponding amides proceed via the usual Michaelis–Becker mechanism and lead to the corresponding ω-aminoalkylphosphonates [5,55,101–105]. Thus diethyl phthalimidomethylphosphonate was obtained in 40% yield by the reaction of sodium diethyl phosphite with *N*-bromomethylphthalimide [101]:

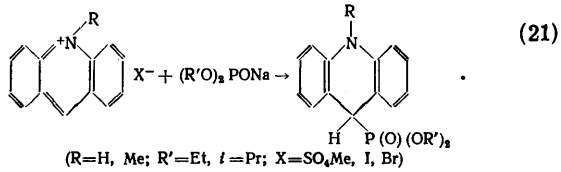


The more reactive α-chloroalkylamines can react directly with dialkyl phosphites to form the hydrochlorides of aminophosphonates in 47–95% yields [102,106]:

$$R_2NCH(R')Cl + (R''O)_2PHO \rightarrow R_2NCH(R)P(O)(OR'')_2 \cdot HCl , \qquad (20)$$

where $R_2 = (CH_2)_4$ or $(CH_2)_5$, R' = H, Et, i-Pr, or $CONC_5H_{10}$, and R'' = Me or Et.

The reaction of diaryl phosphites with diphenylbromoethyl isocyanate in the presence of triethylamine led to the formation of diaryl isocyanatodiphenylmethylphosphonates [107] in 32–88% yields. Sodium dialkyl phosphites readily react with acridinium salts to form dihydroacridylphosphonate esters [108] (yield 63–68%):



(R=H, Me; R'=Et, *i*=Pr; X=SO_4Me, I, Br)

The reaction of lithium, potassium, sodium, and magnesium phosphides with ω-chloroalkylamines has been proposed as a general method for the synthesis of ω-aminoalkylphosphines [109–116]. 2-Diethylaminoethyldialkyl(phenyl)phosphines have been obtained in this way in 40–65% yields [110]:

$$Et_2NCH_2CH_2Br + MPR_2 \rightarrow Et_2NCH_2CH_2PR_2 \cdot$$
$$(M=Li, K;\ R=Et, Ph, C_6H_{11}\text{-cyclo.}) \qquad (22)$$

The Arbuzov reaction is widely used for the synthesis of aminoalkyl organophosphorus compounds. Triethyl phosphite readily reacts with *N*-chloromethylpiperidine to form piperidinomethylphosphonate in 52% yield [117]:

$$(EtO)_3P + ClCH_2NC_5H_{10} \rightarrow (EtO)_2P(O)CH_2NC_5H_{10} + EtCl . \qquad (23)$$

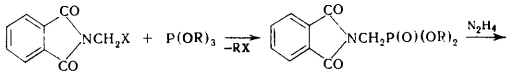
Aminoalkylation of neutral phosphites by halogenoalkyl amines has been used successfully to synthesise aminoalkylphosphonates with various functional groups [103,104,106,118–123]: aminomethyltriphosphonates were obtained in

71–77% yield by the reaction of trichloromethylamines with triethyl phosphite in chloroform at −40°C:[121]

$$3\,(EtO)_3P + R_2NCCl_3 \xrightarrow{CHCl_3,\,-40^\circ} [(EtO)_2P(O)]_3CNR_2 + 3\,EtCl \qquad (24)$$

where R = Me and $R_2 = (CH_2)_5$.

The reaction of *N*-halogenomethylphthalimides with trialkyl phosphites gave rise to the formation of phthalimidomethylphosphonates in 82–94% yields[55,124–128]. Treatment of the latter with hydrazine leads to aminomethylphosphonates:



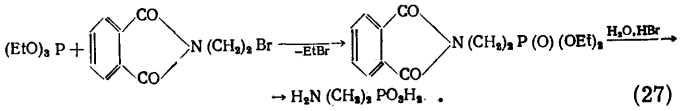
$$\longrightarrow H_2NCH_2P(O)(OR)_2\,. \qquad (25)$$

(X = Cl, Br; R = Me, Et)

When dialkyl phosphonites and alkyl phosphinites are used instead of trialkyl phosphites, the products are aminoalkylphosphinic acids and aminoalkylphosphine oxides[129–131]. The reactions of chloromethyl isocyanate with trialkyl phosphites and alkyl phosphinites takes place similarly. Isocyanatomethylphosphonates and isocyanatomethylphosphine oxides were obtained by this procedure in 7–40% yields[132]:

$$R_2P(OR') + ClCH_2NCO \rightarrow R_2P(O)CH_2NCO + R'Cl\,. \qquad (26)$$
(R=OR', Pr)

Dialkyl phosphorochloridites and phosphorofluoridites and alkyl phosphorodichloridites and phosphorodifluoridites also react with chloromethyl isocyanate[133–135]. When di- and tri-chloromethyl isocyanates instead of chloromethyl isocyanate are used in the reaction with phosphites, products phosphorylated to different extents are obtained, depending on the ratio and reactivities of the reactants[135–138]. The method has been used also to synthesise ω-aminoalkylphosphonates[12,55,105,139–141]: 2-aminoethylphosphonic acid has been synthesised in 50% yield by the reaction of *N*-(2-bromoethyl)phthalimide with triethyl phosphite and subsequent hydrolysis[12]:

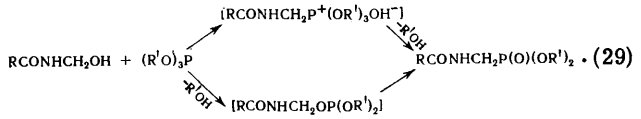


$$\rightarrow H_2N(CH_2)_2PO_3H_2\,. \qquad (27)$$

Apart from halogenoalkylamines and the corresponding amides, *N*-trimethylammoniummethylformamide[142], *N*-acetoxymethylamides[143], and the corresponding amines[144] have also been introduced into this reaction. Trialkyl phosphites[142,143], triphenyl phosphite, and phosphorous hexaethyltriamide[144] have been used as the phosphorus-containing components. In the reactions with triphenyl phosphite and phosphorous hexaethyltriamide the desired products were isolated in 54 and 73% yields respectively:

$$PX_3 + MeCOOCH_2NEt_2 \rightarrow [X_3P^+CH_2NEtMeCOO^-] \rightleftarrows [X_3P^+CH_2NEt_2(OCOMe)\,X^-] \rightarrow$$
$$\rightarrow X_3P(O)CH_2NEt_2 + MeCOX\,. \qquad (28)$$
(X=OPh, NEt_2)

N-Hydroxymethylamides are also capable of aminoalkylating trialkyl phosphites at 100–160°C with a 30–59% yield of the desired products[145,146]. It is suggested that under these conditions the phosphite is either alkylated directly or there is a preliminary transesterification and a subsequent Arbuzov rearrangement[145]:



(R = Me, Ph; R' = Me, Et, Pr, Bu)

A mixture of an amide and paraformaldehyde can be introduced into the reaction instead of *N*-hydroxymethylamides[147]. Aminophosphonates have been obtained under the same conditions from secondary amines, aldehydes, and trialkyl phosphites in 21–94% yields[147–150]:

$$RR'NH + R''CHO + (R'''O)_3P \rightarrow RR'NCH(R'')P(O)(OR''')_2 + R'''OH\,, \qquad (30)$$

where R and R' = Me or Et, RR' = $(CH_2)_5$, R'' = H or Ph, and R''' = Et, Pr, or Bu.

In the presence of acetic acid at 100–160°C trialkyl phosphites are capable of being aminomethylated by aminoacetals of formaldehyde and by diethylaminoacetonitrile[151,152]:

$$(RO)_3P + R'R''NCH_2X \xrightarrow{MeCOOH} R'R''NCH_2P(O)(OEt)_2 + MeCOOEt + HX\,. \qquad (31)$$
(X=CN, OR; R=Me, Et, Pr, Bu; R', R''=Me, Et, Ph)

The yields of aminophosphonates are 50–65%. The authors believe[151,153] that the role of acetic acid reduces either to an increase of the polarity of the medium, which promotes the ionisation of the aminoalkylating agent, or to transesterification of the latter and a subsequent reaction of type (28).

N-Aminomethyl- and *N*-alkoxymethyl-amides of carboxylic acids are also capable of reacting under these conditions with trialkyl phosphites to form carbamoylmethylphosphonates in 52–85% yields[153,154].

N-Aminomethylamides of carboxylic acids containing a hydrogen atom at the amide nitrogen atom readily react with trialkyl phosphites also in the absence of acetic acid, forming acetamidomethylphosphonates[154] (50–70%); a secondary amine and an alcohol have been isolated as side products:

$$RCONHCH_2NR'_2 + P(OR'')_3 \rightarrow RCONHCH_2P(O)(OR'')_2 + HNR'_2 + R''OH + R''NR'_2\,, \qquad (32)$$

where R = Me, Ph, or $CH_2{=}C(CH_3)$–, R' = Me or Et, and R'' = Et or Bu.

The authors suggest that this is caused by acid catalysis due to the imidine form (I).

In the presence of acid agents, trialkyl phosphites are capable of being aminoalkylated by Schiff bases[155,156]. Thus trialkyl phosphites react with benzylideneaniline in the presence of phenol at 100–130°C, giving rise to 20–30% yields of aminophosphonates[155]:

$$(RO)_3P + ArN{=}CHPh \xrightarrow{PhOH} (RO)_2P(O)CH(Ph)NHAr + PhOR\,. \qquad (33)$$
(Ar=Ph, C_6H_4Me-*p*; C_6H_4Cl-*m*; R=Et, Pr).

When aminoacetals are treated with PCl_3, aminoalkylphosphonates are also formed ultimately[157,158]. It is suggested that the reaction proceeds via the formation of α-chloromethylamine and a phosphite[157]:

$$3\,R'_2NCH_2OR + PCl_3 \rightarrow 3\,R'_2NCH_2Cl + P(OR)_3\,, \qquad (34)$$
$$P(OR)_3 + R'_2NCH_2Cl \rightarrow R'_2NCH_2P(O)(OR)_2 + RCl\,,$$

where R = Et, R' = Et, and $R'_2 = (CH_2)_5$.

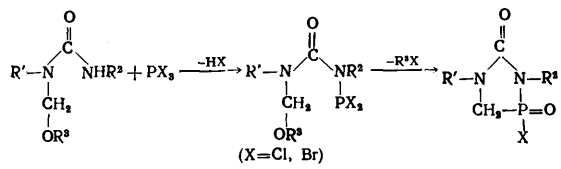
The occurrence of the first stage was demonstrated by the isolation of α-chloromethylamines[117]. Phosphorochloridites[119,159] and chlorophosphines react similarly with aminoacetals[160]. An analogous mechanism probably

operates in the reactions of diaminals and aminoacetals of formaldehyde with mixed anhydrides of diethylphosphorus acid on the one hand and acetic, benzoic, and diethylphosphoric acids on the other and with tetraethyl pyrophosphite [161]:

$$(EtO)_2POY + R_2NCH_2X \rightarrow X(EtO)P(O)CH_2NR_2 + YOEt\ , \qquad (35)$$

where Y = COMe, COPh, $P(OEt)_2$, or $P(O)(OEt)_2$, X = OBu, NMe_2, or NEt_2, R = Me, and $R_2 = (CH_2)_5$. The yields of aminophosphonates in these reactions amount to 43–65%.

1,3-Dialkyl-4-halogeno-2,4-dioxo-1,3,4-diazaphospholans have been obtained in 40–86% yields by the reaction of phosphorus trihalides with *NN'*-dialkylalkoxyalkylureas [162]:



(X=Cl, Br) . (36)

The reaction of *N*-hydroxymethylamides with phosphorus trichloride, which probably proceeds via the formation of the corresponding phosphorochloridite and its rearrangement, leads to amidomethylphosphonic acids after hydrolysis [101,163–167] (yields 20–34%):

$$RCON(R')CH_2OH + PCl_3 \rightarrow [RCON(R')CH_2OPCl_2] \rightarrow$$

$$\rightarrow [RCON(R')CH_2P(O)Cl_2] \xrightarrow{H_2O} RCON(R')CH_2PO_3H_2\ , \qquad (37)$$

where R = Me, $Me(CH_2)n$ (n = 10–16), or β-pyridyl and R' = H, alkyl, or aryl.

The reaction of diethyl phosphorochloridite and chlorodiphenylphosphine with *N*-hydroxymethylamidine, which is similar to those already discussed, leads to amidomethylphosphonates and amidomethylphosphine oxides in yields up to 80% [37,145]:

$$R_2PCl + HOCH_2NHCOR' \xrightarrow{NEt_3} R_2P(O)CH_2NHCOR'\ . \qquad (38)$$

(R=OEt, Ph; R'=Me, Ph)

The reaction of dialkyl phosphorochloridites with 4-(*NN*-diethylamino)but-2-yn-1-ol in the presence of bases proceeds with isomerisation and the formation of dialkyl-(α-*NN*-diethylaminomethyl)allenylphosphonates [168,169]:

$$(RO)_2PCl + HOCH_2C\equiv CCH_2NEt_2 \xrightarrow[-NR_3\cdot HCl]{NR_3} [(RO)_2POCH_2C\equiv CCH_2NEt_2] \rightarrow$$

$$\rightarrow CH_2=C=CP(O)(OR)_2\ . \qquad (39)$$

$$\quad\quad CH_2NEt_2$$

(R=Et, Pr)

The α-aminoalkylation of tertiary phosphines, leading to α-aminoalkylphosphonium salts, can be carried out only when effective α-aminoalkylating agents, such as α-halogenoalkylamines and the corresponding amides [102,170–173] and ureas [174,175], are used:

$$R_2NCH(R')X + R''_3P \rightarrow R_2NCH(R')P^+R''_3X^-\ . \qquad (40)$$

The yields of the α-aminoalkylphosphonium salts are 40–98%.

Reactions of Dialkyl Phosphites and Their Analogues with Amines and Carbonyl Compounds

In 1952 Kabachnik and Medved' [176] and Fields [177] proposed independently a new general method for the synthesis of α-aminophosphonates by the reaction of dialkyl phosphites and aldehydes or ketones† with ammonia (Kabachnik and Medved') and amines (Fields):

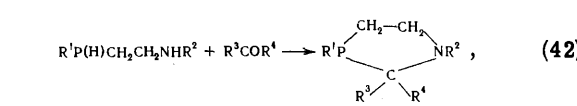
$$(RO)_2PHO + HN\langle + \rangle C=O \rightarrow (RO)_2P(O)\overset{|}{\underset{|}{C}}-N< + H_2O\ . \qquad (41)$$

Aminophosphonates are obtained after only brief heating of the reactants in solvents (water, alcohol) or in their absence. The yields of aminophosphonates vary within wide limits and depend on the structures of the initial reactants. The desired products are isolated from the reaction mixture by distillation in the form of hydrochlorides or picrates.

By varying the amines, aldehydes, ketones, and the phosphorus-containing component, it is possible to obtain by this method a wide variety of α-aminoalkyl phosphorus-containing compounds. The following amines (or ammonia) were introduced into the reaction: ammonia [176,178–189]‡, aliphatic primary and secondary amines [86,177,180,187,190–202], aromatic and heterocyclic amines [177,203–207], alkylenediamines and alkylenepolyamines [78,208–213], and hydroxyalkylamines [214–221].

$$(EtO)_2PHO + CH_2O + NH_3 \rightarrow [(EtO)_2P(O)CH_2]_2NH + [(EtO)_2P(O)CH_2]_3N\ .$$

Aziridine [57] and carboxamides [147] could not be made to undergo this reaction. Formaldehyde [86,214][114 ? (Ed. of Translation)] [177,180,187,190–193,195–197,199–204,209,211,218,219,221] as a 40% aqueous solution or paraformaldehyde, aliphatic and alicyclic aldehydes and ketones [78,177,178,180,181,183,186,188,194,199,206–208,210–213], and aromatic and heterocyclic aldehydes and ketones [176,178,179,183,185,189,190,205,210] have been used as the carbonyl components. Apart from dialkyl or diaryl phosphites [76,176–179,181–184,187–189,194,198,199,203,204,208–214,216–222], other compounds with a phosphorus-hydrogen bond readily enter into the reaction: dialkyl phosphorothioites [186,189], monoalkyl phosphonites [211], dialkyl(aryl)-phosphine oxides [86,180,196,200], dialkylphosphine sulphides [192], hypophosphorus acid [185,193,205–207,223–227]§, and phosphines [71,115,190,195,201,228]. In all cases the reaction proceeds via mechanism (41), i.e. with formation of a product resulting from the substitution of a hydrogen atom at the phosphorus atom by an α-aminoalkyl residue. 2-Aminoethylphosphines with hydrogen atoms at nitrogen and phosphorus readily react with carbonyl compounds to form intramolecular aminoalkylation products—1,3-azaphospholidines [114,115,229,230] (yields 47–91%):



(42)

where R^1 = H, Et, Bu, or Ph, R^2 = H or Et, R^3 and R^4 = H, Me, Et, or Ph, and $R^3R^4 = (CH_2)m$ (n = 4–6) or

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†Kabachnik and Medved' studied this reaction in relation to ketones somewhat later [178].

‡When ammonia, a primary amine, and a sterically unhindered aldehyde are used, products substituted to different extents at the nitrogen atom are obtained, depending on the reactant ratio and the reaction conditions [182,187,209,220].

§The aminoalkylation of hypophosphorous acid with a mixture of an amine and an aldehyde leads to mono- and bis-aminoalkylation products—aminoalkylphosphonic and di(aminoalkyl)phosphinic acids respectively [193,206,223]:

$$H_3PO_2 + CH_2O + R_2NH \rightarrow R_2NCH_2P(O)(H)OH \xrightarrow{R_2NH+CH_2O} (R_2NCH_2)_2POOH\ .$$

R=Me, Et; $R_2 = (CH_2)_5$, $(CH_2)_2O(CH_2)_2$; $R_2N{=}N(CH_2CH_2)_2N$.

$(CH_2)_2O(CH_2)_2$. *o*-Aminophenylphosphines[231], 3-aminopropylphenyl(butyl)phosphine[232-234], and 4-aminobutylphenylphosphines[233] react similarly with aldehydes and ketones.

Compounds containing a phosphorus–phosphorus bond are readily aminoalkylated under these conditions with formation (among other products) of mixtures of organophosphorus compounds with different degrees of aminoalkylation and oxidation of the phosphorus atom[191,197,202,235-238]. Thus the reaction of tetraphenyldiphosphine with formaldehyde and diethylamine yields diethylaminomethyldiphenylphosphine and phosphine oxide together with other products[235,236]:

$$Ph_2P{-}PPh_2 + CH_2O + HNEt_2 \xrightarrow{H_2O} Ph_2PCH_2NEt_2 + Ph_2P(O)CH_2NEt_2 + Ph_2PH + Ph_2PHO . \quad (43)$$

An even more complex mixture of products is formed in the aminoalkylation of white phosphorus[191,202,236]:

$$P_4 + CH_2O + HNR_2 \xrightarrow{H_2O} R_2NCH_2PO_2H_2 + (R_2NCH_2)_2PO_2N + (R_2NCH_2)_3PO + (R_2NCH_2)_2PH + (R_2NCH_2)_3P + (HOCH_2)_2PO_2H + HOCH_2PO_2H_2 , \quad (44)$$

where R = Me, Et, Bu, or cyclo-C_6H_{21} and R_2 = $(CH_2)_4$, $(CH_2)_5$, or $(CH_2)_2O(CH_2)_2$.

Depending on the reactant ratio and the type of amine employed, the main product (trisdialkylaminomethylphosphine oxide) is obtained in yields up to 47%.[191,236] It is believed that the dialkylhydroxymethylamine, formed from formaldehyde and a secondary amine, initially cleaves the phosphorus–phosphorus bond and then aminoalkylates the dissociation products[202,236]:

$$R_2NH + CH_2O \longrightarrow R_2NCH_2OH ,$$

$$Ph_2P{-}PPh_2 + R_2NCH_2OH \longrightarrow \begin{matrix} Ph_2P{-}PPh_2 \\ | \quad\quad | \\ R_2NCH_2{-}O{-}H \end{matrix} \longrightarrow$$

$$\longrightarrow Ph_2POCH_2NR_2 + Ph_2PH , \quad (45)$$

$$Ph_2POCH_2NR_2 \xrightarrow{+H_2O} Ph_2PHO + HOCH_2NR_2 ,$$

$$Ph_2PHO + HOCH_2NR_2 \longrightarrow Ph_2P(O)CH_2NR_2 ,$$

$$Ph_2PH + HOCH_2NR_2 \longrightarrow Ph_2PCH_2NR_2 .$$

The aminoalkylation of phosphorus acid must be considered in connection with the practical importance of aminoalkylphosphonic acids formed by this method in high yields in a single stage and readily isolated from the reaction mixture[239]:

$$H_3PO_3 + H{-}N\!\!<\!\!\!> + CH_2O \xrightarrow{H^+} H_2O_3PCH_2N\!\!<\!\!\!> + H_2O . \quad (46)$$

A significant difference between the method for the aminoalkylation of phosphorous acid and those discussed above is that a satisfactory reaction is achieved only in strongly acid media (pH 1–3). The reaction is carried out with heating to 120–150°C in the course of 1–2 h and goes a most to completion. The yields of the products of exhaustive phosphonomethylation amount to 49–96% when primary amines and polyamines are used[239]. Ammonia (in the form of ammonium salts)[239-241], primary amines[239,242-245], ethanolamine[239,246], glycine[239,247], diethanolamine[239,246], iminodiacetic acid[239,247], alkylenediamines[239,248], polyethyleneimines[245], and other amines[78,250-254] were used in the reaction. Apart from formaldehyde (in the form of the 40% solution), other aldehydes and ketones can be made to react[242-244,250-253,255,256]. A promising method for the aminomethylation of phosphorous acid is its reaction at 100–160°C with aminopolyacetic acids[257-259]. For example, nitrilotri(methylphosphonic) acid was obtained in 93% yield by heating phosphorous acid with nitrilotriacetic acid[259]:

$$N(CH_2COOH)_3 + H_3PO_3 \xrightarrow{160^\circ} N(CH_2PO_3H_2)_3 . \quad (47)$$

In the presence of phosphorus trichloride, the reaction proceeds under milder conditions.

Two views have been expressed about the mechanism of reaction (41), which in many respects resembles the Mannich reaction[260]. One of these is based on a study of the reactions of diethyl phosphite with benzaldehyde and ammonia: it is suggested that in the first stage the dialkylphosphite adds to the carbonyl compound [reaction (48a)] under the influence of the catalyst (ammonia) and then the hydroxy-group in the α-hydroxyalkylphosphonate is substituted by the amino-group[179,180] [reaction (48b)].

$$(RO)_2PHO + R'R''CO \xrightarrow{NH_3} (RO)_2P(O)CR'R''OH , \quad (48a)$$

$$(RO)_2P(O)CR'R''OH + NH_3 \rightarrow (RO)_2P(O)CR'R''NH_2 + H_2O . \quad (48b)$$

This hypothesis was put forward because the main product of the reaction of diethyl phosphite with ammonia and benzaldehyde in the cold is α-hydroxybenzylphosphonate $(EtO)_2P(O)CH(Ph)OH$; the formation of α-aminobenzylphosphonate $(EtO)_2P(O)CH(Ph)NH_2$ is observed only on heating the reaction mixture[179]. Stage (48a) constitutes the addition of dialkyl phosphites to carbonyl compounds in the presence of a base (in the present case ammonia), which has been thoroughly investigated[261]. The possibility of the second stage—the nucleophilic substitution of the hydroxy-group by the amino-group—has been demonstrated by the formation of α-aminobenzylphosphonate on heating α-hydroxybenzylphosphonate with an alcoholic solution of ammonia[179].

The second view is based on the reaction of dialkyl phosphites with formaldehyde and secondary amines; it is suggested that the first stage involves the addition of the amine to formaldehyde with formation of hydroxymethylamine [reaction (49a)] and the subsequent interaction of the latter with the dialkyl phosphite, leading to the dialkylaminomethylphosphonate[177] [reaction (49b)]:

$$R_2NH + CH_2O \rightleftarrows R_2NCH_2OH , \quad (49a)$$

$$(R'O)_2PHO + R_2NCH_2OH \rightarrow (R'O)_2P(O)CH_2NR_2 + H_2O . \quad (49b)$$

This hypothesis arose in view of the absence of the exchange of the hydroxy-group for the dialkylamino-group on heating diethyl hydroxymethylphosphonate with diethylamine[177]. The possibility of stage (49b) was demonstrated by the formation of aminophosphonates in high yields on reaction of dialkyl phosphites with bisaminals and aminoacetals of formaldehyde[177,198]:

$$R_2NCH_2X + (EtO)_2PHO \rightarrow R_2NCH_2P(O)(OEt)_2 + HX . \quad (50)$$
$$(R=Et, i\text{-}Pr, Bu;\ X=OMe, NR_2)$$

Thus on the basis of this mechanism the reaction can probably be regarded as a process of the Michaelis–Becker type in which the amine catalyses the formation of a highly nucleophilic dialkyl phosphite anion and the dissociation of α-hydroxyalkylamines at the C–O bond leads to a stable carbonium–immonium ion[262-264]:

$$R_2N{-}CH_2OH \rightleftarrows [R_2N{-}CH_2^+ \longleftrightarrow R_2N^+{=}CH_2] + OH^- , \quad (51)$$

$$(R'O)_2P(O)H \overset{B}{\rightleftarrows} [(R'O)_2PO]^- + BH^+ ,$$

$$[(R'O)_2PO]^- + R_2N^+{=}CH_2 \rightarrow (R'O)_2P(O)CH_2NR_2 .$$

There are at present no data for the mechanism of the reactions of phosphorous acid with formaldehyde and

amines [reaction (46)] in a highly acid medium. One can only suppose that in this case the aminoalkylating species is the carbonium-immonium ion and the object of electrophilic attack is phosphorous acid [containing phosphorus(III)], the reversible formation of which is promoted by the high acidity of the medium.

In conclusion one should note that, despite the conflict between mechanisms (48) and (49) although there is evidence in support of each), the proposed versions of reaction (41)—amination of the α-hydroxyalkyl organophosphorus compounds [reaction (48)] and aminoalkylation of organophosphorus compounds with a phosphorus–hydrogen bond by aminoacetals and bisaminals [reaction (50)]—are of preparative value. The first version—the amination of α-hydroxyalkylorganophosphorus compounds¶—has been investigated mainly for hydroxymethyl derivatives of phosphines and for hydroxymethylphosphonium salts. The value of this method is due to the availability of such compounds, which obviates the necessity for the employment of the relatively inconvenient phosphines: heating of hydroxymethylphosphines with diethylamine in a sealed tube at 150–160°C for 8 h leads to diethylaminoethylphosphines in 57–88% yields [265]:

$$Pr_nP(CH_2OH)_{3-n} + (3-n)\,Et_2NH \rightarrow Pr_nP(CH_2NEt_2)_{3-n} + (3-n)\,H_2O\,. \quad (52)$$

When tri(hydroxymethyl)phosphine is treated with aniline under the conditions of azeotropic distillation of water, tri-(*N*-phenylaminomethyl)phosphine is formed in 81% yield [266]:

$$P(CH_2OH)_3 + 3\,PhNH_2 \rightarrow P(CH_2NHPh)_3 + 3\,H_2O\,. \quad (53)$$

Acetoxymethylphosphines can be used in the reaction instead of hydroxymethylphosphines. In this case the reaction is carried out in an aqueous or aqueous alcoholic medium in the presence of potassium hydroxide and involves the preliminary hydrolysis of the acetoxymethylphosphines to the corresponding hydroxymethylphosphines [267,268]. An advantage of this method compared with those described above is the ease of the purification of the initial acetoxymethylphosphines, which has a significant influence on the purity of the desired products [267]. The use of hydroxymethylphosphonium salts instead of hydroxymethylphosphines leads to aminomethylphosphines [269,270]. This method is used also to synthesise aminomethylphosphine oxides: diethylaminomethyldiphenylphosphine oxide was obtained in a quantitative yield by heating hydroxymethyldiphenylphosphine oxide with diethylamine [271]:

$$Ph_2P(O)CH_2OH + HNEt_2 \rightarrow Ph_2P(O)CH_2NEt_2 + H_2O\,. \quad (54)$$

There are patent data concerning the condensation of hydroxymethylphosphonium salts and tri(hydroxymethyl)-phosphine oxide with amines to form high-molecular-weight compounds [272–274].

The second version of reaction (41) (aminoalkylation of compounds with a phosphorus–hydrogen bond by bisami als and aminoacetals) has also found applications in the synthesis of a wide variety of aminoalkyl derivatives of phosphorus. The high yields of the desired substances, the absence from the reaction mixture of water which is difficult to remove, and the possibility of employing aminals with different functional groups make this synthetic procedure extremely useful and in many cases the only one possible. Aminophosphonoacetate esters have been obtained in yields of 73–82% from the aminoacetals of glyoxylic acid esters [106]:

$$R_2NCHCOOMe + (EtO)_2PHO \rightarrow (EtO)_2P(O)CHCOOMe + MeOH\,. \quad (55)$$
(OMe; NR$_2$)

(R=Me; R$_2$= (CH$_2$)$_5$)

The reaction of the dimethylacetal of dimethylformamide with diethyl phosphite leads to a 62% yield of aminomethylenediphosphonate [275,276]:

$$Me_2NCH(OMe)_2 + 2\,(EtO)_2PHO \rightarrow [(EtO)_2P(O)]_2CHNMe_2 + 2\,MeOH\,. \quad (56)$$

Cyclic bisaminals and aminoacetals readily react with dialkyl phosphites, forming aminophosphonates containing amino- and hydroxyalkyl substituents at the nitrogen atom [277–280]:

$$(EtO)_2PHO + \begin{array}{c} CH_2-X \\ | \\ CH_2 \\ \diagdown \\ N \\ \diagup \\ R' \end{array} \begin{array}{c} | \\ CHR \end{array} \rightarrow (EtO)_2P(O)CH(R)N(R')CH_2CH_2XH\,. \quad (57)$$

(R=H, Me; R'=H, CH$_2$CH$_2$OH; X=O, NH)

Aminoalkylphosphonamides were obtained by this method from phosphoramidites in 35–79% yields [281–283]:

$$(R_2N)_2PHO + (R'_2N)_2CHR'' \xrightarrow{Na} (R_2N)_2P(O)CH(R'')NR'_2 + R'_2NH\,. \quad (58)$$
(R=Me, Et, Bu; R$_2$= (CH$_2$)$_5$; R'=Me, Et; R''=H, Ph)

Apart from dialkyl phosphites and phosphorodiamidites, hypophosphite esters [284,285], dialkyl(aryl)phosphine oxides [180,286], alkylphosphonous and phosphonothious acids [287], and phosphines [265] react readily with bisaminals and aminoacetals.

The Addition of Compounds with a Phosphorus–hydrogen Bond to Multiple Carbon–nitrogen and Carbon–carbon Bonds

Dialkyl phosphites readily add to aromatic Schiff bases, forming α-aminoalkylphosphonates in 67–91% yields [288,289]:

$$(RO)_2PHO + ArHC{=}NAr' \rightarrow (RO)_2P(O)CH(Ar){-}NHAr'\,. \quad (59)$$

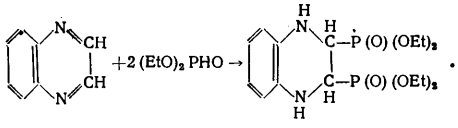
The reaction proceeds slowly even when the reactants are mixed in the cold in the absence of a solvent and is rapid in the presence of catalytic amounts of alkali metal alkoxides [288,289] or acids (HCl, $SnCl_2$) [290–293] in alcohol. When carefully purified reactants are used, the desired products can be obtained in nearly quantitative yields by the reaction without a solvent and without heating [294].

The above method of synthesis is of undoubted interest, although its applications are limited to the formation of *N*-monosubstituted α-aminoalkyl derivatives of phosphorus. Its usefulness is primarily due to the ready availability of the aromatic Schiff bases and the high yields of the desired products.

Under the conditions described above, dialkyl phosphites readily add not only to Schiff bases obtained from aromatic amines, aldehydes, and ketones [288–299] but also to those synthesised from aromatic amines and heterocyclic aldehydes [300–303], from heterocyclic amines and aromatic aldehydes [304,305], from aliphatic amines and diamines and aromatic aldehydes [306–311], and from aliphatic amines and aldehydes [310,312–314]. Certain heterocyclic compounds containing multiple carbon–nitrogen bonds are capable of combining with dialkyl phosphites to form phosphorus-containing heterocycles [315,316]. For example,

¶ This method is probably not general, since in many cases the corresponding α-aminoalkyl compounds could not be obtained by treating hydroxyalkyl organophosphorus derivatives with amines [177,185,196].

the addition of two dialkyl phosphite molecules to quinoxaline in sodium ethoxide leads to 1,4-dihydro-2,3-bis-(diethoxyphosphinyl)quinoxaline in 77% yield[315]:



(60)

Imines containing functional groups at the nitrogen and carbon atoms also readily combine with dialkyl phosphites, forming α-aminoalkyl phosphonates with different functional groups in 23–84% yields[317–320]†:

$$PhN{=}CXY + (RO)_2PHO \rightarrow PhNHC(X)(Y)P(O)(OR)_2 , \quad (61)$$

where X = H, P(O)(OEt)$_2$ or P(O)Ph$_2$ and Y = P(O)(OEt)$_2$ or P(O)Ph$_2$.

The synthesis of optically active α-aminobenzylphosphonic acid by the addition of diethyl phosphite to the Schiff base derived from benzaldehyde and α-phenylethylamine enantiomers has been described. The reaction proceeds with asymmetric induction; subsequent hydrolysis and hydrogenolysis of the addition product resulted in the formation of the enantiomers of α-aminobenzylphosphonic acid[322]‡:

$$PhCHO + PhC^*H(Me)NH_2 \rightarrow PhCH{=}NC^*H(Me)Ph \xrightarrow{(EtO)_2PHO} \underset{(II)}{\rightarrow (EtO)_2P(O)C^*HPhNHC^*HMePh} \xrightarrow{HCl,\ H_2O} H_2O_3PC^*HPhNHC^*HMePh \xrightarrow{H_2,\ Pd/C} \rightarrow H_2O_3PC^*HPhNH_2 . \quad (62)$$

$[\alpha]_D = -18{,}1°$ [from (+) - II];
$[\alpha] = +18{,}1°$ [from (−) - II].

Apart from dialkyl phosphites, other organophosphorus compounds with a phosphorus–hydrogen bond readily add to azomethines: diaryl phosphites[291,324–326]; monoalkyl phosphites[327], dialkyl phosphorothioites[328–332], phosphorodiamidites[281], hypophosphorous acid[205,206,227,333–336], alkylphosphonites[337], dialkyl(aryl)phosphine oxides[180,318,320] and sulphides[338,339], dialkyl(aryl)phosphines[318,340], and triphenylphosphine hydrobromide[318]. Instead of diaryl phosphites, the more readily available triaryl phosphites can be introduced into the reaction in the presence of water and hydrochloric acid[341]. The imides of α-aminoalkylphosphonates have been synthesised in 36–95% yields by the addition of the anilides and phenylhydrazides of dialkylphosphorous acids to Schiff bases[342–345]:

$$(EtO)_2PNHX + PhCH{=}NC_6H_4R \rightarrow (EtO)_2P(=NX)CH(Ph)NHC_6H_4R . \quad (63)$$
(R=H, Me, NO$_2$; X=C$_6$H$_4$R, NHC$_6$H$_4$R)

α-Aminoalkyl organophosphorus compounds are formed also following the addition of compounds with a phosphorus–hydrogen bond to enamines[346–348]; for example, the reaction of diphenylphosphine oxide with 2-dialkylaminovinyldiphenylphosphine oxides resulted in the formation of tetraphenyldialkylaminoethylenediphosphine dioxides in 67–75% yield[347]:

$$Ph_2P(O)CH{=}CHNR_2 + Ph_2PHO \rightarrow Ph_2P(O)CH_2CH(NR_2)P(O)Ph_2 . \quad (64)$$
(R=Me, Et)

It is noteworthy that the mode of addition to 1-acetamidoacrylic acid is determined by the presence of an electron-accepting substituent and leads after hydrolysis to β-amino-β-carboxyethylphosphonic acid in 50% yield[1]:

$$CH_2{=}\underset{NHCOMe}{C}{-}COOH + P(OMe)_3 \rightarrow CH_2{=}\underset{NHCOMe}{C}COOMe + (MeO)_2PHO \rightarrow \rightarrow (MeO)_2P(O)CH_2{-}\underset{NHCOMe}{CH}COOMe \xrightarrow{HCl,\ H_2O} H_2O_3PCH_2\underset{NH_2}{CH}COOH . \quad (65)$$

The addition of dialkyl phosphites and phosphorothioites to aziridine has been proposed as a method for the synthesis of 2-aminoethylphosphonates and 2-aminoethylphosphonothioates[349]:

$$(RO)_2PHX + \underset{NH}{CH_2{-}CH_2} \longrightarrow (RO)_2P(X)CH_2CH_2NH_2 \quad (66)$$
(X = O, S; R = Et, Pr, *i*-Pr, Bu)

Phosphine[350,351], alkyl(phenyl)phosphines[232,234,352–355], and dialkylphosphines[350] add to allylamines in the presence of radical catalysts contrary to the Markovnikov rule with formation of 3-aminopropylphosphines.

Several studies have been made on the mechanism of the addition of compounds with a phosphorus–hydrogen bond to Schiff bases. The following mechanism has been proposed for reaction (59) catalysed by alkoxides[289]:

$$(RO)_2PHO + RONa \rightleftarrows (RO)_2PONa + ROH , \quad (67)$$
$$(RO)_2PONa + R'R''C{=}NR''' \rightarrow (RO)_2P(O)C(R')(R'')N(Na)R''' ,$$
$$(RO)_2P(O)C(R')(R'')N(Na)R''' + (RO)_2PHO \rightarrow (RO)_2P(O)C(R')(R'')NHR''' + (RO)_2P(O)Na .$$
etc.

Recently this mechanism was confirmed by kinetic investigations[356]. The catalytic effect of acids in reaction (59) has been explained both by the enhancement of the electrophilicity of the Schiff base and by an increase of the dialkyl phosphite content in the reactive symmetrical [with phosphorus(III)] form[357].

The employment of an equimolar mixture of the amine and the carbonyl compound instead of the complete Schiff base[291,319,324,325], i.e. the reaction carried out under conditions analogous to those described in the preceding section, constitutes a modification of the process discussed above. This evidently shows that the methods are related: one cannot rule out the possibility of the occurrence of reactions of type (41) employing primary amines and ammonia, via a stage involving the formation of an azomethine and their subsequent course in accordance with Eqn. (59).

Synthesis of α-Aminoalkylphosphorus Derivatives by the Reaction of Phosphoramidites with Carbonyl Compounds

The full ester-amides and triamides of phosphorus(III) acids react with carbonyl compounds to form α-aminoalkylphosphorus derivatives in many instances. Such a reaction was investigated for the first time§ in relation to dialkyl *NN*-dialkylphosphoramidites, aldehydes[361], and ketones[362]. In such cases the desired products are formed in 9–53% yields[361–364]:

$$(RO)_2PNR'_2 + R''(R''')CO \rightarrow (RO)_2P(O)C(R'')(R''')NR'_2 , \quad (68)$$

where R = Pr, Bu, or Pe, (RO$_2$) = C$_2$H$_4$O$_2$, R′ = Me or Et, R″ = H, Me, or Et, R‴ = H, Et, Pr, C$_6$H$_{13}$, or Ph, and R″R‴ = (CH$_2$)$_4$ or (CH$_2$)$_5$.

†Subsequently it was concluded on the basis of spectroscopic data that the reverse order of addition obtains for X, Y = P(O)(OEt)$_2$ and P(O)Ph$_2$ [Eqn. (61)].[321]

‡Diethyl α-aminobenzylphosphonate was resolved into its enantiomers by the fractional crystallisation of its salt with dibenzoyltartaric acid[323].

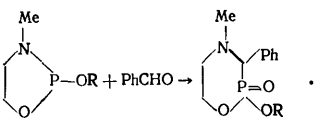
§The formation of an adduct in the reaction of *o*-phenylene *N*-phenylphosphoramidite with benzaldehyde was described as early as 1959.[358,359] Later it was shown that the proposed structure of the adduct is incorrect and that the reaction product is an aminophosphonate[360].

It has been shown that reaction (68) probably does not involve the preliminary hydrolysis of the initial phosphoramidite by traces of water to the dialkyl phosphite and the amine with subsequent interaction via mechanism (41).[361] Dialkyl *N*-arylphosphoramidites[360,365], propyl *NN*-diethylphenylphosphonamidite[366,367], phosphorous triamides[364], and diphenylphosphinamidous acids[365,368] react similarly with aldehydes. Acid alkylphosphoramidites can also react with aldehydes and ketones to form the acid esters of phosphonamidic acids[369] (45–65%):

$$(RO)(R'_2N)PHO + R''(R''')CO \rightarrow HO(RO)P(O)C(R'')(R''')NR'_2, \qquad (69)$$

where R = Me, Et, Pr, or Bu, R′ = Me or Et, R″ = H or Me, R‴ = Me or Ph, and R″R‴ = $(CH_2)_5$.

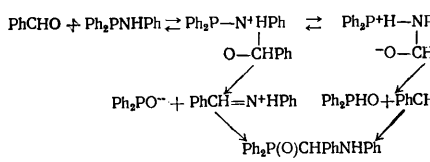
The reaction of benzaldehyde with 2-alkoxy-3-methyl-1,3,2-oxazaphospholans takes place with ring expansion and leads to 2-alkoxy-2-oxo-3-phenyl-4-methyl-1,4,2-oxazaphosphorinanes[370]:



(70)

It is noteworthy that the formation of aminophosphonates in reactions of phosphorus(III) amides and carbonyl compounds is by no means observed in all cases and frequently other processes take place[371]. This factor and also the relatively low availability of the initial amines reduce the practical value of this method.

Several hypotheses have been put forward concerning the mechanism of reaction (68). Some workers suggest a preliminary nucleophilic attack by the phosphorus atom on the carbonyl carbon atom with a subsequent series of rearrangements[360,361], while others believe, on the basis of experimental data, that nucleophilic attack by the nitrogen atom (analogous to that in the Wittig and PO–olefin addition reactions) is most likely with a subsequent rearrangement of the adduct in accordance with mechanism (71) to an aminoalkyl compound[365]:



(71)

The catalytic effect of amine hydrochlorides in reactions of type (68) can also be accounted for[364] within the framework of a mechanism analogous to mechanism (71).

Synthesis of Aminoalkyldiphosphonic Acids by the Reaction of Phosphorus(III) Trihalides with Nitriles

When nitriles are heated with phosphorus trihalides in the presence of organic and inorganic oxygen-containing acids with subsequent hydrolysis of the reaction mixture, aminoalkyldiphosphonic acids are formed[372–375]:

$$R{-}CN + P(Hal)_3 \xrightarrow[2.H_2O]{1.t^\circ} (H_2O_3P)_2C(R)NH_2. \qquad (72)$$

The desired products were obtained in yields of 28 and 51% respectively by the reaction of phosphorus tribromide with acetonitrile (R = Me) and benzonitrile (R = Ph)[374]. If instead of being hydrolysed, the reaction mixture is subjected to alcoholysis, acid esters are formed[372,373]. The reaction of cyanomethylated polystyrene copolymers with phosphorus trihalides and phosphorous acid in the presence of carboxylic acids leads after hydrolysis to phosphorus-containing complex-forming ion-exchange resins[376]. The reactions with phosphorous acid of the adducts of HCl or HBr and nitriles $[(H_2N{-}CRHal)^+Hal^-]$ or the products of the interaction of PCl_5, $COCl_2$, $(COCl)_2$, etc. with carboxamides $[(RR''N{=}CRHal)^+Hal^-]$ are modifications of the method under consideration. These also lead to aminoalkyldiphosphonic acids (4–78%); in the latter case nitrogen-substituted aminoalkyldiphosphonic acids are produced[377]. Formamides react directly with PCl_3 to form aminomethyldiphosphonic acids, which are or are not substituted at the nitrogen atom[378,379].

III. PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

The first members of the series of aminomethylphosphonates $[RR'NCH_2PO(OR'')_2$, R,R′ = H, Me, or Et and R″ = Me or Et) are soluble in water[177]; their salts (hydrochlorides, hydrobromides, and picrates) are much more soluble in water and are sparingly soluble in organic solvents (alcohol and ether). The latter properties are frequently used for their isolation and purification. Aminophosphinates and phosphine oxides are oily liquids or solids which dissolve in organic solvents and are sparingly soluble in water; they are isolated from the reaction mixture by distillation, crystallisation, or in the form of salts.

Acid esters of aminophosphonic acids and aminophosphonic and aminophosphinic acids are to some extent soluble in water and much less so in organic solvents. The surfactant properties of these compounds have been investigated[2,380]. Infrared spectroscopic and NMR data for many substances of this class have been published[3,124,201,267,320,363,381–385].

CHEMICAL PROPERTIES

The chemical properties of aminoalkyl organophosphorus compounds are determined by the presence in their molecules of the phosphorus-containing residue, the amino-group, and the methylene or methylidyne groups linked directly to nitrogen and phosphorus atoms. In many reactions these groups behave in the same way as in the corresponding compounds with a single heteroatom, exhibiting in a few instances certain chemical properties due to the mutual influence resulting from the close proximity of the nitrogen- and phosphorus-containing fragments.

Reactions Involving the Organophosphorus Fragment

One of the most important reactions involving the organophosphorus fragment is hydrolysis of α-aminoalkylphosphonic acid esters to the free acids on heating the esters with hydrochloric acid at 100–140°C for several hours:

$$H_2NC(R)(R')P(O)(OR'')_2 \xrightarrow{HCl,H_2O} H_2NC(R)(R')PO_3H_2. \qquad (73)$$

Aminoalkylphosphonic acids[178,179,181] are obtained in 35–85% yields. The hydrolysis of *N*-mono- and *N*-disubstituted α-aminoalkylphosphonates[187,203,210,386] and the analogous phosphinates[310,387], β- and γ-aminoalkylphosphonates[17,20], and ω-trialkylammoniumalkylphosphonates[388]

proceeds similarly. α-Aminoalkylphosphonothionates are converted into aminoalkylphosphonic acids under these conditions[186]. To remove hydrogen chloride from the hydrochlorides of aminoalkylphosphonic acids, the latter are treated in some cases with silver oxide and then with hydrogen sulphide[208] or epoxyalkanes[1,208].

The method described above has been used to eliminate both alkyl groups from dialkylaminoalkylphosphonates. The method involving the thermal decomposition of the hydrochlorides and hydrobromides of aminoalkylphosphonates until the complete elimination of the alkyl halide has proved convenient for the removal of only one alkyl group, i.e. for the preparation of the acid ester[389-391]. Thus acid esters were obtained in 78–97% yields by heating the hydrochlorides and hydrobromides of dialkylaminomethylphosphonates[389]:

$$R_2NCH_2PO(OR')_2 \cdot HX \rightarrow R_2NCH_2PO(OR')(OH) + RX. \quad (74)$$
(X=Cl, Br; R=Me, Et; R'=Et, Bu)

This method proved to be unsuitable for aminophosphonates containing aromatic substituents at the nitrogen atom and at the α-carbon atom owing to their complete cleavage in an acid medium. Such aminophosphonates are hydrolysed in an alkaline medium[299,392,393], since under these conditions both the esters themselves and their hydrolysis products are fairly stable[297]. The hydrolysis is usually carried out in an aqueous or alcoholic solution of alkali; the acid is isolated from the resulting salt by acidification[392,393]. It is noteworthy that in the alkaline hydrolysis of alkyl esters it is possible to obtain only the acid esters[299,392]. Phenyl esters, which are completely hydrolysed under severe conditions in an alkaline medium, are used for the synthesis of the free acids[393]:

$$ArNHCH(Ar')P(O)(OR)_2 \xrightarrow{KOH} \begin{cases} \xrightarrow{R=Alk} ArNHCH(Ar')P(O)(OR)OH \\ \xrightarrow{R=Ph} ArNHCH(Ar')PO_3H_2. \end{cases} \quad (75)$$
(Ar=Ph, *m*, *p*-C_6H_4Me; Ar'=Ph, *p*-$C_6H_4CHMe_2$)

Acid esters and acids are obtained in 63–92% yields. This method is also suitable for the synthesis of acid esters of *N*-alkylaminoalkylphosphonic acids[392]. The resulting ω-aminoalkylphosphonic acids have three dissociation constants corresponding to the protonation of the phosphonate anion in the titration with an acid (pK_1), the second dissociation of the phosphonate group (pK_2), and the dissociation of the betaine proton in the titration with alkali (pK_3):[394]

$$\begin{aligned} &H_3N^+(CH_2)_nPO_3^-H + H^+ \rightleftarrows H_3N^+(CH_2)_nPO_3H_2 \quad pK_1, \\ &H_3N^+(CH_2)_nPO_3^-H \rightleftarrows H_3N^+(CH_2)_nPO_3^{2-} + H^+ \quad pK_2, \\ &H_3N^+(CH_2)_nPO_3^{2-} \rightleftarrows H_2N(CH_2)_nPO_3^{2-} + H^+ \quad pK_3. \end{aligned} \quad (76)$$
(n=1, 2, 4, 5, 10)

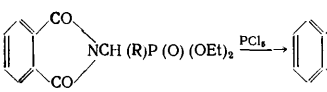
For the compounds under consideration, the above dissociation constants are $pK_1 = 2.35–2.6$, $pK_2 = 5.9–8.0$, and $pK_3 = 10.8–11.25$.[394] For comparison, we may quote the first and second dissociation constants of alkylphosphonic acids: $pK_1 = 2.35–2.6$ and $pK_2 = 7.1–8.25$ for $Me(CH_2)_{n-1}PO_3H_2$ (n = 1, 2, 6, or 12). Owing to the high pK_3 values of such acids, due to the high basicity of the amino-residue, they are titrated as mono-basic acids in the presence of indicators[395]. γ-Anilinopropylphosphonic acid also has the betaine structure, but, owing to the low basicity of the nitrogen atom, it is titrated as a dibasic acid [$pK_1 = 2.10$, $pK_3 = 4.25$, and $pK_2 = 7.15$ for $PhNH_2^+(CH_2)_3PO_3^-H$].[394] The same observations have been made also for the acid esters of aminophosphonic acids: whereas the acid esters of dialkylaminomethylphosphonic acids are neutral in an aqueous medium[389,392], the acid esters of *N*-arylaminophosphonic acids behave as acids themselves[392]. Owing to this difference, the former acid esters do not form stable salts with many metals[392]. The acid properties of polyaminopolyalkylphosphonic acids and mixed polyaminopolyalkylphosphonic and polyacetic acids are characterised by a large set of dissociation constants whose values are determined both by the nature of the dissociating functional groups and by their mutual influence¶.

Other reactions involving the phosphorus atom have been well investigated. Thus aminophosphonic acids are esterified by expoxyalkanes[397] and orthoformates[123].

Phenyl *N*-arylaminobenzylphosphonates are readily transesterified by alcohols in the presence of alkoxides[393]:

$$ArNHCH(Ar')PO(OPh)_2 \xrightarrow[-PhONa]{ROH,\ RONa} ArNHCH(Ar')PO(OR)_2. \quad (77)$$
Ar=Ph, *m*, *p*-C_6H_4Me, *p*-C_6H_4Cl, *p*-$C_6H_4CHMe_2$; Ar'=Ph, *p*-C_6H_4Me; R=Me, Pr, Bu.

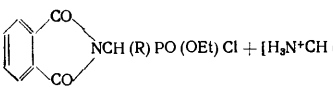
Treatment of diethyl ω-dialkylaminomethyl(ethyl)phosphonates with phenyl-lithium leads to ω-dialkylaminomethyl(ethyl)diphenylphosphine oxides[398]. Phthalimidobenzyl(methyl)phosphonates are quantitatively converted into ester-acid chlorides by reaction with phosphorus pentachloride[128,399]:



(78)

(R=H, Ph)

The resulting acid chlorides were used to synthesise peptides containing aminoalkylphosphonic acid moieties in 70–88% yields[128,399]:

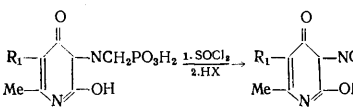


(79)

(R=H, Ph; R'=H, *d*, *l*-Me, *l*-CH_2Ph)

β-Phthalimidoethylphosphonyl chloride, obtained by treating the corresponding acid with thionyl chloride or its diethyl ester with phosphorus pentachloride, has been used to synthesise lipids and kephalins containing aminoethylphosphonic acid residues[400,401].

The conversion of pyrimidinylmethylphosphonic acids into the dimethyl and dibutyl esters and *NN'*-diphenyldiamide in 29–50% yields by successive treatment with thionyl chloride, methyl or butyl alcohol, and aniline has been described[54,402]:



(80)

(R_1=H, Br; X=OMe, OBu, NHPh)

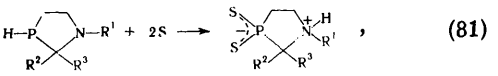
Treatment of *N*-substituted α-aminobenzylphosphonates with thionyl chloride and then with *p*-nitrophenol and triethylamine is accompanied by the cleavage of the phosphorus–carbon bond and leads to di(nitrophenyl)phosphate[403]. Phosphorus pentachloride completely cleaves nitrilotri(methylphosphonic)acid to tri(chloromethyl)amine and phosphoryl chloride; the hexaethyl ester is cleaved similarly[123].

¶Detailed data on their acid dissociations are quoted in the review of Kabachnik et al.[396]

Like other phosphines, ω-aminoalkylphosphines are converted into the corresponding sulphides and oxides on treatment with sulphur or hydrogen peroxide [24,110,111,114,230,234,265,267,340,352,353,355].

Phosphinic and phosphinodithioic acids are formed under these conditions from di-(β-aminoethyl)phosphines and β-aminoethylphenylphosphines [114,115].

1,3-Azaphospholidines containing a hydrogen atom at the phosphorus atom are converted into inner salts of phosphinodithioic acids in 71–81% yields by treatment with sulphur in benzene [230]:



(81)

where R^1 = H or Et, R^2 = H, R^3 = Ph, and R^2R^3 = $(CH_2)_5$.

The oxidation of *NNN'N'*-ethylenediaminetetra(methylenephosphonous) acid with mercury(II) chloride to the phosphonic acid has been proposed as a method of synthesising the latter in an analytically pure form [404].

The alkylation of β-diethylaminoethyldialkyl(aryl)phosphines by ethyl iodide involves the phosphorus atom and results in the formation of aminophosphonium salts in 74–87% yields [110]:

$$Et_2NCH_2CH_2PR_2 + EtI \rightarrow [Et_2NCH_2CH_2P^+(R_2)Et]\,I^- . \quad (82)$$
(R=Et, Ph, cyclo-C_6H_{11})

Aminoalkylphosphonimidates readily exchange the imino-residue for oxygen and sulphur on treatment with carbon dioxide and carbon disulphide; treatment with acids leads to ester-amides [343]:

$$(EtO)_2PCH(Ph)NHAr' \xrightarrow{NAr} \begin{cases} \xrightarrow{CO_2} (EtO)_2P(O)CH(Ph)NHAr' \\ \xrightarrow{CS_2} (EtO)_2P(S)CH(Ph)NHAr' \\ \xrightarrow{AcOH} (EtO)(ArNH)P(O)CH(Ph)NHAr' . \end{cases} \quad (83)$$

Reactions Involving the Nitrogen Atom

The amino-group of aminoalkyl phosphorus derivatives enters into many of its characteristic reactions. *N*-Alkyl-substituted and unsubstituted aminoalkyl organophosphorus compounds form stable salts with acids. In contrast to alkylation, the protonation of aminoalkylphosphines also takes place at the nitrogen atom [23,231]. The alkylation of the nitrogen atom is of preparative interest. Thus, on reaction with dimethyl sulphate (DMS) in an alkaline medium and subsequent acidification, *NN*-di(carboxymethyl)aminomethylphosphonic acid is converted into its *N*-methylbetaine [26]:

$$H_2O_3PCH_2N(CH_2COOH)_2 \xrightarrow[2.\ H^+]{1.\ NaOH,\ Me_2SO_4} HO_3^-PCH_2N^+Me(CH_2COOH)_2 . \quad (84)$$

Depending on the methylating agent, aminoalkylphosphonic acid containing an unsubstituted amino-group are converted into dimethylaminoalkylphosphonic acids (formaldehyde and formic acid) or into fully methylated derivatives—betaines (DMS in an alkaline medium or methyl iodide in methanol) [395,405]. It has been suggested that polyaminoalkylpolyphosphonic and polyaminoalkylpolyphosphonicpolyacetic acids be obtained by alkylating aminoalkylphosphonic acids with alkylene dihalides and chloroacetic acid in an alkaline medium [48,406–410].

The full esters of dialkylaminoalkylphosphonic acid are readily alkylated by alkyl halides and DMS even at room temperature in inert solvents (dioxane, ether) or in the absence of a solvent on heating with formation of salts of trialkylammoniumalkylphosphonates [63,75,411–414].

Thus alkylation of diethyl ω-dimethylaminoalkylphosphonates with methyl iodide in ether at 0°C leads to the corresponding methiodides in 61–81% yields [388]:

$$Me_2N(CH_2)_nP(O)(OEt)_2 \xrightarrow{MeI} Me_3N^+(CH_2)_nP(O)(OEt)_2I^- . \quad (85)$$

A characteristic feature of these compounds is their tendency to undergo dealkylation to the betaines—slowly at room temperature and rapidly on heating [411,414,415]. For example, when trimethylammoniummethylenediphosphonate is refluxed for 3 h in benzene, the betaine is formed in 97% yield [411]:

$$(EtO)_2P(O)CHP(O)(OEt)_2 \xrightarrow{t^\circ} (EtO)(O)PCHP(O)(O)(OEt)_2 + EtI . \quad (86)$$
($^+NMe_3I^-$; $-O^+NMe_3$)

It has been noted that the tendency towards betaine formation depends not only on the type of substituent in the alkoxy-group (increases with decrease of the length of the substituent) but also on the nucleophilic properties of the anion: the perchlorates and methyl sulphates are more stable than the bromides and iodides [414].

A simple method for the synthesis of such betaines is the coupled *N*-alkylation and *O*-dealkylation of aminophosphonates occurring when these are heated [346,415]: a betaine was obtained in 50% yield by heating dimethyl α-dimethylaminoisobutylphosphonate [346]:

$$(MeO)_2P(O)CH[CHMe_2]NMe_2 \xrightarrow{t^\circ} (MeO)O_2^-PCH[CHCMe_2]N^+Me_3 . \quad (87)$$

Toluene-*p*-sulphonic acid is used as a catalyst for this process [415]. The *N*-dealkylation of aminoalkyl phosphorus derivatives has been less thoroughly investigated. *N*-Benzylaminoalkylphosphonic and the analogous phosphinic acids are readily dealkylated [310] by hydrogenolysis in glacial acetic acids over a palladium catalyst at a temperature as low as 20°C, the yields being 92–98%:

$$PhCH_2NHCH(R)P(O)(OH)X \xrightarrow{AcOH,H_2/Pd-C} H_2NCH(R)P(O)(OH)X . \quad (88)$$
(X=OH, Ph; R=Me, Et, Pr, Bu, Ph)

When the iodide of diethyl triethylammoniummethylphosphonate is heated with triethylphosphite, the latter is alkylated and an ethyl group is removed from the nitrogen atom [416]. The ethyl esters of *N*-t-butylaminomethylphosphonic and *N*-t-butyliminodi(methylphosphonic) acids are hydrolysed and cleaved by hydrochloric acid to aminomethylphosphonic and iminodi(methylphosphonic) acids respectively [312,314].

Aminoalkyl organophosphorus compounds, both unsubstituted and mono-substituted at the nitrogen atom, are readily acylated. Thus, on heating with acetic anhydride, aminomethylphosphonic acid is converted into acetamidomethylphosphonic acid in 57% yield [417]:

$$H_2NCH_2PO_3H_2 + (MeCO)_2O \rightarrow MeCONHCH_2PO_3H_2 . \quad (89)$$

Fusion of this acid with phthalic anhydride leads to phthalimidomethylphosphonic acid [417]. In this case the chlorides of chloroacetic, benzoic, and *p*-nitrobenzoic acids are also effective acylating agents in an alkaline medium [417,418]. The full esters of aminoalkylphosphonic and aminoalkylphosphonothioic acids are smoothly acylated by acetic anhydride [417,418], acyl chlorides in the presence of pyridine and by the Schotten–Baumann reaction [329,418,419], aryl isocyanates [420], keten [421], mixed anhydrides of aminocarboxylic and carbonic acids [422,423], phthalimidoacetic acid in the presence of dicyclohexylcarbodi-imide [399], and phosgene [424]. The acylation of aminoalkylphosphinates and phosphine oxide has also been described [72,387].

Phosphonic acids containing a tertiary nitrogen atom can be converted by treatment with hydrogen peroxide in alkaline or neutral aqueous and aqueous alcoholic media

into the *N*-oxides of aminophosphonic acids and into their salts[425-432]; for example, the oxidation of nitrilotri-(methylphosphonic) acid with hydrogen peroxide leads to the *N*-oxide in 49% yield[425]:

$$N[CH_2PO_3H_2)_3 \xrightarrow{H_2O_2} ON(CH_2PO_3H_2)_3 . \quad (90)$$

The oxidation of *NN*-disubstituted aminomethylphosphine oxides takes place similarly[86,433]. The oxidation of aminoalkylphosphonic acids and their esters, containing a primary amino-group, with sodium hypochlorite leads to azodi(alkylphosphonic) acids and their esters[434]:

$$2\,(RO)_2P(O)C(R')(R'')NH_2 \xrightarrow{NaOCl} (RO)_2P(O)C(R')(R'')N{=}NC(R')(R'')P(O)(OR)_2 . \quad (91)$$
(R=H, Alk)

The diazotisation of aminoalkyl organophosphorus compounds with a primary amino-group is of considerable preparative interest. The reaction with α-aminoalkylphosphonic acids proceeds with evolution of nitrogen and the formation of α-hydroxyalkylphosphonic acids[28,183,387]:

$$H_2O_3PCH(R)NH_2 \xrightarrow{HNO_2,\ \text{nitrogen oxides}} H_2O_3PCH(R)OH + N_2 . \quad (92)$$
(R=H, Ph)

Aminomethylphosphonate esters are converted into diazomethylphosphonates in 46–64% yields on diazotisation with sodium nitrite in aqueous acetic acid[125-127]:

$$(RO)_2P(O)CH_2NH_2 \xrightarrow{HNO_2} (RO)_2P(O)CHN_2 . \quad (93)$$
(R=Me, Et)

α-Diazoalkylphosphine oxides were obtained similarly in 45–90% yields by the diazotisation of α-aminoalkylphosphine oxides[18,36,127]:

$$R_2P(O)CH(R')NH_2 \xrightarrow{HNO_2} R_2P(O)C(R')N_2 . \quad (94)$$
(R=Ph, CH_2Ph, R'=H; R=Ph, R'=Ph)

The possibility of such diazotisation of aminophosphonates and phosphine oxides is probably due to their high α-C–H acidity and the considerable stability of the resulting α-diazoalkyl derivatives of organophosphorus compounds: comparison of the thermal stabilities of α-diazoalkyl organophosphorus compounds with those of the carbonyl analogues showed that the former are just as stable and in some cases even more stable than the latter[435].

The diazotisation of β-amino-αα-dimethylethyldiphenylphosphine oxide takes place with deamination and is accompanied by the isomerisation of the intermediate carbonium ion, to a large extent owing to the migration of the diphenylphosphinyl group[10]:

$$Ph_2P(O)CMe_2CH_2NH_2 \xrightarrow[\text{or } C_5H_{11}ONO]{NaNO_2,\ H_2SO_4} [Ph_2P(O)CMe_2CH_2^+] \longrightarrow$$
$$\longrightarrow Ph_2P(O)CH_2{-}C(Me){=}CH_2\ (25\%) + Ph_2P(O)CH{=}CMe_2\ (8\%) +$$
$$+ Ph_2P(O)CH_2CMe_2OH\ (38.8\%) + Ph_2P(O)CMe_2CH_2OH\ (6.8\%) +$$
$$+ Ph_2P(O)C(Me)\begin{matrix}CH_2\\ \diagdown\\ \diagup\\ CH_2\end{matrix}\ (14.7\%) . \quad (95)$$

The primary amino-group in aminomethylphosphonates and aminomethylphosphine oxides is converted in the usual way into the isonitrile group in 72–80% yield[142,436]:

$$R_2P(O)CH_2NHCHO \xrightarrow[NEt_3]{COCl_2} R_2P(O)CH_2N{=}C . \quad (96)$$
(R=Ph, CH_2Ph, OEt)

Reactions Involving the α-Carbon Atom

These reactions are usually accompanied by the dissociation of carbon–nitrogen and phosphorus–carbon bonds or the elimination of an α-hydrogen atom and the formation of phosphorylated nitrogen yields.

When the carbon–nitrogen bond in aminoalkyl derivatives of organophosphorus compounds is broken, the amino-group is substituted by other organic residues. For example, heating of tri(dimethylaminomethyl)phosphine with aniline leads to tri(anilinomethyl)phosphine in 45% yield[266]:

$$(Me_2NCH_2)_3P + 3\,H_2NPh \xrightarrow[-3Me_2NH]{} (PhNHCH_2)_3P . \quad (97)$$

The substitution of the diethylamino-group in *NN*-diethylaminomethylphosphines by the diphenylphosphine residue has been suggested[190] as a method for the synthesis of compounds with a P–C–P bond system (yields 31–100%):

$$Ph_nP[CH_2NEt_2]_{3-n} + m\,HPPh_2 \xrightarrow[Et_2NH]{} Ph_nP[CH_2NEt_2]_{3-n-m}[CH_2PPh_2]_m . \quad (98)$$
($n=0-2$, $m=1-3$)

The formation of a cyclic product in 76% yield on dehydrochlorination of tetra(anilinomethyl)phosphonium chloride with triethylamine probably proceeds via a mechanism involving the cleavage of the P–C and C–N bonds[266]:

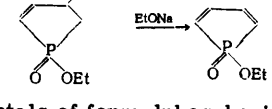
$$(PhNHCH_2)_4P^+Cl \xrightarrow[-Et_3N\cdot HCl]{Et_3N} \left[\begin{matrix}PhNCH_2 & & CH_2NHPh\\ & P^+ & \\ PhNHCH_2 & & CH_2NHPh\end{matrix}\right] \longrightarrow$$
$$\longrightarrow \left[\begin{matrix}PhNCH_2 & & CH_2NHPh\\ & CH_2\ \ P & \\ PhN: & \longrightarrow & CH_2{-}NHPh\\ H & & \end{matrix}\right] \longrightarrow \begin{matrix}Ph\\ N{-}CH_2\\ CH_2\ \ \ PCH_2NHPh + PhNH_2\\ N{-}CH_2\\ Ph\end{matrix} . \quad (99)$$

The removal of the amino-group from aminoalkyl derivatives of phosphorus is facilitated in the presence of an acid hydrogen atom in the β-position[122,348]. For example, α-amino-γ-oxophosphonates are spontaneously deaminated to the corresponding vinylphosphonates in 18–44% yields even at room temperature[122]:

$$(EtO)_2P(O)CH[NMe_2]CH_2COR \xrightarrow[-Me_2NH]{} (EtO)_2P(O)CH{=}CHCOR , \quad (100)$$

where R = *p*-C_6H_4X (X = Br, H, or OMe) or CH = CHPh.

1-Ethoxyphosphole 1-oxide has been synthesised by treating the iodide of 1-ethoxy-4-trimethylamino-2-phospholen 1-oxide with sodium ethoxide[437]:



(101)

The aminoacetals of formylphosphonic acid esters and formyldiphenylphosphine oxides react with diethyl phosphite and diphenylphosphine oxide to form diphosphorylated trimethylamines[103] in 52–60% yields:

$$R_2P(O)\begin{matrix}CH(OMe)\\ \diagdown\\ \diagup\\ NMe_2\end{matrix} + R'_2P(O)H \xrightarrow{-MeOH} [R_2P(O)][R'_2P(O)]CHNMe_2 . \quad (102)$$
(R,R'=OEt, Ph)

NNO-Trimethylaminoacetal of formyldiethylphosphine readily disproportionates on heating to bisdiethylphosphinyldimethylaminomethane and the dimethyl acetal of dimethylformamide (DMF)[116]:

$$2\,Et_2PCH(OMe)NMe_2 \rightarrow (Et_2P)_2CHNMe_2 + HC(OMe)_2NMe_2 . \quad (103)$$

Immoniumphosphonates were synthesised by treating aminoacetals of formylphosphonic acid esters with thionyl chloride[103]:

$$(RO)_2P(O)CH\langle^{OMe}_{NMe_2} \xrightarrow{SOCl_2} (RO)_2P(O)CH{=}N^+Me_2Cl^- + SO_2 + MeCl \quad (104)$$

(R=Me, Et)

The products are very reactive with respect to compounds with a mobile hydrogen atom[122]:

$$(EtO)_2P(O)CH{=}N^+Me_2Cl^- + RH \xrightarrow[-NEt_3\cdot HCl]{NEt_3} (EtO)_2P(O)CH(R)NMe_2 \quad (105)$$

(R=R'S, R'_2N, R' O, $R'_2P(O)$, $(MeCO)_2CH$, $ArCOCH_2$)

The chemical and thermal instability of certain aminoalkyl organophosphorus compounds is due to the lability of their phosphorus–carbon bond. The lability is manifested most clearly in α-aminoalkylphosphonium salts[170–173]: *NN*-disubstituted aminomethyltriphenylphosphonium halides are unstable even at room temperature and are fully hydrolysed by water[173]:

$$Ph_3P^+CH_2NR_2X^- \rightleftarrows Ph_3P + CH_2{=}N^+R_2X^- \xrightarrow{H_2O} Ph_3P + CH_2O + H_2NR_2X \quad (106)$$

X=Cl, Br; R=Me; $R_2 = (CH_2)_5$, $(CH_2)_2O(CH_2)_2$

The replacement of the phenyl groups at the phosphorus atom by alkyl groups[171,173] (i.e. an increase of the basicity of the initial phosphine) and a decrease of the stability of the carbonium-immonium ion by the introduction of acyl groups at the nitrogen atom[172] appreciably stabilise such compounds, but they too decompose in an alkaline medium or under the influence of powerful nucleophilic agents (MeONa, NEt_3, MeLi, t-BuOK) with formation of trialkyl(aryl)phosphines[171–173]. The introduction of substituents stabilising the positive charge (for example, the *p*-dimethylaminophenyl group) at the α-carbon atoms reduces sharply the thermal and hydrolytic stability of α-aminoalkylphosphonium salts[170]. An ethynyl group at the phosphorus atom is cleaved[438]:

$$Bu_3PC{\equiv}CH + HOCH_2NEt_2 \rightarrow [Bu_3\overset{+}{P}(C{\equiv}CH)CH_2NEt_2]OH^- \rightarrow Bu_3P(O)CH_2NEt_2 + C_2H_2 . \quad (107)$$

The stability of the carbonium-immonium ion formed determines also the lability of the carbon–carbon bond in β-aminoalkylphosphonium salts[89]:

$$[Ph_3PC(Ph){=}CH_2]Br^- + HNC_5H_{10} \rightleftarrows [Ph_3\overset{+}{P}CH(Ph)CH_2NC_5H_{10}]Br^- \rightarrow$$
$$\rightarrow Ph_3P{=}CHPh + [CH_2{=}\overset{+}{N}C_5H_{10}]Br^- . \quad (108)$$

On heating (distillation), certain α-aminoalkylphosphonates undergo partial cleavage of the phosphorus–carbon bond with formation of enamines and dialkyl phosphites[102,363]:

$$R_2NCHP(O)(OR'')_2 \xrightarrow{t^\circ} R_2NCH{=}CR'R'' + (R''O)_2PHO , \quad (109)$$

(CHR'R'')

where $R_2 = (CH_2)_4$, R'R'' = Me, and R''' = Et or $R_2 = (CH_2)_5$, R' = H, R'' = Me, and R''' = Me.

Aminophosphonates containing aromatic groups at the nitrogen and α-carbon atoms are relatively stable in an alkaline medium[297], but, when treated with acetic or hydrochloric acid at 40–60°C, they are fully decomposed into an amine, aldehyde, alcohol, and phosphorus acid[291,439]:

$$ArNHCH(Ar')P(O)(OR)_2 \xrightarrow{HCl \text{ or } MeCOOH} ArNH_2 + Ar'CHO + H_3PO_3 + 2\,ROH \quad (110)$$

β-Aminoalkylphosphonates, which are intermediates in the PO–olefin addition reaction (17), undergo a further conversion into an olefin and a phosphoramidate in the presence of bases[94] or acids[98]:

$$PhCHP(O)(OEt)_2 \xrightarrow[-NH_3]{NaNH_2} PhCH + PhN(Na)P(O)(OEt)_2 . \quad (111)$$

(CHPh, NHPh; HCPh)

Like α-aminocarboxylic acids, aminomethylphosphonic acid is cleaved by ninhydrin with formation of a blue dye and a mixture of phosphates[440].

The phosphonate carbanions obtained from aminophosphonates readily enter into the PO–olefin addition reaction[275,319,441]. For example, phosphorylated enamines were obtained in 60–75% yields by treating dimethylaminoethylenediphosphonates with sodium hydride in dioxane and then with aldehydes (ketones do not enter into this reaction)[275]:

$$[(EtO)_2P(O)]_2CHNMe_2 \xrightarrow[2.RCHO]{1.NaH} (EtO)_2PO_2Na + RCH{=}CP(O)(OEt)_2 , \quad (112)$$

(NMe$_2$)

where R = Ph, *p*-$C_6H_4NO_2$, PhCH=CH, or 3,4-(OCH_2O)Ph. When nitroso-compounds are introduced into this reaction instead of aldehydes, amidines are formed in 45–97% yields[319,324,441]:

$$(PhO)_2P(O)CH(NHR'')R \xrightarrow[2.\ R'NO]{1.NaH \text{ or } KOH} (PhO)_2PO_2Na + R'N{=}C(R)NHR'' .$$

(R=Ph, *p*-$C_6H_4NO_2$; R' = Ph, *o*-C_6H_4Me; R''=Ph, *p*-$C_6H_4NO_2$, *o*-C_6H_4Me, *p*-C_6H_4OMe) (113)

Phosphorylated nitrogen ylides have been obtained by the reaction of α-ammoniumalkylphosphonates with bases[414,442]:

$$(RO)_2P(O)CH(R')N^+R''_3X^- \xrightarrow[-B\cdot HX]{B} (RO)_2P(O)C^-(R')N^+R''_3 . \quad (114)$$

In this case, where R' is a group capable of stabilising the negative charge [COR', COOR', PO(OR')$_2$], the formation of the ylide is observed even on treatment with potassium carbonate[414,442], whereas stronger bases (sodium hydride or dimsyl sodium) are needed when R' = H.[443] The chemical properties of these compounds have been little investigated: only alkylation with methyl iodide leading to a *C*-methylated ammoniumalkylphosphonate[414] and PO–olefin addition on treating *N*-diphenylphosphinylmethylpyridinium salts with aromatic aldehydes in the presence of diethylamine[444] have been described. The carbanions obtained by the reaction of diethylphosphinylmethyl isocyanide with butyl-lithium also react with carbonyl compounds to form vinyl isocyanides[142] (68–84%).

IV. APPLICATIONS OF AMINOALKYL ORGANOPHOSPHORUS COMPOUNDS

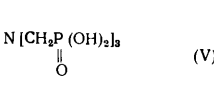
Owing to their ready availability and their chemical properties, compounds of this class can find extensive applications in various branches of science and engineering. Much interest is shown at present in the employment of aminoalkylphosphonic acids as effective complexones with electron-donating functions of the nitrogen atoms and the oxygen atoms in the phosphoryl groups, which are capable of forming chelate rings and of assuming various conformations depending on the configurations of the metal ions being chelated. Numerous publications have been devoted to this problem and have been described exhaustively in the review of Kabachnik et al.[396] Here only some data on the employment of these compounds as complexones are quoted.

Polyaminoalkylpolyphosphonic acids [for example (III)–(VI)], which are analogous of polyaminoalkylpolyacetic acids, are capable of effective complex formation with many metal ions:

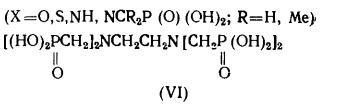
$(HO)_2PCNH(CH_2)_nNHCP(OH)_2$ (III)

(*n*=2 – 5; R=H, Me)

$(HO)_2PCNHCH_2CH_2XCH_2CH_2NHCP(OH)_2$ (IV)



(V)



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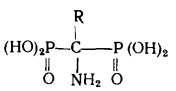

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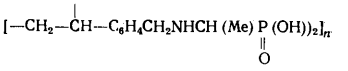
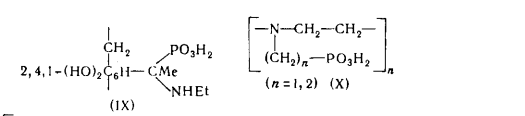


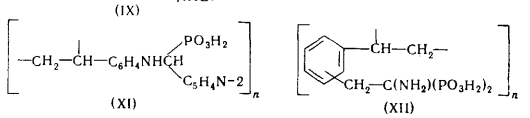
(VIII)

However, owing to their stereochemical characteristics and the high electron-donating capacity of the phosphonate group, they form relatively unstable complexes with alkaline earth metal ions, while their complex-forming capacity with respect to transition metal, lanthanide, and beryllium ions is very high [78,104,375,396,445-450]. An important feature of organophosphorus complexones is the formation of very stable "acid" or "hydrogen" complexes at low pH in which the metal is not coordinated to the nitrogen atom owing to the protonation of the latter [396]. This property is of undoubted interest in studies with readily hydrolysable salts. For these reasons, certain organophosphorus complexones [for example (III) and (VI)] can be used for the extraction of valuable elements and for the separation of lanthanides and actinides within their respective groups [448-452].

The high complex-forming capacity of these compounds is used also in the ion-exchange resins (VIII)-(XII) containing aminophosphonic acid residues [50,79,249,376,453-459]. For example, ion exchangers of the type (VIII)-(XI) effectively extract Cu^{2+} ions from an acetate buffer (capacity 1.1-1.4 mequiv. of Cu^{2+} per gram of resin) [453,459]:

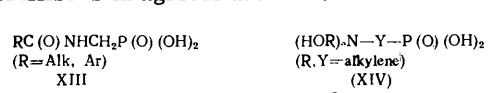


(IX) (n = 1, 2) (X)

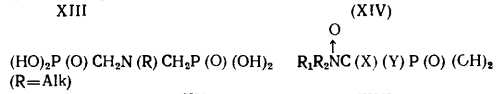


(XI) (XII)

Aminophosphonic acids can also find application in most cases where it is necessary to bind metal ions giving rise to undesirable effects. It has been suggested that they be used for water softening and to prevent the formation of scale [375,460] [compounds of type (V) and (VII)], as antioxidants [compounds (XIII)] [167] and as corrosion inhibitors [461], for the removal of rust and for the etching of aluminium alloys [compounds (VII) and (XIV)], [53,462] for the passivation of metals [253] [compounds (V), (VI) and (XV)], and as metal deactivating additives to lubricating oils [compounds (XIII)]. [45,167] The effective dispersing and deflocculating properties of salts (Li, Na, K, NH_4) of aminophosphonic acids [240,244,253] permit their employment for the formation of oil gels [164] [compounds (XIII)], as components of a boring solution [compound (V)], [182] for the prevention of ice formation in water-containing hydrocarbon fuels [compounds (XV)], [242] and in detergent compositions [45,240,243] [compounds (V) and (XV)]. Their manganese, copper, zinc, etc. salts can be used as microfertilisers in agriculture [53,373].

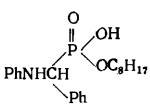


(XIII) (XIV)

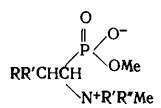


(XV) (XVI)

Aminophosphonic acid N-oxides [of the type of compound (XVI)] and their salts have been suggested as complexones [425,428,431], stabilisers of peroxide compounds, antioxidants for oils and soaps, water softening agents, metal corrosion inhibitors, and metal passivators [428-432]. In view of its ability to form complexes soluble in ligroin with a number of metal atoms, mono-octyl anilinobenzylphosphonate (XVII) has been proposed as an effective extractant at the interface between organic and aqueous phases [385,463-465].



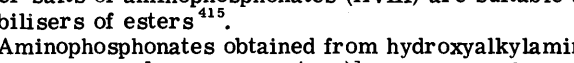
(XVII)



(XVIII)

Inner salts of aminophosphonates (XVIII) are suitable as stabilisers of esters [415].

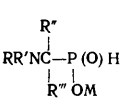
Aminophosphonates obtained from hydroxyalkylamines and polyamines [for example (XIX)] and also the hydroxyalkyl esters of aminophosphonic acids [for example (XX)], which contain hydroxy- and amino-groups, have been suggested as fire-resistant polyhydroxy-components in the manufacture of polyurethanes [213,215,218-220,277,279,280,397,466,467].



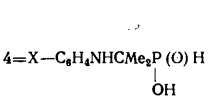
(XIX) (XX)

Their non-combustibility and thermal and chemical stability permit the employment of certain aminophosphonates as hydraulic liquids, heat exchangers, lubricators, and plasticisers [146,194,466,468]. These compounds can also be used as surfactants, emulsifying agents [194,222], and extractants [469].

Aminoalkylphosphonous acids and their salts of the general type (XXI) have been suggested as surfactants, antioxidants, and complex-forming agents [33,205,206,223].



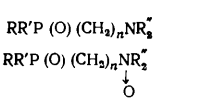
(M=H, Na, NH_4) (XXI)



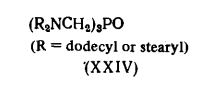
(X=HO, RR'N) (XXII)

Compounds of the general type (XXII) have been patented as photographic developers which are stable in air, readily soluble, and free from allergic effects [225].

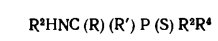
Aminoalkylphosphine oxides and N-oxides of type (XXIII) are promising extractants suitable for the extraction of uranium and for the separation of lanthanides and actinides within their respective groups [86,286,433,470]:



(n=1, 2) (XXIII)



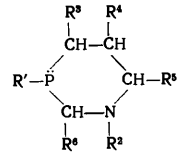
(XXIV)



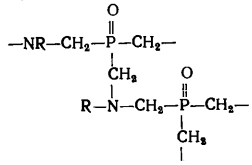
(XXV)

Tri(aminomethyl)phosphine oxides (XXIV) have been proposed as additives which reduce the static electric charge of synthetic fibres and impart fire resistance to them [237]. Aminoalkylphosphine sulphides (XXV) are suitable as lubricating materials and additives to oil [338].

Aminoalkylphosphines of the general type (XXVI) can be employed to modify carbonyl catalysts in oxo synthesis[471].

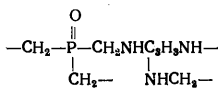


(XXVI)

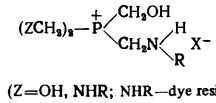


(XXVII)

Products obtained by the condensation of tetra(hydroxymethyl)phosphonium halides, tri(hydroxymethyl)phosphine and the corresponding phosphine oxide with nitrogen-containing compounds (primary amines, ammonia, urea, guanidine, melamine, etc.) of type (XXVII) and (XXVIII) are thermostable non-combustible resins suitable for impregnating veneers, wool, textiles, etc.[272-274,472-477].



(XXVIII)

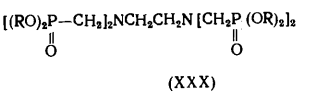


(Z=OH, NHR; NHR—dye residue

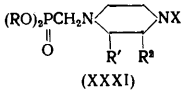
(XXIX)

When the aim was to make fabrics non-combustible, best results were obtained by condensation directly on the fibre[478]. Dyes with amino-groups give rise to wear-resistant colours on cellulose fibres on treatment with tetra(hydroxymethyl)phosphonium halides (XXIX).[479] Certain polyamides based on di(aminoalkyl)phosphine oxides and phosphinic acids have the self-quenching property and exhibit an enhanced adhesion to metals[355,480-482].

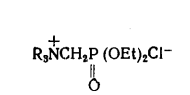
The biological activity of aminoalkyl organophosphorus compounds has been comparatively little studied. It has been established that 2-aminoethylphosphonic acid and some of its derivatives enter into the composition of the proteins and polysaccharides of some marine animals and lower organisms[483-488]. Many aminoalkyl organophosphorus compounds exhibit a low toxicity to warm-blooded animals[489]. Their much higher toxicity to plants and insects permits the employment of some of them [for example (V), (XVI), (XXI), (XXX)–(XXV)] as insecticides, fungicides, antiparasite agents, herbicides, growth regulators, and defoliants[33,194,203,209,431,490-492]. The chelate complexes formed by aminoalkylphosphonic acids with iron(III) ions are suitable for the protection of plants from chlorosis[52,59]. The low toxicity of aminoalkylphosphonous acids (XXI) and ammoniumalkylphosphonates (XXXII) to warm-blooded animals permits their use as antibacterial agents[58,205,224,334-336]. It has been suggested that salts of aminophosphonic acids of the type (V) and (XIII) be used to improve the contrast of X-ray photographs[493] and to increase the concentration of 5-hydroxytetracycline in blood[494]; their salts with microelements are suitable for the introduction of the latter into the organism[165]. The high complex-forming capacity of polyaminoalkylpolyphosphonic acids [for example (III), (IV), and (VI)] with respect to beryllium and certain heavy elements gives rise to the possibility of using them for the effective treatment of intoxications caused by the presence of these metals in the organism[396].



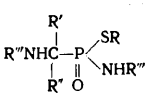
(XXX)



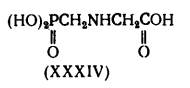
(XXXI)



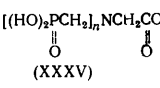
(XXXII)



(XXXIII)



(XXXIV)



(XXXV)

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After the review had been sent to the editors, a number of publications dealing with methods for the synthesis and properties of aminoalkyl organophosphorus compounds appeared.

β-Dialkoxyphosphinylethyl isocyanate was obtained by the Curtius rearrangement of the azide of β-dialkoxyphosphinylpropionic acid[495].

A number of α-aminophosphonic acids were synthesised by the Hofmann degradation of the amides of α-diethoxyphosphinylcarboxylic acids[496,497].

α-Aminophosphonates, tri-(γ-aminopropyl)phosphine, and the corresponding phosphine oxide were obtained by reducing the oximes of α-ketophosphonates[498], tri-(β-cyanoethyl)phosphine, and the corresponding phosphine oxide[499].

1-Alkyl-4-alkoxy-4-oxo-1,4-azaphosphorinanes and silicon-containing β-aminoethylphosphonic acid esters have been synthesised by the addition of primary amines and silicon-containing amines to divinylphosphinic[500] and vinylphosphonic[501] acid esters.

The interaction of alkali metal derivatives of benzyl phosphonates and phosphine oxides with β- and γ-chloramines led to the formation of a number of phosphorus analogues of methadone and their analgesic activity was studied[502].

The synthesis of dialkylphosphinobis(dimethylamino)methanes by the reaction of *NNN'N'*-tetramethylformamidinium chloride with lithium dialkyl phosphites and their disproportionation to bis(dialkylphosphino)dimethylaminomethane and tris(dimethylamino)methane have been described[503].

The condensation of trialkyl(aryl) phosphites with thiourea and urea has been suggested as a general method of synthesising α-ureidophosphonates[504].

Methods have been patented for the synthesis of nitrilotri(ethylenephosphonic) acid by the reaction of sodium and potassium dialkyl phosphites with tri-(2-chloroethyl)amine[505] and for the synthesis of ureidomethylphosphonyl halides by the reaction of phosphorus trihalides with alkoxymethylureas[506]. They have been suggested as fire resistant agents.

New polydentate *PN*-ligands have been obtained by the reaction of *N*-substituted ethylenediamines with diphenylphosphine and formaldehyde and their properties have been investigated[507].

The phosphonomethylation of silicon-containing[508,509] and heterocyclic[510] amines and glycine[511] with phosphorous acid and formaldehyde in hydrochloric acid has been described. The compounds thus obtained have been suggested as inhibitors of corrosion and scale formation and as complex-forming agents.

Dialkyl 1-(*N*-acylamino)-2,2,2-trichloroethylphosphonate esters have been obtained by treating *N*-1,2,2,2-tetrachloroethylbenzamide and *N*-acetyltrichloroacetaldimine with trialkyl phosphites and dimethyl phosphite[512,513].

It has been shown that magnesium derivatives of phosphorodiamidites readily add to Schiff bases[514];

N-allyl- and *N*-pyridyl-aminophosphonates have been synthesised by the reaction of dialkyl phosphites with Schiff bases [515,516]. A new method has been proposed for the synthesis of α-aminobenzylphosphonates by heating benzaldazines with an excess of diethyl phosphite in the presence of sodium diethyl phosphite—in the course of the reaction two molecules of diethyl phosphite add to the C=N bonds with subsequent reduction of the resulting 1,2-bis(diethoxyphosphinylbenzyl)hydrazine [517].

The kinetics and mode of the reactions of dialkyl(phenyl) phosphites with Schiff bases have been discussed [518,519].

The chromatographic determination of many aminophosphinic acids has been described [520,521], and it is suggested that they be identified with the aid of crystalline *N*-di- and *N*-tri-nitrophenyl derivatives [522]; the infrared and ^{1}H NMR spectra of certain aminoalkyldiphosphonic acids have been investigated [523,524].

It has been shown that the deamination of 2-amino-1-hydroxy-1-phenylethylphosphonic acid involves appreciable rearrangement with formation of phenylacylphosphonic acid [525].

Ion-exchange resins based on chloromethylated styrene-divinylbenzene copolymers containing β-aminoethylphosphonic [526] and (−)-α-aminobenzylphosphonic [527] acid groups have been synthesised and investigated; the synthesis and polymerisation of *N*-methacryloyl-β-aminoethylphosphonic acid has been described [528].

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Gas Chromatography in the Functional Group Analysis of Organic Compounds

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The role and trends in the development of chromatographic methods for the functional group analysis of organic compounds are discussed. Attention is concentrated on the analytical possibilities of using chemical reactions of the test compounds together with gas-chromatographic separation (chemical-chromatographic method).
The bibliography includes 192 references.

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I. INTRODUCTION

With the introduction of gas-chromatographic methods appreciable changes have occurred in recent years in methods for functional group analysis, particularly for the functional group analysis of volatile organic compounds. The application of combined methods in conjunction with gas chromatography has revealed a number of new possibilities. These include the following: (1) an improvement of the resolving power of methods for functional group analysis which have been transformed from methods for group identification into methods for the identification of individual compounds: this has permitted the successful solution of problems which could hardly be solved by earlier methods[1,2]; (2) an improvement in the reliability of the method, in particular a decrease of the errors associated with the stage involving the intermediate isolation of the pure substance; (3) reduction of the time required for analysis; (4) decrease in the amount of substance necessary for functional group analysis.

The application of gas chromatography is useful and justified also in combination with any traditional methods for functional group analysis. For example, the employment of physical (spectroscopic and electroanalytical) methods, which are used at the outlet from the chromatographic column for the analysis of the eluate, makes it possible to proceed from group identification to the identification of individual compounds; the employment of chemical methods in combination with chromatographic procedures makes it possible to increase greatly the range of reactions studied, whose products may be not only coloured or gaseous substance but in general any volatile compounds; this of course greatly extends the scope of the method. In combination with chemical methods for functional group analysis, gas-chromatographic procedures can be used also as kinetic techniques, since the reactivities of isomers are frequently different.

II. RETENTION PARAMETERS

The retention parameter of a compound is its chromatographic constant, which is directly proportional to its distribution constant between the gas and stationary phases (the determination of this constant taking into account adsorption interactions has been discussed, for example, by Berezkin[3]). The retention parameters depend on the structure of the molecule of the compound, in particular on the size and number of functional groups present in the molecule. Various workers have successfully used additive schemes to calculate the retention parameters[4-8]. The possibility, in principle, of detecting certain functional groups on the basis of retention indices should be noted[9]; however, this is possible only provided that the structure of the carbon skeleton of the compound being analysed is first established and the procedure is not very reliable[10]. We may note that, in order to improve the accuracy, the relative rather than absolute retention characteristics (relative retention time, relative retention index, etc.) are usually employed in such cases.

The properties of retention parameters can be used for functional group analysis. For example, the linear variation of the logarithm of the retention parameter with the number of methylene groups in a molecule is generally known for homologous series[11,12]. This permits a relatively simple solution of one of the complex problems of functional group analysis—the determination of the number of carbon atoms in the hydrocarbon group. The solution of this problem by other methods is much more difficult. Sakharov and coworkers[13,14] have shown that fractional-linear functions can be usefully employed to characterise the variation of the retention parameters.

In assigning the components of the mixture under analysis to a particular class of organic compounds, the variation of the retention volumes on two[15,16] or more[17,18] stationary phases of different polarity can be of significant assistance: $\lg V_{1i} = A \lg V_{2i} + B$, where V_{1i} and V_{2i} are the retention volumes of the ith compound in a particular homologous series on the first and second phases and A and B are constants.

It has been suggested that organic compounds of different types can be characterised by graphical relations for differences between logarithmic functions of relative retention parameters, for example relations of the type $\Delta I_{12} = f(\Delta I_{34})$, where ΔI_{12} and ΔI_{34} are the differences between the retention indices of the given compound on phases 1 and 2 and phases 3 and 4 respectively. The points corresponding to compounds of a given class are located on the above graphs in specific characteristic regions, which can be

usefully employed to identify the functional groups in organic compounds[19].

The method of identification based on the variation of the retention time with the reciprocal of the absolute temperature in one chromatographic column, proposed by Arakelyan et al.[20], is fairly laborious but relatively reliable.

All the methods indicated above have been used successfully in analytical practice and have been described in detail in monographs on chromatography[21–24].

III. INVERSE GAS CHROMATOGRAPHY

Inverse gas chromatography (IGC) is based on the use of a direct interaction between standard compounds and the test substance and the establishment of definite relations between the chromatographic characteristics of the standard compounds and the structure of the compounds used as the stationary phase. IGC is particularly useful in the study of involatile compounds (high-molecular-weight compounds and compounds unstable at elevated temperatures).

The IGC method permits the group identification of compounds used as the stationary phase. When the relative retention times of substances of different polarity (methanol, heptane, and toluene) are plotted in a triangular coordinate system using straight-chain paraffins, aliphatic alcohols, and acids as the stationary liquid phase, each of the above homologous series is characterised by a distinct range of values of the retention times for the standard compounds. We may note that certain isomeric compounds can also be distinguished with the aid of this method. Thus the spectra of the volatile standard compounds 1,3-butylene glycol and 1,4-butylene glycol and those of primary and secondary octyl alcohols are different. The above data indicate a fairly high sensitivity of the IGC method with respect to the nature and structure of the compounds. Similar results can be obtained also for polymeric systems.

The extensive factual data accumulated in gas chromatography on the application of polymers as stationary liquid phases for the separation of mixtures of volatile compounds lead to the conclusion that polymers can also be identified by the IGC method. Thus the retention volumes of phosphine are 1.75, 1.58, and 2.52 cm^3 on columns with silicone oils 702, VKZh-94 V, and PFMS-4 respectively[25]. In another example two polymeric compounds of the same type —poly(propylene glycol) with M = 1760 and poly(ethylene glycol) with M = 1540 — are characterised by markedly different retention parameters[26], which permits their identification by the IGC method.

The IGC method has been developed in greatest detail to characterise (identify) asphaltenes (M = 500–1000)[27].

Dorrence and Peterson[28] demonstrated the usefulness of employing in IGC chemical reactions with the stationary liquid phase investigated. In order to study the functional groups in asphaltenes, the asphaltene test specimen in the column was silylated, as a result of which the active hydrogen atoms in the hydroxy- and carboxy-groups were replaced by trimethylsilyl groups. Treatment of asphaltene with *NN*-bis(trimethylsilyl)acetamide at 160°C led to a sharp decrease in the specific coefficients for the interaction with the chosen volatile standards (phenol and propionic acid). This method can be used to characterise various polymeric compounds with functional groups.

We may note that, whereas the amount of test substance required for the IGC method on a packed column is about 0.4 g, it decreases to 3–4 mg when a capillary column is used[27]. The microversion of IGC is particularly important for polymers which are difficult to synthesize and in general for compounds which are difficult to obtain.

Since the problem of identifying polymers in may cases reduces to the determination of their molecular weights, we may mention the possibility of employing the relation between the retention parameters of volatile standard compounds and the molecular weight of the stationary liquid phase[29].

IV. SELECTIVE DETECTORS

One of the major requirements which must be met by detecting systems in gas chromatography, namely their universality, i.e. equal sensitivity to all the mixture components emerging from the chromatographic column, is a disadvantage in the identification of organic compounds. In functional analysis the main requirement which must be met by the detector is its selectivity and an ideal system would be one having specific sensitivity only to compounds of specified classes, whose signal would be proportional to the content of the corresponding functional group.

The automatic titrator[11] and the spectrofluorimetric detector[30] meet this requirement most closely. The first is designed for the selective determination of acids and bases in the eluate and is based, as its name suggests, on the automatic maintenance of a specified pH in the titration cell. The operation of the spectrofluorimetric detector, which is designed for the detection of aromatic groups, is based on the employment of the fluorescence[30] or ultraviolet light absorption[31] characteristic of aromatic compounds.

The detector with selective sensitivity to compounds having multiple bonds is of undoubted interest[32]. The detection principle involves passing the mixture of saturated and unsaturated compounds to be analysed through an ionisation chamber together with krypton, which is excited to a metastable state by radioactive emission. The metastable krypton atoms are capable of ionising the molecules of the unsaturated compound and in the presence of the latter an ionisation current is generated.

The electron capture detector, proposed for the first time by Lovelock and Lipsky[33], exhibits an enhanced sensitivity to alkyl halides, sulphides, carbonyl compounds with conjugated double bonds, organometallic compounds, nitriles, and nitro-compounds. The sensitivity of the detector to many types of compound reduces its value for the purpose of identification, but makes it irreplaceable in the determination of certain compounds present in nanogram amounts.

Other selective detectors, which can be divided into three main groups, exhibit a much higher specificity. Thermionic detectors, based on the increased conductivity of the flame in a flame-ionisation detector on combustion of organic compounds containing heteroatoms in the presence of alkali metal or alkaline earth metal salts, were used in early investigations mainly for the selective detection of halogen- and phosphorus-containing compounds[34,35]. When rubidium and potassium salts are used[36], the sensitivity for nitrogen-containing compounds increases, but the greatest sensitivity is achieved when caesium bromide is employed[37]. In the presence of caesium the thermionic detector may be used for the highly sensitive determination of silicon, tin, and lead compounds[38]. It has also been shown[39] that the signal of the thermionic detector with rubidium sulphate is proportional to the content of heteroatoms in the molecules of the substances being analysed and a formula has been proposed whereby it is possible to calculate the content of the heteroatoms (halogens, sulphur, phosphorus, and nitrogen).

The coulometric detector[40], which exhibits selective sensitivity to compounds containing halogens, sulphur, nitrogen and phosphorus, may prove to be of significant assistance in the identification of organic compounds. The detector design was developed further in studies by Stepanenko and Krichmar[41–44]. The ion-selective electrodes, which have recently come to be widely used in analytical chemistry, have also found applications in coulometric detectors for the determination of fluorine[45], sulphur, and chlorine[46]. Among other electrochemical detecting systems, mention should be made of a selective galvanic detector[47], which is sensitive to alcohols and aromatic and unsaturated hydrocarbons.

The group of spectroscopic detectors, a major advantage of which is (apart from a fairly high sensitivity in the determination of heteroatoms) a very high selectivity, has been developed vigorously in recent years. The simplest example of this group is the halogen detector based on the Beilstein effect, i.e. on the green light emission arising when halogen-containing compounds are introduced into the flame through a copper mesh[48]. The flame-photometric detector, which was initially proposed for the selective determination of phosphorus and sulphur[49], has been modified to determine many other elements. The operation of the detector is based on the measurement of the intensity of the characteristic emission lines of the flame in the presence of heteroatoms using a photo-multiplier. In the determination of sulphur- and phosphorus-containing compounds, 394 and 526 nm light filters are usually employed, but it has also been stated that the positions of these maxima have been determined inaccurately[50]. When the flame-photometric detector is sensitised by indium salts, its sensitivity to halogen atoms is increased selectively with a maximum in the region of 360 nm[51,52] or at 409.9 nm, which corresponds to the maximum in the emission spectrum of indium iodide[53]. The photometric recording of the flame emission from an alkali metal thermionic detector made it possible to distinguish chlorine, bromine, and iodine atoms[54] and the employment of metallic calcium ensures a selective determination of fluorine in the region of the spectrum near 529.9 nm.[55] Organomercury[56,57] and boron[58] compounds can also be analysed. It has been suggested that the disadvantage of the flame photometric detector, due to the mutual interference of the heteroatoms present (and also of their concentrations) on the observed emission, be eliminated[59] by measuring the ratios of the spectral line intensities for the elements being determined (at 256 nm for chlorine, 206.2 nm for iodine, 253.3 nm for phosphorus, 182.04 nm for sulphur, and 292 nm for bromine) to the intensity of the spectral line of the carbon atom at 247.9 nm, which is almost independent of the structure of the compound and the elements present in it[60].

Many other detectors are used for identification purposes (the mass-spectrometric detector has been particularly successful); selective detectors were surveyed in detail in an earlier review[61].

One should note that almost all specific detectors (with the exception of those mentioned at the beginning of this section) have only an indirect bearing on functional analysis, since they cannot show unambiguously within which functional group the given heteroatom is located. Therefore their application is more effective in elemental analysis of organic compounds, particularly when it is necessary to determine substances present in microamounts. However, there is no doubt that the detecting systems developed so far have assisted in the identification of unknown compounds. The preliminary introduction into the test compounds of a specific heteroelement using reactions characteristic of the given functional group (for example the introduction of bromine at the site of a double bond) with subsequent employment of a detector selective for the element introduced can probably be of some interest. When the given heteroatom is detected in the compound being identified, the presence of the expected functional group may be postulated with considerable certainty.

V. CHEMICAL-CHROMATOGRAPHIC METHODS

The combination of chemical and gas-chromatographic methods appears to be the most effective and flexible procedure in functional group analysis. There has been a steady increase in the proportion of studies involving chemical-chromatographic methods among all the investigations on gas chromatography. Fig. 1 shows that the contribution of these methods increased in 1972 almost by a factor of 1.5 compared with 1966 (data quoted in the bibliographic section of the Journal of Chromatography were used to plot this graph).

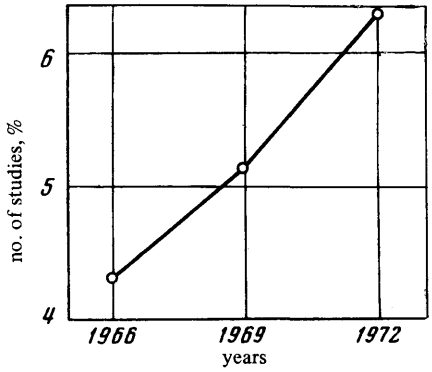

Figure 1. The number of studies on chemical-chromatographic analytical methods in relation to the total number of publications on gas chromatography.

Various methods are used to carry out the chemical reactions: reactions carried out outside the chromatographic system, reactions before the column, reactions in the column, and reactions after the chromatographic column. The choice of the reactions and of the conditions governing their occurrence is governed by the problem to be solved.

The effect of the reaction of the analytical mixture before the chromatographic process, involving a selective removal of components, makes it possible to assign the latter to specific classes by comparing the chromatograms obtained with and without the treatment of the sample by the selected reagents. This method has been called the substraction method.

The substraction process is carried out in a small column (reaction loop) filled with the selected chemical reagent, usually deposited on an inert carrier, like the stationary liquid phase. Under these conditions, it is even possible in many cases to use volatile reagents when the latter are deposited on a strongly adsorbing carrier[62,63].

If the sample analysed is introduced simultaneously into two columns connected in parallel having detector cells operated in a differential mode (the reaction loop is used in series with only one of the columns), then the chromatograph will show only the components eliminated[64]. The system suffers from the disadvantage that it is necessary to achieve an absolutely exact reproducibility in all the working parameters of both chromatographic columns; this can be obviated by including the reaction loop between the two detector cells[65] and by employing one column. The main requirement which the system must meet in this case is a small volume, which should be comparable to the peak width.

It is quite unnecessary that the compounds removed should be fully retained in the reactor in the form of involatile compounds. Even if reactions result in volatile products, the latter will have different elution times from those of the initial compounds, which can be clearly shown by subsequent chromatography. Moreover, the incomplete adsorption in the reaction column may be used to secure additional information about the structure of the compounds analysed. Thus the incomplete removal of *cis*-dienes in a reactor with maleic acid chloride makes it possible to distinguish them from the *trans*-isomers, which react faster and are completely eliminated in the reactor[66]; the employment of a reactor with boric acid ensures the separation of primary and secondary alcohols from their tertiary isomers[67,68].

The fillers in the reaction loops, used for the selective removal of a wide variety of different classes of compounds, have been described in detail in the literature[69,70].

Tricyclohexyl borate has been suggested for the selective absorption of alcohols[71]; metal hydrides can be used for the same purpose[72–74] and it has been noted[73] that aluminium hydride and lithium tetrahydroborate remove all compounds with oxygen-containing functional groups, except ethers. The complete elimination of aldehydes from the mixture analysed is achieved when *o*-dianisidine[74], sodium tetrahydroborate[73], or hydroxylamine hydrochloride[72] are used. The difference in the reactivity of boric acid towards various alcohols has been used to separate tertiary alcohols from primary and secondary alcohols[73,74] and the employment of sodium tetrahydroborate, which reacts slowly with ketones, makes it possible to distinguish the latter from aldehydes[73]. Prokopenko et al.[75] showed that the selectivity in the elimination of different oxygen-containing substances in reactors containing boric acid and lithium tetrahydroaluminate depends on the amount of the reagent. Thus tertiary alcohols can be completely removed in a reactor with a high boric acid content.

The method for the preliminary absorption of alcohols and carbonyl compounds in a reactor filled with 40% of 3-nitrophthalic anhydride and semicarbazide on Celite-545, placed directly before the separating chromatographic column[76], is also of interest.

The formation of adducts with urea is a characteristic reaction for the removal of n-alkanes[77,78] and methyl esters of aliphatic acids[79]. Ohtaki et al.[80] showed that all hydrocarbons with a straight-chain structure can be removed by the reaction with urea. In the subsequent treatment (reactions with hydroborates and oxidation) the olefins can be isolated in the form of the corresponding alcohols and can be determined gas-chromatographically. The overall olefin content in the initial mixture can probably be found also by determining the amount of hydroborate which has reacted.

Columns with *NN*-di-(2-cyanoethyl)formamide[81], mercury perchlorate[82], and alumina[83] have been used for the selective retention of aromatic hydrocarbons. Mercury perchlorate is also an effective absorber for unsaturated compounds[82,83]. It has been suggested that the group isolation of organomercury compounds be carried out either by including in the chromatographic system a short reactor with a powdered metal or by removing them by reaction with various sulphur-containing compounds[84].

A novel method has been proposed for the determination of the overall admixture of involatile organic substances[85].

In many instances it is useful to employ a reaction column with phosphoric acid, which permits the selective removal of nitrogen-containing organic bases from complex mixtures[86].

Examples of the determination of alcohols, ketones, aldehydes, esters, and aromatic hydrocarbons by reactions in a syringe have been described[87].

Qualitative chemical tests after chromatographic separation constitute a less common way of identifying the components of complex mixtures. One of the reasons for this is the low sensitivity of colour reactions, so that considerable amounts of the substance analysed, not less than 20–100 μg, have to be used[88]. It is possible to specify the two most interesting procedures for rapid qualitative tests. The first consists of the subdivision of the eluate from the chromatographic column into several approximately equal streams which are directed to test-tubes with group reagents for a specific class of compounds[88]. A colour change in one of the test tubes at the instant of the emergence of the peak is evidence that the substance belongs to the given class. The second method provides for the employment of a sorbent layer impregnated with the reagent for the given functional group and moving continuously relative to the stream of eluate from the column[89]. If the eluate contains a compound of the given class, then a coloured spot appears on the sorbent layer. By changing the reagent impregnating the sorbent and by comparing the results of the chemical study with the separation chromatograph, it is easy to determine the class of the compound corresponding to each peak. The advantages of the first method are the possibility of testing each peak for several functional groups and also the possibility of determining the nature of the components present at microconcentrations insufficient for the appearance of an appreciable colour by the successive introduction of several samples (provided that the colour of the solution remains stable for a sufficiently long time). The sensitivity of the method based on the subdivision of the eluate stream can be improved significantly by concentrating the substances in short porous glass traps filled with alumina[90]. When the flow rate through the trap is of the order of 5 ml min^{-1}, the majority of compounds investigated (aldehydes, ketones, alcohols, ethers, and aromatic and sulphur-containing substances) are trapped by the layer of packing 2–3 mm thick in the form of a concentrated band, which makes it possible to reduce the detection limit to the level of 0.1–1 μg. The specific reagents used for qualitative tests after chromatographic separation have been discussed[69,70].

All the methods for group analysis described above are applicable only to mixtures of volatile compounds which can be subjected to gas-chromatographic separation. In order to separate the components of mixtures of involatile or high-boiling compounds and assign them to specific groups, special procedures are used, many of which are also carried out in non-chromatographic reactors. Thus a number of procedures (esterification, decarboxylation, silylation, etc.) have been developed or applied in the gas chromatography of involatile compounds and also of highly polar substances whose separation is difficult. In particular, acetylation[91], silylation[91,92], and methylation[93] are used in the gas-chromatographic analysis of hydroxy-compounds; carboxylic acids are converted into the more volatile methyl esters or decarboxylated, etc. Without going into the details of these procedures (reactions of this kind for many classes

of compounds have been described in the literature[94]), we may say that the chemical reactions themselves can be regarded as one of the methods for group identification. In fact, the reagents employed are usually highly selective, for instance, when aldehydes or ketones are identified among the reaction products on treatment of the solid mixture with, for example, iodic acid and subsequent chromatography[95,96], it is possible to conclude with a high degree of certainty that the initial mixture contains α-hydroxycarboxylic acids.

Yet another useful feature of the above procedures should be indicated, namely the possibility of securing additional information about the qualitative composition of the mixture analysed on the basis of gaseous side products which are at present disregarded. Thus, in the conversion of phenols into methyl ethers by the reaction with diazomethane[97] nitrogen is evolved, ammonia is a side product in the silylation of involatile hydroxy-compounds[98], and in the decomposition (described above) of α-hydroxycarboxylic acids by iodic acid to yield the corresponding ketones or aldehydes[95,96] (which are not always convenient for chromatography) an equivalent amount of carbon dioxide is formed, etc.

Pyrolytic methods give rise to extensive possibilities for the identification of unknown compounds. Compounds which permit qualitative and quantitative inferences concerning the presence of specific functional groups in the specimen are as a rule formed in the pyrolytic decomposition of the substance analysed.

The thermal decomposition of organic compounds in the presence of sulphur vapour at 850–880°C gives products which yield information for the identification of many functional groups[99]. Thus the products formed in the pyrolysis of aldehydes, ketones, ethers, esters, alcohols, sulphonic acids, amino-compounds, and acids have been investigated in this way. The nature and ratios of the volatile pyrolysis products (nitrogen, hydrogen sulphide, carbon monoxide, carbon dioxide, carbon disulphide, and sulphur dioxide) are largely determined both by the structure of the initial compounds and by the presence of functional groups in the molecules.

The pyrolysis products (hydrogen, carbon monoxide and dioxide, methane, water, etc.) of substances in an inert gas atmosphere and their ratios also characterise the functional groups in the initial specimen[100–102]. Thus ketones and aldehydes give rise to CO, alcohols to CO_2 and H_2O, esters to CO_2, H_2O, and CO, acids to CO_2, mercaptans to hydrogen sulphide, halogen-containing compounds to the corresponding hydrogen halides, and the decomposition of amines results in the evolution of ammonia[101]. However, since the quantitative aspects of the formation of characteristic products were not determined in the published investigations, the methods based on pyrolytic decomposition are at present applicable mainly to qualitative analysis only.

On thermal decomposition in the presence of a catalyst [copper(II) oxide], hydrazine derivatives evolve methane; this made it possible to devise a method for their quantitative chromatographic determination[103].

The possibility of employing the effects of electron impact and of electric discharges in functional analysis has been studied[104,105]. It has been shown that, by decomposing the specimen analysed in an electric discharge, it is possible to assign the substance to a particular homologous series[104]. The study of the products formed in the decomposition of alcohols, aliphatic and aromatic hydrocarbons, ethers, esters, ketones, and aldehydes in an electric discharge established that methane is formed from all the test compounds and acetylene is generated by compounds with an ethyl group. The decomposition products of all aromatic compounds contain benzene and carbon monoxide and dioxide are present in those of oxygen-containing compounds.

Examples of the employment of thermal decomposition methods for the analysis of certain other groups will be discussed below.

It is necessary to consider especially methods for the quantitative determination of functional groups. In principle any classical gas-volumetric analytical method can be modified for chromatography but it would be very wrong to assume that the only problem is to replace one method by another, even if the latter is more up to date and more automated (although these advantages are important, particularly in routine determinations). Chemical-chromatographic methods give rise to distinctly new possibilities. These include simultaneous qualitative (from the retention time) and quantitative (from the signal intensity) determination of the desired reaction product in the complex reaction mixture, the possibility of the simultaneous determination of several reaction products with similar chemical properties, which in chemical methods can be determined only as a single group, the separation of the desired reaction product from side products, which is frequently a potential source of errors in classical methods, the possibility, in principle, of employing reversible reactions, since one of the products is continually removed from the reaction system by the carrier gas, a high sensitivity of the determination, which makes it possible to carry out a complete analysis of microspecimens, rapidity of the determinations, and finally the possibility of complete automation of the entire analytical process.

The use of chemical reactions (or specific thermal decomposition), leading to reaction systems of two types, has now been described for the quantitative analysis of functional groups in organic compounds. If the reaction products are compounds with physicochemical properties similar to those of the other ingredients of the reaction mixture, then an aliquot part of the latter is chromatographed. This procedure involves a decrease of the sensitivity of the determination (only part of the mixture is analysed), the possibility of loss of the required product and hence of a decrease in the accuracy of the analysis, and also additional difficulties in the automation of the analytical process. It is more convenient although not always possible to employ reactions which lead to the formation of either a gaseous or a volatile product, which characterises specifically the functional group being determined. The final product (or products) are in this case directed to chromatographic analysis either immediately from the reactor or after intermediate concentration.

The employment of chemical-chromatographic methods for the quantitative determination of specific functional groups is discussed below.

1. Determination of Active Hydrogen

The quantitative determination of active hydrogen is based on the known reactions of the compounds analysed with a Grignard reagent or with lithium tetrahydroaluminate. In the first case the reaction results in the evolution of methane, the gas-chromatographic determination of which is fairly simple. It is noteworthy that all the errors of the classical method[106], associated with additional gas evolution (for example, the evolution of ethane appearing as a result of the decomposition of the Grignard reagent) can be readily eliminated in the final chromatographic step[107–110].

The employment of lithium tetrahydroaluminate[111–114], which reacts with active hydrogen atoms in several seconds even at room temperature, is of considerable interest. Methyl, ethyl, n-propyl, and n-butyl ethers, tetrahydrofuran

(THF), dioxane, and ethylmorpholine[115] can be used as solvents, which greatly extends the range of applications of the method compared with the classical chemical determination. THF is a particularly satisfactory solvent for many organic compounds[111,118].

The method for determining active hydrogen was largely the same in all the studies mentioned. A solution of lithium tetrahydroaluminate in a suitable solvent is poured into the reaction cell, a sample of the substance analysed is positioned without coming into contact with the solution (for example the specimen can be put in a dish resting on the reactor stopper[114]), the reaction cell is flushed with the carrier gas and then disconnected from the chromatographic system, and the sample is plunged into the solution. After the completion of the reaction, the cell is reconnected to the chromatograph and the hydrogen evolved is determined in a column with activated charcoal or molecular sieves. A cell designed as a standard attachment of a chromotograph[117], which we believe to be the most convenient for the analysis of liquid substances, has been described for reactions with lithium tetrahydroaluminate.

However, we may note that the high reactivity of lithium tetrahydroaluminate can in many cases constitute a disadvantage, since certain compounds which do not contain active hydrogen are converted into substances containing such hydrogen as a result of the reduction by the reagent.

In this connection we may mention the methods for the determination of active hydrogen linked to a silicon atom, based on the hydrolysis of the organosilicon compound in the presence of potassium hydroxide for 15s and accompanied by the evolution of an equivalent amount of hydrogen, which is determined gas-chromatographically[118].

2. Determination of Amino-groups

Various modifications of the gas-chromatographic method for the determination of primary amino-groups in organic compounds, based on the well-known deamination reaction first used for the quantitative determination of amines by Van-Slyke[124], have now been proposed[119–123]. The nitrogen evolved as a result of the reaction can be readily separated from the accompanying gases in a column with 5 Å molecular sieve for routine analyses, reaction systems[122,123] are preferable in which provision is made for the stirring of the solution during the deamination reaction, a bubbler-type reactor is used (which guarantees freedom from errors associated with the solubility of nitrogen in the reaction mixture), and provision is also made for the absorption of nitrogen oxides which corrode the metallic components of the chromatograph. The duration of analysis does not usually exceed 15 min, the error is not more than ±0.3–0.4%, and the sensitivity of the determination reaches 0.07 mg of amino-nitrogen.

A modification of the method[125], in which solid sodium nitrite deposited on Celite C-22 is suggested instead of the nitrite solution normally employed, is of interest. In addition an internal standard (THF) is introduced into the reaction solution, which obviates the necessity of daily calibration of the apparatus.

The reaction with acrylonitrile has been suggested for the determination of amino-groups[126]; the excess of acrylonitrile which has failed to react is determined gas-chromatographically on a column with poly(ethylene glycol)-300 at 100°C. A similar method, also based on determination of an excess of the reagent which has failed to react, has been proposed for the analysis of relatively involatile primary amines by reaction with benzaldehyde[127]. All the characteristics of the method for the determination of amino-groups with a final gas-chromatographic step are superior to those of the classical Van-Slyke method. An important advantage of the former is also that it fully eliminates errors associated with the presence in the gas mixture of nitrogen oxides and other gaseous substances[128–130] which are not absorbed by an alkaline potassium permanganate solution and which constitute a potential cause of unduly high results.

3. Determination of Alkoxy-groups

The determination of alkoxy-groups in the form of the corresponding alkyl iodides, which are formed by the Zeisel reaction[131] when the compound analysed is refluxed in hydriodic acid, constitutes the basis of almost all gas-chromatographic methods. The classical chemical analysis of alkoxy-compounds is one of the most time-consuming and laborious methods in functional group analysis and yields only the overall content of alkoxy-groups. The ease of gas-chromatographic separation and quantitative determination of alkyl iodides (for example, the separation of 24 C_1–C_{10} alkyl iodides has been described[132]) from the very beginning indicated the likely usefulness of chromatography in analysis, which has been reflected also in the number of publications on this problem[133–147]. In early investigations the alkyl iodides were usually subjected to intermediate concentration in cooled traps with the liquid solvent (n-heptane) and as early as 1961 the contents of C_1–C_4 alkoxy-groups were determined by this procedure[137]. Silica gel[139,141], kieselguhr[140], and Apiezon L on silica gel[143] were employed to concentrate the mixture using high-temperature desorption at 150–170°C. Ehrenberger[140] was able to determine as many as five C_1–C_4 alkoxy-groups present simultaneously. To improve the accuracy of the analysis, the gas-chromatographic separation was employed together with gravimetric[139] and iodometric[140] determination of the amount of alkyl iodide, the accuracy of determination improving to ±0.05 abs.%. The overall duration of analysis is determined by the duration of the reaction with hydriodic acid and ranges from 1 to 3 h.

In 1968 Chumachenko and Kolesnik[148] showed that, in the reaction of organic substances with hydriodic acid in a hermetically sealed tube at 130°C, alkyl iodides are quantitatively split off in the course of 5–10 min, which made it possible to develop methods for the rapid determination of methoxy-[145] and ethoxy-groups[146] in organic compounds. The apparatus is illustrated schematically in Fig. 2. The sample of the substance (1–2 mg) was placed in a 10 × 0.8 cm test tube, 0.3 ml of hydriodic acid (or a mixture of 50 mg of potassium iodide and 0.05 ml of orthophosphoric acid) was poured in, the tube was closed, and kept at 130°C for 10–15 min in the determination of ethoxy-groups or 5 to 12 min in the case of methoxy-groups. The stream of nitrogen was then switched to flush the reactor and the alkyl iodides split off were transferred by the carrier gas to a column with Polysorb-1, where they were separated. Absorption tubes with potassium carbonate and calcium chloride were used to absorb moisture and the acid vapour. The entire apparatus was made of glass and Teflon. The overall duration of the analysis was 15–20 min or 25–30 min in the determination of methoxy- and ethoxy-groups respectively and the accuracy was at least to within 0.2 abs.%. The determination of the relatively volatile methyl and ethyl iodides was possible when these were transferred directly by the carrier gas from the reactor to the chromatographic

column, but in the analysis of C_3-C_5 alkoxy-groups intermediate concentration will probably be a necessary step.

The method for the determination of alkoxy-groups in carboxylic acid esters which are difficult to hydrolysed, based on their alkaline fusion at 240–360°C in the presence of sodium alkoxide, merits consideration[149]. The alcohols evolved in this process are trapped in a cooled trap and then analysed gas-chromatographically. Fig. 3 presents a chromatogram for the separation of the alcohols formed in the analysis of a mixture of polychloroacrylates. Calculation showed that the reaction proceeds with quantitative liberation of the alcohols from the corresponding esters. The alkaline fusion method has been used also to determine the alkoxy-groups in polysiloxane[150].

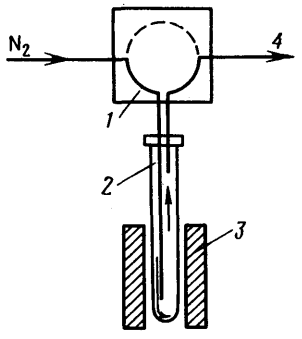

Figure 2. Apparatus for the determination of alkoxy-groups[148]: *1*) diaphragm valve; *2*) reactor; *3*) heater; *4*) outlet to chromatographic column.

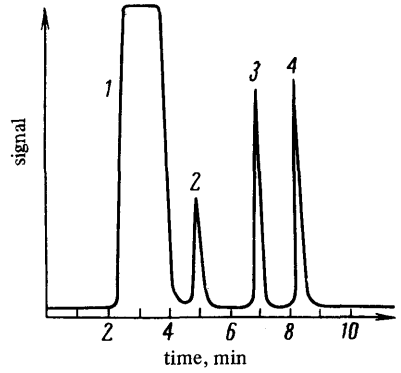

Figure 3. Chromatogram of the products of the alkaline fusion of poly(methyl α-chloroacrylate), poly(ethyl α-chloroacrylate), and poly(isopropyl α-chloracrylate)[149]: *1*) water; *2*) methanol; *3*) ethanol; *4*) isopropyl alcohol.

A method has been described for the determination of ethoxy-groups by oxidising the specimen with CrO_3 and subsequent analysis of an aliquot part of the reaction solution for acetic acid[151].

Among other methods, mention should be made of the determination of hydroxy-ethyl groups in the form of acetanilide, formed quantitatively from the initial specimen on pyrolysis carried out at 400°C for 10 min[152], and also the determination of alkoxy-groups by a hydrogenation method[141]. The latter procedure is particularly attractive, since the alkoxy-groups are eliminated in a flow reactor, which significantly reduces the duration of the determination and the saturated hydrocarbons formed on hydrogenation can be extremely conveniently separated and detected. The substance analysed enter a hydrogenation tube containing 2.0–2.5 ml of the catalyst (5% of platinum on kieselguhr or 1.5% of platinum on porous glass) and heated to 325°C. On hydrogenation, the alkoxy-groups are split off in the form of hydrocarbons, which either enter a 5 cm column with activated charcoal at 20°C (determination of C_1-C_2 alkoxy-groups) or a 50 cm column with silica gel (determination of C_3-C_5 alkoxy-groups).

It is noteworthy that, despite their inadequate reproducibility, the gas-chromatographic methods for the determination of alkoxy-groups are fairly widely used nowadays and in the immediate future may completely replace classical chemical analytical methods.

4. Determination of *S*-, *N*-, and *Si*-Alkyl Groups

The rupture of C–N, C–S, and C–Si bonds is many times more difficult than the rupture of the C–O bond. Therefore much more severe conditions than those described above are used for the determination of the corresponding alkyls. At the same time the different reactivities of the alkyls bound to S, N, and Si atoms can be used for their separate determination. Thus a method has been proposed for the quantitative determination of alkoxy- and *N*-alkyl groups present together[153]. In the first stage the alkoxy-groups are split off and determined under conditions analogous to those already described, after which the reactor is heated to 300°C (20 min) and then to 350°C (10 min). Under these conditions, the N–C bonds are broken and the resulting alkyl iodides are determined gas-chromatographically with intermediate concentration at a low-temperature.

The dissociation of C–S bonds in organic sulphides can be achieved with the aid of a suspension of Raney nickel in ethyl, n-butyl, or cyclohexyl alcohol[154]. The reaction is carried out in a simple microreactor (Fig. 4) consisting of a test-tube with two syringes for the injection of the reactants and for the removal of the gaseous reaction products. The corresponding hydrocarbons formed from the alkyl groups are separated and identified in a gas chromatograph connected to the reaction cell.

A similar reaction system was used also to determine alkyl groups linked to a silicon atom[155,156]. In this case the reaction with concentrated sulphuric acid in the presence of a vanadium catalyst was employed. Heating of the organosilicon compound being analysed to 175°C for 15 to 20 min in the above medium leads to the elimination of alkyl groups linked to silicon in the form of the corresponding hydrocarbons (methane from methyl groups, benzene from phenyl groups, etc.), the gas-chromatographic separation and identification of which presents no difficulty. Ethyl and phenyl groups can also be determined quantitatively by their thermal dissociation from the silicon atom with formation of ethane and benzene[157]. The reaction is carried out in the presence of phosphorus pentoxide in water, with the temperature raised from 20° to 500–580°C (depending on the group being determined).

A method has also been described for the determination of alkyl groups in aromatic compounds by their catalytic abstraction in a stream of hydrogen to yield saturated hydrocarbons[158–159].

It was shown recently[158] that the alkoxy-groups in organosilicon compounds can be identified by determining the products of the reaction of the substances analysed with boron tribromide. The alkoxy-groups are split off in the form of alcohols (which are then converted into unidentified compounds).

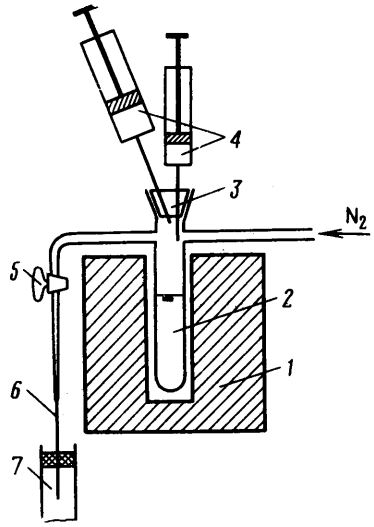

Figure 4. Schematic illustration of the microreactor[154]: *1*) heated block; *2*) glass reactor; *3*) rubber stopper; *4*) syringes; *5*) shut-off tap; *6*) needle for injection into the column; *7*) upper part of chromatographic column.

5. Determination of Acyl Groups

Virtually all the methods developed so far are based on the transesterification of the initial specimen with sulphuric acid, a mixture of methanol with hydrochloric or toluene-*p*-sulphonic acid, and a mixture of toluene-*p*-sulphonic acid and its methyl ester[160–165]. In the first gas-chromatographic method described[160] the simultaneous qualitative and quantitative determination of formyl and acetyl groups on a single sample was already achieved. The sample of the test substance, toluene-*p*-sulphonic acid, and methanol were introduced into the reactor and the reaction was carried out at 70–80°C for 30 min. The reaction products were then collected in a cooled trap and an aliquot part of the distillate was analysed. Methyl formate and methyl acetate were separated from one another and from methanol in a column with Carbowax-1500.

The gas-chromatographic separation of acyl groups up to butyryl and isobutyryl groups was described later[164,165]. The transesterification was carried out in a mixture of toluene-*p*-sulphonic acid and its methyl ester at 225–230°C for 20 min and the substances evolved were chromatographed on compound columns with poly(ethylene glycol adipate) and a T-1 emulsifier by passing the carrier gas through the reactor. In this analytical method the accuracy, reproducibility, and sensitivity are naturally higher than in the analysis of only part of the solution. It was noted[164] that the yield of methyl acetate in the transesterification reaction is 90% and therefore an appropriate correction factor must be applied in the calculation.

Alkaline hydrolysis[162] with subsequent gas-chromatographic determination of acetic acid can also be used to identify the acetyl group.

6. Determination of Hydroxy-, Carboxy-, and Carbonyl Groups.

The quantitative determination of hydroxy-groups can be achieved by estimating the active hydrogen[166]. The methane evolved in the reaction between a hydroxyl-containing polymer and a Grignard reagent is determined with the aid of a column containing a 5 Å molecular sieve connected directly to a column filled with 10% of *N*-methylpyrrolidinone on alumina, in which methane is separated from the solvent. The authors showed that the gas-chromatographic method permits the determination of hydroxy-groups at concentrations so low that chemical methods are inapplicable.

A more specific method for the determination of primary and secondary alcohols is based on the reaction of the specimen being analysed with acrylonitrile and the determination of the excess of the latter by chromatography on a 3 m column filled with Chromosorb containing 10% of poly(ethylene glycol)-3000.[167]

The microdetermination of carboxy-groups can be achieved by decarboxylating organic acids by pyrolysis in helium in the presence of copper carbonate and quinoline, the specimen being heated for 45 min in a reactor at 225°C.[168] The carbon dioxide evolved is determined gas-chromatographically. To increase the productivity of the method, it is recommended that a system of three reactors, connected in parallel, be used.

The reaction of α-aminoacids with ninhydrin serves as the basis of a method for the determination of carboxy-groups in aminoacids from the amount of carbon dioxide evolved[169]. The reaction is carried out in a system consisting of an attachment to a standard chromatograph. The sample of the substance (3–5 mg), a buffer mixture at pH 4.7, and about 50 mg of ninhydrin are placed in the cooled reaction vessel, which is flushed with the carrier gas, whereupon the latter is disconnected and the system is heated to 100°C. When the reaction is complete (after 3 min), the reaction system is again connected to the chromatograph and the carbon dioxide evolved is determined on a column with AG-3 activated charcoal. The duration of analysis is 10–15 min and the standard deviation of the determination is ±0.39%.

The method for the determination of carboxy-groups by the pyrolysis of the specimen at 1000–1100°C in sulphur vapour is very interesting[170]. The carboxy-groups are then quantitatively split off in the form of carbon disulphide, which is determined using silica gel.

The pyrolytic method has been successfully applied also in the determination of carbonyl groups[171]. The analysis is based on the fact that in the pyrolysis of different ketones and methyl esters of aromatic acids dissolved in carbon tetrachloride in an atmosphere of argon, carbon monoxide is formed in an amount equivalent to the content of the group being determined. The pyrolysis is carried out in a reactor filled with crushed quartz at 800–860°C.

7. Determination of Sulphur-containing Groups

It is recommended that alkane- and arene-thiols be determined quantitatively by reaction with acrylonitrile and

subsequent determination of the excess of the latter which failed to react[167]. The reaction is carried out in a pyknometer for 1–2 min and the solution is analysed gas-chromatographically.

In the determination of sulphate and sulphite groups in organic substances, reductive hydrolysis in phosphoric acid in the presence of a tin(II) salt for 15 min at 300°C can be used[172]. A column with silica gel is employed to separate the hydrogen sulphide evolved from other gases.

It has been suggested that arenesulphonic acids and their salts be determined by alkaline fusion[173] and pyrolysis[174]. In the first case the process is carried out in apparatus (Fig. 5) consisting of a quartz tube part of which is inserted in a cylindrical furnace. Several milligrams of potassium hydroxide and sodium alkoxide are added to the test sample in a platinum boat. The fusion is carried out for 20 min, after which the boat is removed from the hot zone and placed under an outlet with a rubber membrane through which a saturated aqueous solution of maleic acid is injected into the boat from a syringe. The maleic acid displaced phenols from the melt. The boat is then again moved to the heated space and the volatile products are determined chromatographically.

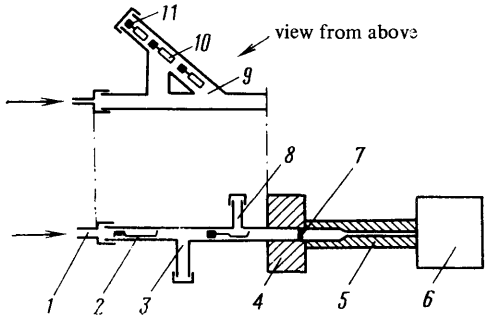

Figure 5. Attachment of alkaline fusion[173]: *1*) inlet for carrier gas; *2*) retraction device; *3*) pocket for the ejection of boats after analysis; *4*) furnace; *5*) heated connection to the chromatograph; *6*) gas chromatograph; *7*) device limiting the travel of boats; *8*) outlet with rubber membrane; *9*) outlet for boats with samples; *10*) platinum boat; *11*) device for moving boats.

Sulphur dioxide in an amount equivalent to the content of the sulpho-groups is evolved by the pyrolysis of arenesulphonic acids and their salts at 710–790°C in the presence of added silicic acid[174]. The pyrolysis products are separated on a column with Porapak Q, which also permits the simultaneous determination of the initial hydrocarbon formed in an amount up to 50% (Fig. 6). The method is particularly interesting, because in certain cases the addition of a hydrogenating agent (for example, a carbohydrazide) to the specimen undergoing pyrolysis increases the yield of the initial hydrocarbon to the theoretical value (thus the yield of benzene from benzenesulphonic acid was 98%), which in principle makes it possible to identify the specimen fully on the basis of a single sample.

8. Determination of Vinyl and Alkyl Groups

The vinyl groups in organosilicon polymers can be determined by the pyrolysis of the initial specimen and subsequent gas-chromatographic determination of the relative amounts of ethylene and methane in the volatile pyrolysis products[175].

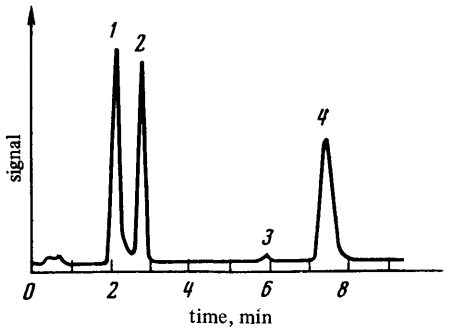

Figure 6. Chromatogram of the pyrolysis products of toluene-*p*-sulphonic acid[174]: *1*) water; *2*) sulphur dioxide; *3*) benzene; *4*) toluene.

The elimination of terminal vinyl groups in the form of ethylene when the specimen of the organosilicon polymer is treated with concentrated sulphuric acid also served as the basis for the development of an analytical method[176]. The sample is placed in a reactor, 450 μl of 90% sulphuric acid is poured in, the solution is heated in a stream of helium from 65° to 250°C (at a rate of 10 deg min^{-1}), and the decomposition products are trapped at low temperatures. When the reaction is complete (after approximately 1.5 h), the trapped volatile products are determined chromatographically. It was shown that vinyl groups are quantitatively converted into ethylene, ethyl groups into ethane, and methyl groups into methane.

Methods have been described for the identification of vinyl groups in the form of ethylene after alkaline hydrolysis[158] and alkaline fusion[150].

It has been suggested that alkyl groups be determined by the degradative decomposition of the test substance in a stream of hydrogen, which serves at the same time as the carrier gas, in the presence of a catalyst: a mixture of aluminium oxide silicate with quartz impregnated by tungsten and molybdenum oxides[177].

9. Determination of Unsaturated Bonds

Before the start of any determination of functional groups, it is important that the investigator knows about the presence and positions of unsaturated bonds for a correct choice of reaction conditions in order to avoid side processes, which frequently involve unsaturated bonds. We therefore feel it useful to consider, if only briefly, the main advances achieved in chromatographic methods in this field.

It is well known that the oxidation of substances containing multiple bonds by oxidising agents such as potassium permanganate and periodate, etc. results in the cleavage of the

molecule at the site of the bond with formation of two or more fragments (depending on the number of unsaturated bonds). Chromatography in all its versions is the most promising procedure for solving the problem of separation and identification of fragments which then arises and this has been reflected in a large number of published studies on chromatographic methods for the determination of the number and location of unsaturated bonds. It is noteworthy that in certain cases involving the formation of complex mixtures of oxidation products identification for the determination of the structure is frequently altogether impossible without a final chromatographic step.

The widely used methods involving oxidation with potassium permanganate in acetic acid[178], frequently resulting in too far reaching oxidation, and with the milder potassium permanganate–potassium periodate mixture[179] have been rapidly giving way recently to the ozonolysis method first proposed by Bon[180]. It is based on the formation of ozonides, their decomposition, and gas-chromatographic identification of the products.

Several types of apparatus, mainly of similar design[181–183], ensuring an ozone concentration of about 2.5–3.0%, have been developed. The usual sequence of steps is as follows[184–188]. The test substance (10–100 μg) in ethyl acetate or carbon disulphide (the use of a solvent for solids is not obligatory[186]) is placed in the reaction tube, the mixture is cooled to a temperature from -70° to 10–15°C (depending on the nature of the substance being analysed), and a stream of oxygen enriched with ozone is passed through the reactor until the initial concentration of ozone is restored at the outlet from the tube. The ozone is detected at the outlet with the aid of a solution of potassium iodide and starch in sulphuric acid. When the reaction is complete (after 0.5–5.0 min), nitrogen is bubbled through the solution and, after the decomposition of the resulting ozonides, the products are analysed gas-chromatographically. Depending on the structure and number of unsaturated bonds, the main products are formaldehyde, acetaldehyde, acetone (in the presence of isopropylidene groups), glyoxal (particularly from compounds with conjugated double bonds), carbon dioxide (in the presence of cumulative bonds), and other aldehydes and aldoesters.

The ozonides are decomposed either with the aid of a triphenylphosphine powder[185,189] or thermally[190,192]. A microreactor in which the specimen with a volume up to 5 μl may be ozonised, decomposed, and injected into the gas chromatograph without any transfer of the test substance and associated losses has been described for the latter case[186].

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In this review the authors deliberately did not consider the methods for the determination of the carbon skeleton of organic compounds, which constitute one of the branches of functional group analysis and significantly facilitate identification. The possibilities and achievements of gas chromatography in this field are very great and require special consideration. The determination of the carbon skeleton by hydrogenation has been described in detail in Beroza's review[192].

The survey of the principal achievements of gas chromatography in the qualitative identification of organic compounds and quantitative determination of functional groups leads to the conclusion that, by virtue of the sum total of its advantages, the application of gas chromatography has now resulted in radical changes in one of the most important branches of organic chemistry–functional group analysis, particularly in the study of multicomponent mixtures. We may note that the traditional chemical methods have not lost their value. On the contary, the greatest advances have been achieved precisely in those cases where gas chromatography is used in combination with traditional chemical methods.

It is noteworthy that the growth in the use of gas-chromatographic methods in analytical practice is now held back by the lack of a universal chromatographic apparatus with different reactors designed for functional group analysis with simultaneous employment of chemical and chromatographic procedures.

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The Periodic Law and Progress in the Study of the Structure of Matter†

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A survey is made of the diverse achievements of Soviet scientists, rising to one of the founders of Russian chemistry—the genius D.I.Mendeleev and his greatest work—the periodic law, which has exerted an immense influence on the development of physics and chemistry at all four conceptual levels in the structure of matter—elementary particles, nuclei, atoms, and molecules. Consideration is given to the fundamental contribution made by Soviet scientists to predicting, discovering, and studying new isotopes and new types of radioactivity, to synthesising new transuranic elements and establishing their valency states (sometimes completely unexpected), and to founding the chemistry of "new atoms", in which proton and electron have been replaced by other elementary particles.

The principal modern methods for studying the structure of matter are based on the recording of hyperfine interactions between electrons and nuclei, electrons of outer and inner shells—i.e. essentially interactions between periodic and monotonic functions of the atomic numbers of the chemical elements. Soviet scientists both discovered the hyperfine interactions and made the most important contribution to their chemical utilisation (the discovery of electron spin resonance, the introduction of e.s.r. and γ-resonance spectroscopy into chemistry, the widespread application of nuclear magnetic resonance to chemistry, the establishment of photoelectronic spectroscopy in the ultraviolet and of accurate X-ray chemical spectroscopy, etc.).

The work of Soviet theoretical chemists in basing the periodicity in the properties of chemical elements on the molecular orbital method is reported, and illustrates how the periodic law preserves its fertility even at the modern quantum-mechanical level of attacking the problem of chemical bonds.

A list of 157 references is included.

The emergence and growth of chemical sciences in our country are indissolubly linked with three great names—M. V. Lomonosov, A. M. Butlerov, and D. I. Mendeleev—which we cannot fail to remember on the anniversary of our Academy. Each of these giants left an indelible mark in the history of science. Among the three, Mendeleev received the fullest recognition during his lifetime. More than 130 honorary titles and diplomas were conferred on him by Russian and foreign scientific societies, universities, and academies. But with all the brilliance of the confirmations of Mendeleev's chief creation—the periodic law—during his lifetime, its immense significance was disclosed still more fully by his successors. Mendeleev's feeling that "... the future will not threaten the periodic law with destruction but will only promise a superstructure and further development..." was realised[1].

For a long time a kind of hierarchy of the natural sciences—mathematics, physics, chemistry, biology—has been established, in which a "senior" science enriches a "junior" science with methods and concepts, thus stimulating its development. The periodic law was a brilliant example of the reverse relation in this hierarchy—an enormous and ramified influence of a chemical discovery on the development of physics.

Rutherford's discovery of the atomic nucleus and Moseley's investigation of X-ray spectra revealed the physical meaning of the serial number of an element in Mendeleev's system as the positive charge on its nucleus. Bohr's theory linked the planetary model of an atom with

† This paper is an expanded text of a lecture at the 250th Anniversary General Meeting of the USSR Academy of Sciences.

the quantum theory, gave a theoretical interpretation of the origin of periodicity in the chemical properties of elements, and enabled the structure of the sixth period in Mendeleev's system and the properties of the then unknown hafnium and rhenium to be predicted. But another consequence of comparing the periodic system with the quantum theory—Pauli's "exclusion principle" formulated in 1925—acquired a special and immeasurable importance. A path could be traced from Mendeleev through the Pauli principle to the Fermi-Dirac statistics and further to the theory of the valency bond, to the theory of atomic nuclei and universal weak interaction, of metals and semiconductors, superconductivity and superfluidity.

Mendeleev's law—or at least his method of systematisation and periodisation of the properties of known materials and extrapolation to new, as yet undiscovered materials—has found and finds wide application at all four levels (elementary particles, nuclei, atoms, molecules) in the science of the structure of matter. All the achievements in revealing a system in what was till recently chaos provide a guarantee of a deeper insight in the future. How clearly the great Mendeleev understood this is evident even from such remarkable words of his: "It can readily be supposed—but cannot yet be proved—that the atoms of elements are composite materials formed by the addition of several still smaller parts, that what we term indivisible (the atom) is indivisible only by ordinary chemical forces, as particles are indivisible under ordinary conditions by physical forces ... Such a view is evidently supported by the periodic relation I have formulated between properties and weight ..."[2].

The present Review will be concerned mainly with the most recent achievements of scientists—especially of Soviet scientists—in studying the structure of matter at the atomic and molecular levels, i.e. chemical structure. But first we must refer to elementary particles, especially to nuclei.

Recent decades have been marked not only by the discovery of a multitude of new elementary particles but also by the first major successes in their systematisation and the prediction of new particles on this basis. The author of the first systematic account of elementary particles, based on the introduction of a new (strangeness) quantum number and on application of the concepts of group theory, the American Nobel prizewinner Gell-Mann, makes a direct reference to the analogy between his work and Mendeleev's discovery of regularities in the properties of the chemical elements. He suggests that the system of particles will lead to a theory explaining their interactions, as the Pauli principle and quantum mechanics arose to explain the regularities and properties of atomic systems found by Mendeleev.

A still closer and still fuller analogy exists between the classification of the elements and the generally accepted classification of atomic nuclei based on the concept of the presence of many neutron and proton shells. This shell model of the nucleus led to the discovery of such an extremely important property of nuclear forces as their well developed dependence on the relative orientation of the spin and the orbital moment of the nucleons (neutrons and protons). Nevertheless, the creation and development of the shell model of the nucleus resulted from advances in the study of radioactivity, in particular the isomerism of artificial radioactive isotopes discovered in the USSR by Kurchatov and his coworkers in 1935.[3]

The fundamental contribution by Soviet scientists to the investigation of radioactivity—the spontaneous transmutation of chemical elements—can be illustrated by Fig. 1, which represents diagrammatically five main elementary types of radioactivity either already observed or predicted. Only two of them—α- and β-disintegration—were known by the end of the nineteenth or the beginning of the twentieth century. The third type—spontaneous fission—was discovered in 1940 in the USSR by Petrzhak and Flerov[4], at that time young students of V. G. Khlopin and I. V. Kurchatov. The fourth type—proton radioactivity—was suggested long ago by Rutherford, but was predicted from modern theories only in the 1950s by Soviet scientists[5-7], and observed experimentally only in 1970 in the cobalt-53m isomer[8]. The fifth and final type—two-proton radioactivity—was predicted in the USSR in 1960[6,9] and has not yet been observed experimentally. An interesting and expected feature of many dozens of nuclei having an even number of protons—the ability to emit a pair of protons together, but not single protons—is due to the pairing of protons having opposite spins, and has its chemical analogue in the formation of coordinate bonds, in which a single atom supplies the pair of electrons.

The coupling of the pairing effect, which is characteristic of all particles having semi-integral spins (electrons, protons, neutrons, etc., to which the general name *fermions* is given), with the presence of a potential barrier around the nucleus even with neutral particles (in this case a purely centrifugal barrier) leads to the possibility,

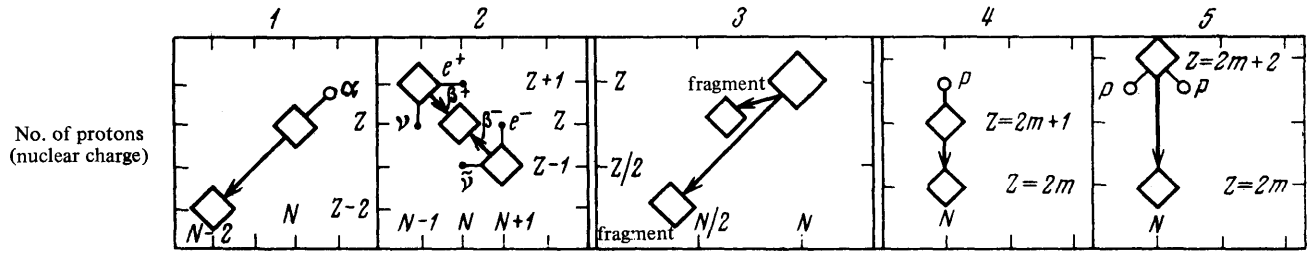

Figure 1. Schemes illustrating the five main types of radioactive disintegration of nuclei—spontaneous transmutation of chemical elements (e^- = electron; e^+ = positron; ν = neutrino; $\tilde{\nu}$ = antineutrino): 1) α-disintegration; 2) β-disintegration (β^-, β^+, and electron capture); 3) spontaneous fission; 4) proton disintegration; 5) two-proton disintegration.

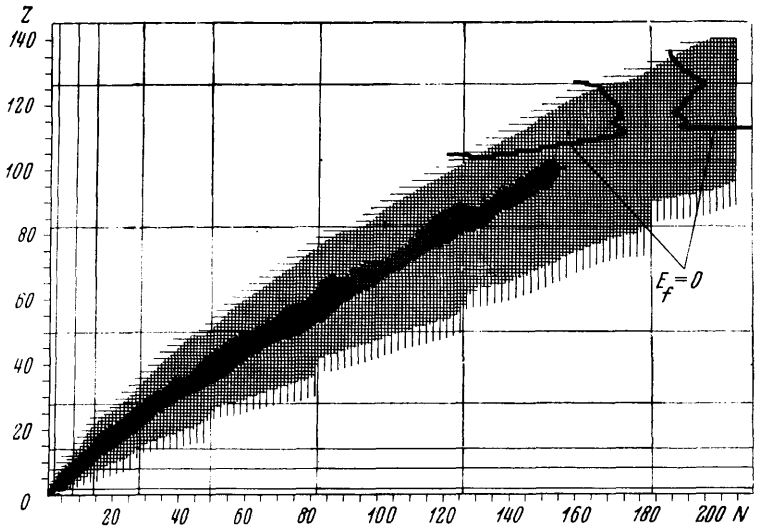

Figure 2. Region of stable and radioactive isotopes known at the present time (Z = No. of protons (atomic No.); N = No. of neutrons). The upper and lower boundaries are determined by the predicted instability for ejection of protons and neutrons respectively. The boundary of a possible "isthmus" of stability to spontaneous fission in the vicinity of $N = 184$ and $Z = 126$, 114 is indicated in the upper right-hand corner. In the absence of shell effects, spontaneous fission would have given a straight horizontal stability boundary near $Z \simeq 110$–112.

recently demonstrated theoretically, of the appearance of a sixth elementary type of radioactive disintegration of nuclei—two-neutron radioactivity, or the emission of a pair of neutrons by long-lived isomeric nuclei[9].

A few two-stage radioactive processes are known or have been predicted, in which the first step is some variant of β-disintegration, which is almost instantaneously followed by escape from an intermediate nucleus of some other particle (excited by part of the energy of β-disintegration) or by its fission. Such processes and the particles emitted in them are said to be *delayed*, the "delay" being due here to the sluggishness of the initial β-disintegration—i.e. not to the disintegration but to the formation of the excited nucleus.

Only delayed α-particles and neutrons were known before the Soviet work. The emission of delayed protons was discovered in the laboratory of G. N. Flerov at Dubna in 1962[10]. Another series of studies showed that the probability of fission of several transuranic nuclei was far higher than that expected from theoretical considerations, which was explained by the delayed fission of uranium and plutonium nuclei produced from neptunium and americium, as a result of slow electron capture from inner shells[11]. Theoretical analysis by Leningrad scientists indicated that tritium and helium-3 nuclei could also be emitted as delayed particles[12].

At the present time around 2000 isotopes of 105 chemical elements are known, of which only 15% are stable isotopes. However, systematisation of the bonding energies of nucleons in nuclei indicates the possibility of detecting almost 4000 more radioactive isotopes with a marked deficiency or a marked excess of neutrons in the nuclei. Fig. 2 shows clearly the relative regions of already known and not yet discovered isotopes. And the question of new isotopes involves not only their number: fundamentally new properties and phenomena await study.

The present stage of research on neutron-deficient and neutron-excess isotopes began in 1959–1960, when Soviet scientists[13,14], in particular Zel'dovich, proposed ways of determining the limits of stability of nuclei based on the shell theory of the nucleus and one of the main properties of nuclear forces—their independence of electric charges—since when dozens of new isotopes even of the lightest elements have been found, and their properties have shown excellent agreement with prediction. An extremely interesting example is the superheavy helium-8, which has double the weight of ordinary helium[15]. The prediction and detection of this isotope by Soviet scientists were marked by a discovery diploma[15]. Helium-8 is a kind of record-holder among atomic nuclei, in which each proton is associated with three neutrons. As a result of three successive radioactive transformations—two β-disintegrations and one α-disintegration (Fig. 3)—each atom of superheavy helium is converted into two atoms of ordinary helium, so that an aerostat filled with helium-8 inflated spontaneously to twice its volume in fractions of a second, without change in the chemical composition of the gas filling it.

In the search for new radioactive isotopes the synthesis of new transuranic elements acquired the widest popularity for understandable reasons, and greatly extended the limits of the Mendeleev periodic system. The first transuranic element (neptunium) was synthesised in 1940 and a fundamental contribution to extending the Mendeleev system was

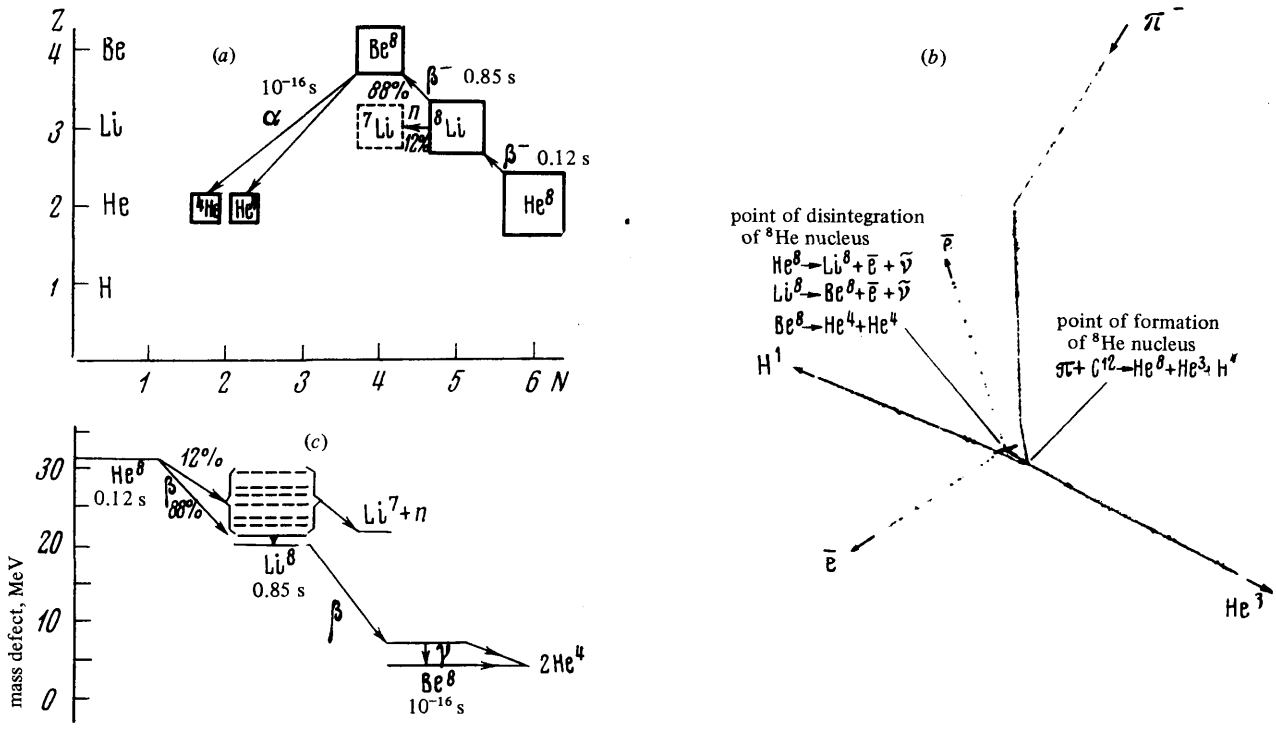

Figure 3. *a*) Illustration of disintegration path of helium-8 nuclei; *o*) pattern of formation of helium-8 nuclei by the bombardment of photographic emulsions with π-mesons ($\pi^- + {}^{12}C \rightarrow {}^1H + {}^3He + {}^8He$) and subsequent disintegration of helium-8 (obtained in the synchrocyclotron in the Laboratory of Nuclear Problems of the Joint Institute of Nuclear Research at Dubna); *c*) scheme of disintegration ($^8He \rightarrow {}^8Li \rightarrow {}^8Be \rightarrow 2{}^4He$).

made by a group of scientists headed by G. T. Seaborg at the Radiation Laboratory in Berkeley (U.S.A.) During 1941–1945 these workers obtained by means of accelerators, nuclear reactors, and nuclear explosions, eight new elements—from plutonium to element No. 101—the last of which they named *mendelevium* "... as a token in recognition of the priority of the great Russian chemist Dmitrii Mendeleev, who was the first to use the periodic system of the elements to predict the chemical properties of then undiscovered elements. This principle is the key to the discovery of almost all the transuranic elements"[16]. In 1958 scientists from Berkeley announced that they had obtained element 102 and in 1961 element 103, which they named respectively *nobelium* and *lawrencium*[17–19].

An enormous contribution to the synthesis and study of transuranium elements has since been made by Flerov's laboratory in Dubna. In 1963 and subsequent years Flerov and his coworkers obtained for the first time many isotopes of elements 102 and 103, which compelled them to revise the mass numbers previously assigned in Berkeley to the isotopes of these elements[20–23]. In 1964 the Dubna scientists achieved the remarkable success of obtaining the first isotope of the new element No. 104, named "kurchatovium Ku".[24] In February 1971 the synthesis was announced in Dubna of the next element 105, for which the name "nielsbohrium Ns" was proposed[25]. Several other isotopes of kurchatovium and of element 105 have since been synthesised in Berkeley.

Some idea of the latest situation is given by Fig. 4, in which are indicated all isotopes of the four newest elements known at the present time and those isotopes of elements 102 and 103 for which the presently accepted characteristics were first established in Dubna. Special emphasis is given to the isotopes discovered there of elements 104 and 105, which were incorporated by Soviet scientists into the Mendeleev system‡.

With regard to the main interest of chemists in the new elements—in their chemical properties—controversies have now continued for nearly thirty years on Seaborg's actinide theory, according to which actinium is followed by completion of a shell of fourteen 5*f* electrons in the elements from thorium to No. 103, analogous to the filling of the 4*f* shell in the rare-earth elements. A tendency sometimes develops to regard the periodic system as analogous not to a geographical atlas but to a plan which must indicate every street and every house, and to see any distinction between actinides and lanthanides as the overthrow of the actinide theory.

Nevertheless, the actual properties of elements in chemical compounds, the greater or lesser stability of their different valency states, are influenced by extremely

‡ In July 1974 the Dubna group announced the synthesis of new isotopes of kurchatovium (mass numbers 255 and 256) and the first isotope of element 106 (apparently A = 259).[25a]

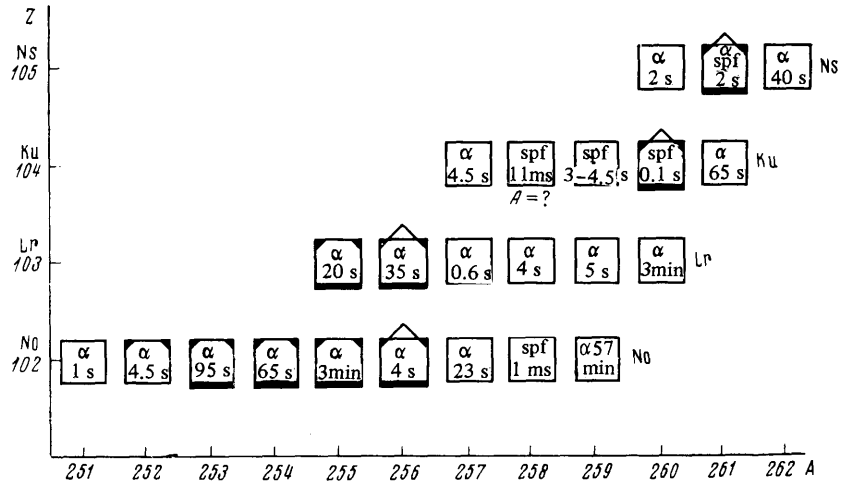

Figure 4. Isotopes of elements 102–105. The shaded corners and underlining denote those isotopes for which the presently accepted characteristics were first established at Dubna in the USSR. The triangles above the boxes indicate the first isotopes of each element, whose properties have not since been revised. The boxes contain the type of disintegration (spf = spontaneous fission) and the half-lives.

diverse factors. The problem can hardly be solved by model calculations. Even calculation of the energetics of the electron configurations of the free atoms and ions requires complicated programmes and high-speed electronic computers (as an illustration, it was thus established that the electron configuration $7s^27p$ for a free lawrencium atom was ~ 0.5 eV more advantageous, because of relativistic effects and spin-orbit splitting, than the lutetium-like configuration $6d7s^2$). No systematic molecular-orbital calculations have yet been made even for isolated molecules of lanthanide and actinide compounds. The same applies to real solutions and solid compounds, where the solvation energy as well as interionic and intermolecular interactions must also be taken into account, and with radioelements also the various effects of autoradiolysis. Here the chemist has the final say: comprehensive chemical investigations would prepare the ground for future calculations, and any new, especially unexpected facts lay the foundations for future general theoretical constructions.

For this reason it is difficult to overestimate the value of research on the chemistry of transuranium elements made during the past seven or eight years under the general direction of V. I. Spitsyn in the Institute of Physical Chemistry of the USSR Academy of Sciences. This led to the discovery of extreme valency states—septivalent neptunium, plutonium[26-29], and americium[30], bivalent californium, einsteinium[31], and fermium[32], and univalent mendelevium[33].

The septivalent states of the three actinides could be achieved by oxidation only in alkaline media, in which neptunium could be oxidised by more than twenty oxidants, and plutonium by more than ten, including ozone, persulphate, hypobromite, and the radical-ion $O^{\cdot-}$, the last being formed by the radiolysis of aqueous alkalis. It was most difficult to obtain septivalent americium: this required the radiolysis of alkaline solutions of americium(VI) cooled almost to 0°C and supersaturated with nitrous oxide, which is an acceptor of the strong reductant—the hydrated electron—produced by radiolysis. Around twenty solid compounds of septivalent neptunium and plutonium have been obtained—mainly perneptunates and perplutonates of alkali and alkaline-earth metals.

Fermium and mendelevium were reduced to the lowest valencies by the action of magnesium in aqueous–ethanolic solutions of chlorides of inert carriers. The lowest valency state of mendelevium was detected with only a few hundred atoms of the mendelevium-256 isotope (half-life 1.5 h) available.

The experimental valency states found by Soviet scientists for the above five actinides are indicated by crosses in Fig. 5, which includes all such states known for lanthanides and actinides (the most stable states are denoted by small squares). Fig. 5 shows both properties common to the two groups and their differences, which are due to the close approach in bonding energy of the ns, np, $(n-1)d$, and $(n-2)f$ electrons that is characteristic of the heavier elements. The results of these investigations by Spitsyn and his coworkers indicate a certain affinity between the far actinides ($Z \geqslant 98$) and the transition d-elements, as well as the possibility of discovering octovalent plutonium, quinque- and sexi-valent curium, and quinquevalent berkelium.

Fig. 5 includes also results obtained at Dubna in the USSR by a group of Soviet and Czechoslovak radiochemists under the general direction of Zvara[34-37]. They developed a method, of record rapidity and sensitivity, for establishing the chemical nature of new elements from the volatility of their anhydrous halides. In 1966 this method was used to demonstrate that kurchatovium and hafnium chlorides were closely similar in volatility, and significantly less volatile than the chlorides of actinides[34]. This decisive experiment, which proved that element 104 is already a member of the titanium subgroup of Group IV, and that element 103 sees the completion of the fourteen-electron $5f$ shell, in conformity with the actinide theory,

needed only 16 atoms of kurchatovium. The properties of this element were subsequently confirmed and refined by isolating and recording the radioactive decay of 60 of its atoms[35]. Furthermore, it was shown that nobelium and lawrencium are at most tervalent in their chlorides[35,36]. An outstanding new achievement was the observation that nielsbohrium chloride is more volatile than hafnium tetrachloride but less volatile than niobium pentachloride, as was to be expected for quinquevalent ekatantalum[37]. It must be emphasised that the experiments were made on isotopes of kurchatovium and nielsbohrium whose lifetimes did not exceed a few seconds.

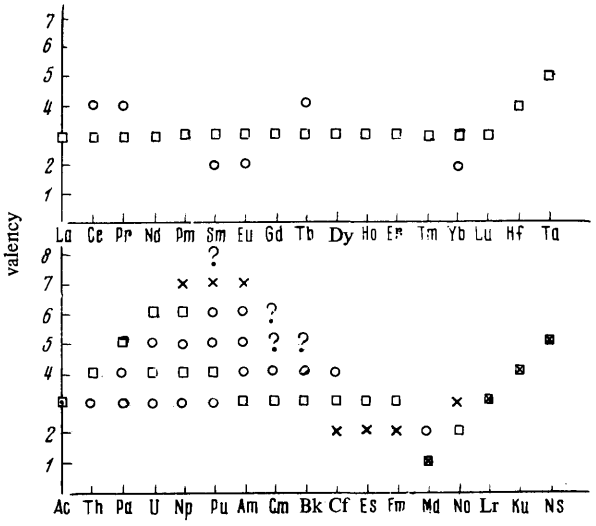

Figure 5. Valency states of lanthanides and actinides (as well as hafnium, kurchatovium, tantalum, and nielsbohrium). The most stable states are indicated by squares, and states first detected in the USSR by crosses (Np, Pu, Am, Cf, Es, Fm, and Md at the Institute of Physical Chemistry of the USSR Academy of Sciences, and No, Lr, Ku, and Ns at Dubna).

Advances in the synthesis and in the study of the properties of the far transuranium elements have enhanced the interest taken in the problem of the limits to which the periodic system can be extended. Only a decade ago it was supposed that spontaneous fission restricts the possibilities of synthesising elements 110–112. However, calculations by Soviet and foreign theoretical nuclear physicists[38–40] indicated that significant stabilisation of nuclei might result from the filling of nuclear shells containing 114, 126, and 164 protons, 184 and 258 neutrons. As a result the "isthmus of stability" shown in Fig. 2 may well appear, and contain many isotopes of elements in the vicinity of positions 114, 126, and even 164 in the Mendeleev system.

With regard to the chemical properties to be expected of these elements, data on the presently known elements and their extrapolation yield the sequence of electron shells depicted in Fig. 6. Each period is represented here by cells containing the symbols of the electron shells filled in the given period: i.e. each cell contains 2, 6, 10, 14, or 18 elements. Element 114 terminates the seventh period, element 164 completes the eighth period, and both are analogues of lead. Element 126 will occur in a new group of 18 elements—"octadecanides", apparently resembling actinium and in whose atoms the 5*g* shell will be completed—forming part of the 50-element eighth period[41–42]. The hypothetical eighth period is completed in Fig. 6 by element 168, and the ninth period by element 218.

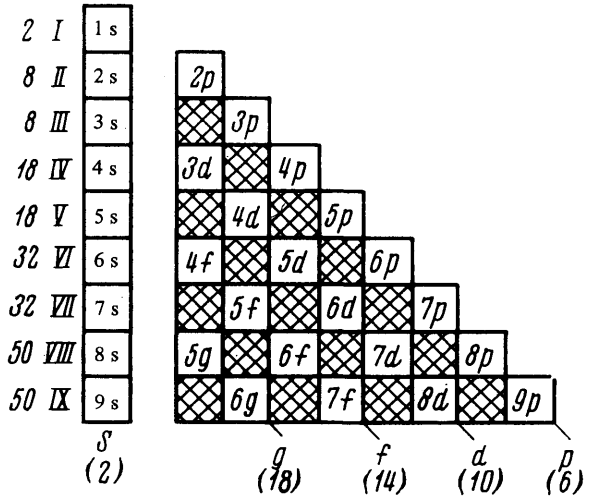

Figure 6. Diagram of sequence in which electron shells are filled in the periodic system. The total number of elements in the period indicated by the Roman numeral (which equals the serial number of the *s*-shell) is listed on the left-hand side. The total numbers of electrons in the various complete shells are given below the diagram.

Quite a number of attempts have been made during recent years to find in Nature or to obtain in accelerators some superheavy elements, but this has not yet been done with sufficient certainty. However, the links between the chemistry and the physics of elementary particles which have appeared recently have opened up completely new prospects for enriching and expanding our ideas on chemical elements. This refers to the numerous examples of so called "new atoms", in which the proton has been replaced by a different positive particle, or the electron by a different negative particle[43]. The possibility of replacing a proton by a lighter positive particle implies that ordinary hydrogen (protium) will cease to be the lightest occupant of the first position in the Mendeleev system. For example, we are now acquainted with kaonium, pionium, and muonium, in which the proton has been replaced respectively by a κ^+, π^+, and a μ^+ meson, and whose atoms are lighter by factors 2, 7, and 9. The lifetimes of these atoms are determined by the decay of the mesons and lie in the range 10^{-8}—10^{-6} s. The lightest conceivable isotope of hydrogen is positronium Ps, whose atom comprises a positron and an electron, and is lighter than hydrogen by a factor of 920. Because a positron has the same mass as an electron, positronium is the only atom completely devoid of a heavy nucleus. Apart from

its extraordinarily small mass, positronium differs from ordinary radioactive hydrogen (tritium) in the most important fact that all the characteristics of its loss by mutual annihilation of the positron and the electron—lifetime, number of γ-quanta emitted on annihilation, their energy and angle of divergence—depend on the properties of the surrounding medium, which permits a completely fresh investigation of these properties. The extremely short lifetime of positronium (10^{-10}–10^{-7} s) hinders its accumulation in concentrations exceeding a few atoms per cubic centimetre, so that none of the classical methods of chemistry can be used to study the reactions of positronium. This can be done only by nuclear methods, which enable the formation and destruction of every single positronium atom to be observed by recording the accompanying γ-quanta. Combining such methods with wide variation in the external conditions—composition of medium, concentrations, temperature, pressure, etc.—has enabled comprehensive quantitative investigations of all types of chemical reactions undergone by positronium to be made in the Institute of Chemical Physics of the USSR Academy of Sciences during the past twelve years[43–45]. Examples are given in Table 1 of oxidation, donor–acceptor interaction, substitution, addition, and conversion. Thus, for the first time in the history of radiochemistry, a detailed study has been made of the chemistry, including the kinetics and the mechanism of the reactions, of atoms which last at most 10^{-7} s.

Table 1. Examples of chemical reactions of positronium.

Type	Example	Method	Medium
Oxidation	$Ps + Fe^{3+} \rightarrow e^+ + Fe^{2+}$	time, angle	aqueous solutions
Donor–acceptor interaction	$Ps + M(C^+ :) \rightleftarrows PsM$ carbonium ion	time	organic solutions
Substitution	$Ps + Cl_2 \rightarrow PsCl + Cl$	time, angle	gases, organic solutions
Addition	$Ps + (CF_3)_2NO \rightarrow (CF_3)_2NOPs$	time, angle	gases, solutions, solid phase
Ortho–para-conversion	$o\text{-}Ps + NO \rightarrow p\text{-}Ps + NO$ (↑↑ ↓ ↑↓ ↑)	time, angle	gases, solutions
"Mixed" interaction (conversion or addition)	$o\text{-}Ps + NO_2 \rightarrow PsNO_2$ / $p\text{-}Ps + NO_2$ (↑↑ ↓ ↑↓ ↑)	time, angle	gases, aqueous and organic solutions

Despite the intrinsic interest of the chemistry of positronium, results obtained by the new positronium method for chemistry as a whole are of greater significance. For example, by using as standard the extremely short "proper" lifetime of positronium (with respect to annihilation), it was possible to measure the rates of several ultra-rapid chemical reactions occurring within fractions of a nanosecond and lifetimes of intermediate products of the order of picoseconds. Varying the temperature and the composition of the solvent in which the reactions of positronium were observed yielded a general technique for delimiting kinetic and diffusion régimes in the kinetics of liquid-phase reactions. Comparison of the rates of various reactions of hydrogen and positronium atoms led to a general conclusion on the mechanism of electron transfer in oxidation by ions of variable valency in solution. Observations on the reactions of positronium with a carbonium ion in different organic structures made it possible to determine the electronic conductance of various groups relative to that of the benzene ring.

Thus the chemistry of positronium has already passed the stage of "fitting" its possibilities to known facts and has entered the second, main stage, when it supplies new information of value to chemistry. The chemistry of other new atoms, sometimes termed in general *mesochemistry*, is still at the first stage, although the results already obtained are extremely promising. Pioneering work on mesochemistry has been done with the synchrocyclotron at the Laboratory of Nuclear Problems (directed by V. P. Dzhelepov) of the Joint Institute of Nuclear Research in Dubna, by the staff of this laboratory and several others, including academic institutes[46–67].

Systematic research on the physicochemical interactions of the hydrogen-like atom of muonium was undertaken at the Institute of Theoretical and Experimental Physics of the USSR State Atomic Energy Commission[43,46–50]. A method was proposed and developed[51–53] for determining the absolute rate constants of the chemical reactions of muonium with organic and inorganic compounds, the mechanism of these reactions was investigated, and quantitative dependences of reactivity on molecular structure were obtained. Known nuclear physical constants of the μ^+ meson and muonium were used as independent time standards, which permitted study of the behaviour of single muonium atoms during times of 10^{-9}–10^{-5} s. Conversion to hydrogen of results for the reactions of muonium in several cases provided more accurate characterisation of the reaction rate for hydrogen atoms themselves than did the corresponding direct experiments. The temperature dependence of the reactivity of muonium was examined, and activation energies of its reaction were determined. A sharp jump in polarisation of the μ^+ meson was revealed for the water–ice phase transition, associated with formation of a closed coordinated system of hydrogen bonds in the ice crystal.

The presence of Larmor precession of triplet muonium was first shown in chemically inert condensed media, and the energy of hyperfine splitting in the muonium atom was determined as a function of the periodic lattice potential of several materials, including semiconductors. Spin-exchange interactions of muonium in solutions of paramagnetic ions have been studied, and a close analogy was shown with results obtained by nuclear magnetic resonance but with substantial broadening of the range of measurements with respect to concentrations and spin–spin relaxation times.

The two-frequency spin precession of the μ^+ meson in the muonium atom, resulting from a quadratic Zeeman effect in the ground-state levels of muonium, was discovered[54] at the Kurchatov Institute of Atomic Energy of the USSR State Atomic Energy Commission. The two-frequency precession was used to study the properties of muonium introduced into the crystalline matrix of several materials. A method for studying diffusion of the μ^+ meson and muonium in a solid was based on the dependence of the interaction between the magnetic moment of the μ^+ meson and those of the nuclei of the medium on the rate of diffusion of the meson in the crystal lattice[55,56]. Spin relaxation of the μ^+ meson caused by dipole–dipole interactions was noted in metals and in light and heavy ice.

The interaction with matter of μ^- and π^- mesoatoms, in which one of the electrons has been replaced by a μ^- or π^- meson, is also of great interest[57-67]. Negatively charged mesons are slowed down in a medium, and ultimately trapped in atomic orbitals to form mesonic atoms and then, in a series of cascade transitions with emission of mesonic X-rays, reach the ground state in the inner K shell. Study of the characteristic X-ray emission spectrum, the lifetimes of the mesons, and their depolarisation enables the interaction of μ^- mesons with matter to be investigated. Observations on the chemical reactions of π^- mesons are based on comparing the specific pattern of their decay on interaction with free protons with the decay within any other π-mesonic atoms. Such work was begun more than ten years ago in the Laboratory of Nuclear Problems of the Joint Institute of Nuclear Research (by Prokoshkin and his coworkers[58,59]); recently the Institute of Chemical Physics of the USSR Academy of Sciences, the State Institute of Applied Chemistry, etc. have taken part in this work.

Since the radii of atomic orbitals are inversely proportional to the mass of the particles occupying them, this radius is minute—around 10^{-11} cm—for atoms of mesohydrogen in the ground state. It would seem that mesonic atoms should not be affected by other chemical bonds at distances of hundreds of mesoatomic dimensions in the molecule. Therefore the discovery of many relations for mesonic atoms which conform to the Mendeleev periodic dependence on atomic number Z was completely unexpected.

Fig. 7 illustrates examples of such regularities for μ^-- and π^--mesonic atoms (given for π^- by the relation

where $W^{exp}_{Z_mH_n}$ is the experimental probability of the nuclear capture of π^- mesons by protons of hydrogen atoms). Such examples led to the so-called "model of large mesomolecules"[60-62] for the properties and transformations of molecules involving excited mesonic atoms, in which the meson is situated not in the ground state but in an orbital remote from the nucleus which has a principal quantum number n and hence a radius increased by a factor n^2, and reaches normal atomic dimensions. Fig. 7 shows that such orbitals are no longer mesoatomic but are mesomolecular. Observations of the formation and the transformations of large mesomolecules yield several conclusions on the properties of other valency bonds in these molecules and on the electronic effects of various functional groups. Furthermore, such observations enable a definite correlation to be established between mesochemical and radiation-chemical reactions and the rate constants of chemical reactions involving mesonic atoms and radicals to be determined.

We have already mentioned the four levels in the structure of matter, and have proceeded from particles through nuclei to atoms and molecules. But the highroad of modern research is based on the synthesis of ideas on

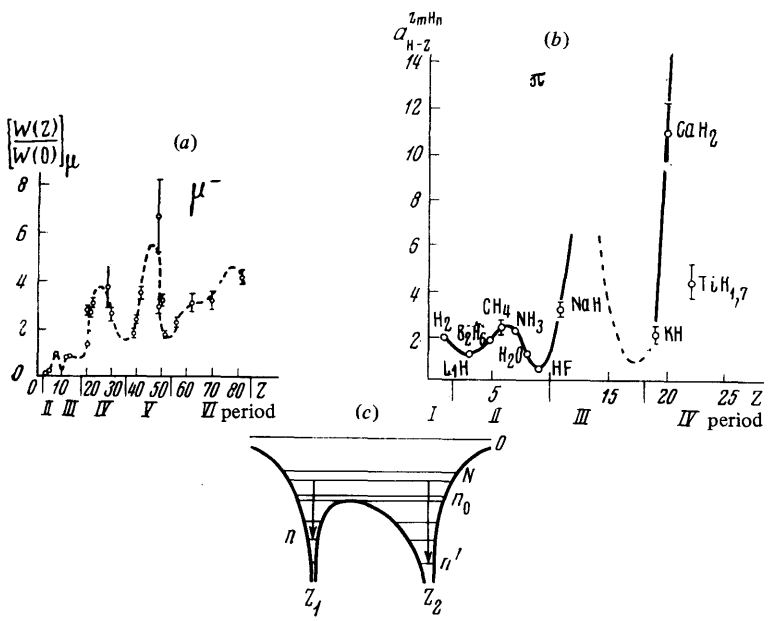

Figure 7. Examples of periodic dependence of certain mesoatomic reactions on atomic number of element Z: *a*) ratio of probabilities of atomic capture of μ^- mesons by element Z and by oxygen chemically combined with it in oxides Z_mO_n;[57] *б*) coefficients $a_{H\text{-}Z} = W(H)/W(Z)$ representing ratio of probabilities of capture of π-mesons by hydrogen and by element chemically combined with it in the saturated hydride Z_mH_n (aggregate of data from several Soviet and foreign papers); *c*) scheme of mesonic levels in diatomic "large mesomolecule" Z^1Z^2. Above n_0 are generalised mesomolecular levels, and below it are located mesoatomic levels Z^1 and Z^2.[60]

the structure of nuclei and electron shells, on the unity of the quantum-mechanical description of the properties of both.

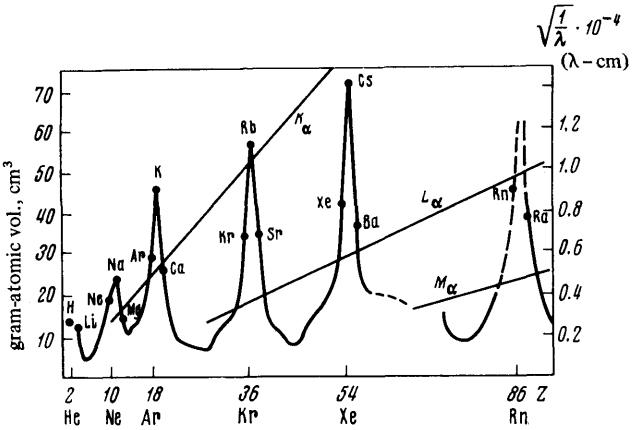

Figure 8. Typical examples of periodic dependence (of atomic volume) and linear dependence (of square root of wave-number of α-lines of K-, Z-, and M-series X-rays—Moseley's law) on atomic number Z of element.

The discovery and interpretation of Mendeleev's periodic law provided for chemistry and physics the two types of dependence of properties of the electron shells on the nuclear charge illustrated in Fig. 8. For the outer, valency shells we have a periodic relation, represented here by the atomic volumes. The relation of the inner, deep shells is a monotonic power dependence represented in Fig. 8 by Moseley's linear law.

The next contemporary stage, to whose establishment and development Soviet scientists have made an enormous contribution, entails the detection, examination, and utilisation in chemistry—and in all other natural sciences—of interactions between outer and inner electrons, outer electrons and nuclei, i.e. interrelations as it were between periodic and power functions of the atomic numbers of the elements (with the atomic numbers themselves as a particular case).

The first example of such interactions, now combined under the name *hyperfine interactions*, was discovered in 1928 by Terenin and Dobretsov[68], and independently by Schüler[69], as a result of accurate investigations on the optical spectra of sodium vapour. It was found that each of the two components of the yellow D-line was split only by 0.02 Å, and this splitting could be explained on the assumption that spins and magnetic moments were present not only in the electrons but also in the nuclei. In the above work, incidentally, Terenin and Dobretsov used for the first time atomic beams—a technique which has since been widely used in various resonance methods.

Table 2 lists the various forms of hyperfine interaction and methods involving their use. One of the main types is the interaction of the electric charges and the magnetic and quadrupole moments of nuclei with the charge of the s-electrons and the intramolecular magnetic and non-uniform electric fields. These hyperfine interactions are used in electron spin resonance (discovered by Zavoiskii[70,71] in 1944) and in other methods of microwave spectroscopy, in particular nuclear magnetic resonance and nuclear quadrupole resonance. Hyperfine interactions play a decisive role also in γ-resonance or Mössbauer spectroscopy, first placed in the service of chemistry by the work of Soviet scientists[72,73]. The hyperfine interaction energy involving valency electrons is in all cases many orders of magnitude smaller than even those of the weakest chemical bonds, and the dependence of this energy on the nuclear charge is represented by most insignificant periodic bumps, as it were, on the background of far stronger periodic or monotonic relations. Fig. 9 shows as example of this situation logarithmic plots of the periodic dependence on atomic number of the density of valency s-electrons in the region of the nucleus and the monotonic increase in total density of all s-electrons on the nuclei of elements from lithium to krypton.

Table 2. Hyperfine interactions and methods of use.

Type of interaction or dependence	Parameter and energy of interaction*	Experimental methods
Magnetic dipole (M1) interaction between nucleus and unpaired ("own" or "foreign") electrons	$\mu_{nucl}H \sim 10^{-6} - 10^{-4}$ eV	microwave spectroscopy—e.s.r., n.m.r.
Electric quadrupole (E2) interaction between nucleus and valency electrons or neighbouring ions	$eqQ \sim 10^{-7} - 10^{-6}$ eV	n.q.r. double resonances, spin echo, etc.
Coulombic (electrostatic—E0) shielding of nuclear charge by s-electrons	$\frac{V_{nucl}}{V} I_1 \sim 10^{-8} - 10^{-7}$ eV	Mössbauer
Coulombic (electrostatic—E0) shielding of charge of inner by outer electrons; dependence of energy of vacant levels on effective charge of atomic core	$\frac{V_{inner}}{V} I_{inner} \sim 0.1 - 10$ eV	X-ray electron and photoelectron spectroscopy or e.s.c.a.
Dependence of Coulombic energy of interaction of electrons with nuclei on nuclear mass (isotope effects in ionisation potentials)	$\frac{m}{M} \cdot \frac{\Delta M}{M} I \sim 10^{-6} - 10^{-2}$ eV	Accurate chemical X-ray spectroscopy, determination of effective charges on atoms
Dependence of energy of vibrational levels on nuclear mass (isotope effects in vibrational levels of molecules)	$\frac{\Delta M}{M} E_{vibr} \sim 10^{-4} - 10^{-3}$ eV	Accurate optical spectroscopy and laser methods for separating isotopes

* μ_{nucl} = magnetic moment of nucleus; H = intramolecular magnetic field on nucleus; e = charge of electron; q = gradient of intramolecular electric field; Q = quadrupole moment of nucleus; V_{nucl} = volume of nucleus; V = volume of atom; V_{inner} = volume of inner shell; I = ionisation potential (I_1 for first electron, I_{inner} for inner electron); m = mass of electron; M = mass of nucleus; ΔM = difference in mass between isotopes; E_{vibr} = energy of vibrational level.

Interaction between the electric charges of the outer and inner electron shells is apparent in changes (of fractions or even a few electron-volts) in the energy of electrons removed from the inner shells of the atoms, and it also leads to the appearance of a specific fine structure in the X-ray spectra. This forms the basis of the so called photoelectron spectroscopy, whose X-ray and ultraviolet forms were established by Siegbahn et al. in Sweden[74,75] and by Terenin et al. in the USSR[76], and also of precision chemical X-ray spectroscopy, founded by workers of the USSR Academy of Sciences at the Vernadskii Institute of Geochemistry and Analytical Chemistry, the Institute of the Mineralogy, Geochemistry, and Crystal Chemistry of the Rare Elements, the Kurnakov Institute of General and Inorganic Chemistry, and the Konstantinov Institute of Nuclear Physics[77-83].

Finally, the isotopic dependence of the vibrational energy levels and the ionisation potentials has recently found most interesting application for the laser separation of isotopes, which has been accomplished in the Institute of Spectroscopy of the USSR Academy of Sciences[84].

A few examples may be cited of the great successes achieved by Soviet scientists in the use of hyperfine interactions in various chemical problems. Some years after the discovery of electron spin resonance by Zavoiskii, and in the same place Kazan, the first observation of hyperfine structure in e.s.r. spectra was made by Kozyrev et al.[85] (and independently in England[86]), which ensured the successful application of the new method in chemistry[86]. Chemical e.s.r. spectroscopy owes its origin largely to Voevodskii[87], who made it a powerful weapon in structural kinetic investigations, in particular the observation of free radicals formed directly during irradiation of various substances, as well as in investigations on so called weak chemical interactions[88,89], whose energy is incomparably smaller than the usual thermal energy but close to the energy of hyperfine interactions. Such interactions are too weak to be observed by methods like optical spectroscopy, measurement of dipole moments, etc.; yet they often control a most important chemical phenomenon—the mutual influence of the reactivities of different functional groups distant from each other—and are apparent in differences (spatial or temporal) in the delocalisation of electrons in the molecules. The e.s.r. method made possible the direct observation of such delocalisation of electrons[90,91], attempts at which had been begun towards the end of the 1950s[90] on radical-anions of the type shown at the top of Fig. 10. But here the left-hand and right-hand rings are not equivalent, owing to the approach of a gegenion (e.g. Na^+, R^+) towards the negative charge, and this prevents delocalisation—"erosion" of the free valency and the negative charge between the two rings. Only quite recently has the exchange of electrons been demonstrated between two distant identical functional groups, in the stable nitroxide biradical shown in the middle of Fig. 10.[91] The e.s.r. spectrum of this biradical in various solvents is characterised by five (bottom right in Fig. 10)—not

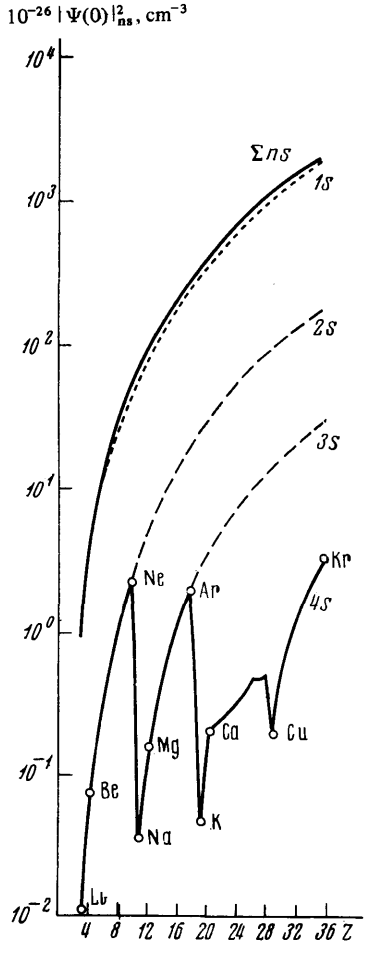

Figure 9. Dependence on atomic number Z of s-electron densities (all calculated per s-electron to a non-relativistic approximation): valency s-electrons $|\Psi(0)|^2_{ns}$ in region of nucleus (bottom full curve); 1s, 2s, and 3s densities (broken curves); total density of all s-electrons (upper full curve).

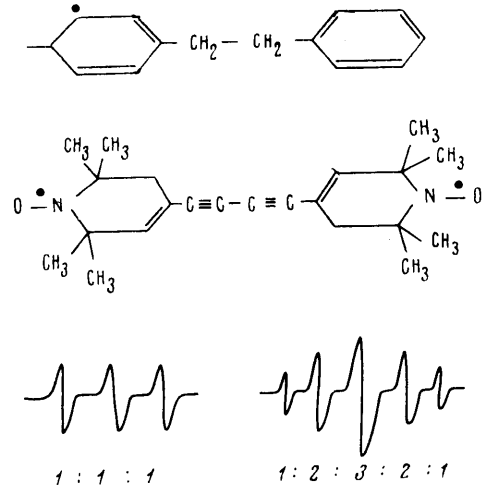

Figure 10. Illustration of e.s.r. investigation of the delocalisation of electrons in molecules: examples of test materials (radical and biradical) (above and centre); typical spectra corresponding to localisation (triplet) and delocalisation (quintet) of electrons in nitroxide biradical (below).[91]

three (bottom left)—hyperfine splitting components, which indicates that each of the unpaired electrons at once undergoes the same interaction with the two (its "own" and the "other") nitrogen-14 nuclei. The frequency of the effective exchange of position by the two electrons here exceeds 10^8–10^9 s^{-1}.

Among other interesting recent chemical applications of e.s.r. we may mention direct observations of the tunnel transfer of electrons in irradiated frozen alkalis at low temperatures, when the distance tunnelled is reckoned in tens of ångströms [92]. The method proved to be sensitive to extremely slow movements of paramagnetic labels, with linear speeds reaching 10^{-7} cm s^{-1} and diffusion coefficients reaching 10^{-17}–10^{-18} cm^2 s^{-1}. [93] It is difficult to overestimate the possibilities which such observations open up for physicochemical biology, the study of molecular kinesis phenomena§, in particular conformational transitions of biopolymer molecules, and various types of motion at molecular, supermolecular, and cellular levels. The e.s.r. method originated in experiments on a condensed phase, to which it was restricted for a long time. Subsequently, however, it found fairly wide application for the study of branched chain reactions in the gas phase [94,95] and from 1967—mainly in the work of Nalbandyan et al. [96–98] and because of the substantial improvement in the sensitivity of e.s.r. instruments—also in the investigation of degenerate branched gas-phase reactions, of particular theoretical and practical interest, such as the oxidation of hydrocarbons, when the concentration of active centres is far smaller.

Further prospects for studying the gas-phase and surface reactions of paramagnetic atoms and free radicals by means of hyperfine interactions are opened up by the maser kinetic method developed by Tal'roze and his coworkers [99,100]. Here, as in e.s.r., use is made of the magnetic hyperfine interaction between electron and nucleus, which in hydrogen atoms causes certain transitions between two hyperfine sublevels of the ground state of wavelength 21 cm. Interaction of a beam of hydrogen atoms from a hydrogen quantum generator (the maser) with various molecules leads to the observed relaxation of the inversion of hyperfine sublevels, so that excellent accuracy can be ensured in the determination of rate constants with around 10^4 improvement in sensitivity relative to e.s.r. in the gas phase.

At the present time about 50% of all e.s.r. spectrometers used in world science are concentrated in the Soviet Union. The widespread introduction of e.s.r. in industry—for rapid analysis or for the optimisation of several technical and in particular catalytic processes using paramagnetic ions of transition metals—promises to have a very considerable economic effect. A theoretical basis for such development may be provided by the comprehensive series of investigations made at the Vernadskii Institute of Geochemistry and Analytical Chemistry [101] on the application of e.s.r. to the study of complex formation by paramagnetic ions in solution. Portable e.s.r. spectrometers suitable for the above purposes have been suggested in the Institute of Chemical Physics [102].

Nuclear magnetic resonance has found extraordinarily wide use by Soviet chemists. Because of the thorough isolation of a system of nuclear magnetic moments from all other degrees of freedom, it is characteristic of this form of microwave spectroscopy that the exchange of energy between this system and the environment in a condensed phase is extraordinarily difficult. Nuclear magnetic spin–lattice relaxation times reach many hours in molecular crystals, and many minutes in pure organic liquids (about the same as the spin–spin relaxation time in liquids). However, the action of the various local fields is averaged out in liquids by Brownian motion, and in the solid phase by the superposition of specially selected external high-frequency fields. Hence under the usual experimental conditions, i.e. with external magnetic fields of $\sim 10^4$ G, when the energy of interaction of the nuclear magnetic moments with the field is of the order of 10^{-7} eV, while the characteristic frequency of precession of these moments $\nu \simeq 10^8$ Hz, n.m.r. lines can be obtained of width reaching $\Delta\nu \simeq 10^{-2}$ Hz. Although the relative width of the n.m.r. spectral lines $\Delta\nu/\nu \simeq 10^{-10}$ is several orders of magnitude larger than for the Mössbauer effect, the n.m.r. method has as yet no peers with respect to absolute line width ($\Delta\nu \simeq 10^{-2}$ Hz corresponds to $\Delta E \simeq 10^{-17}$ eV). Two factors—the chemical shift and indirect spin–spin interaction of nuclei—are responsible for the regular displacement, depending on the molecular structure of the medium, undergone by peaks of such record narrowness. The range of dimensionless chemical shifts varies from 2×10^{-5} for protons to $\sim 10^{-4}$–10^{-3} for heavy atoms. Spin–spin interaction constants vary in absolute value from zero to several kilohertz depending on the density of valency electrons in the region of the nucleus and on the degree of overlap of electrons in the chain of bonds at whose ends are situated the two atoms whose nuclear interaction is under investigation.

The contribution made by Soviet scientists to establishing the theoretical foundations of nuclear magnetic resonance is very great. Work in the Institute of Chemical Physics of the USSR Academy of Sciences, which has acquired a world-wide reputation [103], combined the concepts of a spin temperature and a reservoir of dipole–dipole interactions, and gave widely quoted equations describing the processes in a system of nuclear spins for any value of the saturating field. The Soviet book "Teoriya Yadernogo Magnitnogo Rezonansa" [104], which gave the first general theory of the magnetic shielding of nuclei, became a work of reference for n.m.r. specialists throughout the world.

Studies undertaken in the Institute of Organoelementary Compounds of the USSR Academy of Sciences provide the chief examples of the fundamental experimental results which we have obtained by means of nuclear magnetic resonance. Some time ago Nesmeyanov made a detailed analysis of the close relation between the chemistry of organoelementary compounds and the periodic law [105]. A clear recent confirmation of such a relation was the establishment [106] of periodicity in the shielding of carbon nuclei in cyclopentadienyl ligands of isostructural π-complexes of transition metals (shielding is maximal with the iron subgroup, as shown in Fig. 11). However, n.m.r. reveals far finer regularities. Electronic effects due to different substituents are widely discussed in chemistry, but what occurs at the point of bonding of substituents remained well hidden and was the subject of theoretical speculations, for the key (substituted) atom itself is usually not involved in the range of interactions for which the role of substituents is considered.

Fig. 12 shows the variation in shielding of the key carbon atom in a substituted aromatic system [107]. The effect of substituents on the key atom was found to be stronger in absolute value by factors of 10–10^2 than in the "strictly aromatic" part of the molecule, and furthermore, when the bond with the substituent was weakly polar (with alkyl

§ The term "moleculokinesis", meaning the functional motion of molecules, was introduced by V.A. Engel'gardt.

or methine groups), its sign was opposite to that to be expected from the electron-donor or electron-acceptor character of the substituent. With alternant aromatic systems this alternation of sign is considered also within the region of ring delocalisation of π-electrons; in non-alternant systems the reversed sign of the effect is characteristic only of the key atom. These facts give an experimental guideline for choosing an adequate quantum-chemical description of the electronic effects of weakly polar *C*-substituents. If, however, the bond between the key atom and the α-atom of the substituent is strongly polar, the carbon-13 n.m.r. chemical shifts vary in conformity with the usual views on the inductive effect of a substituent: i.e. alternation of the effect on the key carbon atom is now absent. This is clearly seen from the central portion of Fig. 12, which shows the variation of shielding and the parallel variation of the total electron density of corresponding carbon atoms in a cyclopentadienyl ligand of ferrocene with a carbonium ion as substituent. The lower part of Fig. 12 shows the superposition of effects which is characteristic of substituents of mixed type, e.g. formyl.

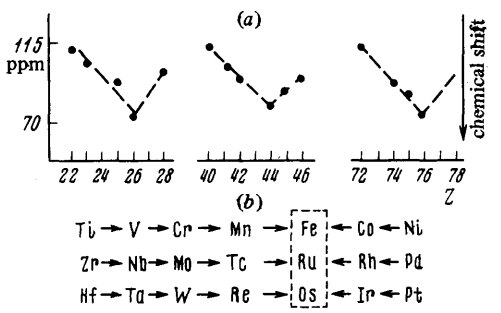

Figure 11. (*a*) Plots of variation in chemical shifts (ppm with respect to tetramethylsilane) of ^{13}C nuclei in n.m.r. spectra of unsubstituted ligands in π-cyclopentadienyl derivatives of transition metals. (*b*) Sequence of increasing shielding of ^{13}C and ^{1}H nuclei in π-cyclopentadienyl derivatives of transition metals.

this applies equally to the two β-atoms; but if an asymmetric atom is adjacent to the ring, spectral differences arise between α- and α'-, and between β- and β'-carbon-13 atoms. Here we are dealing with short-range and long-range intramolecular effects of asymmetric atoms.

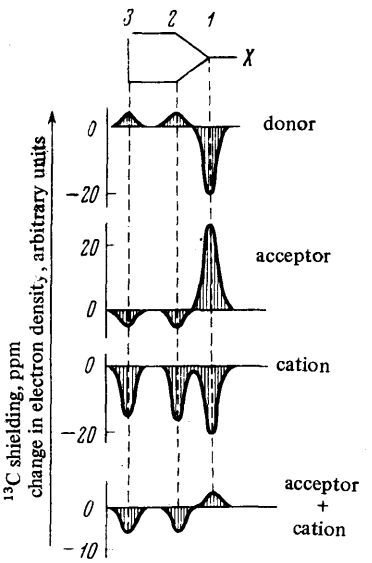

Figure 12. Variation in the shielding of carbon-13 nuclei in a cyclopentadienyl ligand of ferrocene under the influence of substituents attached to the α-carbon atom [107]. Donors (alkyls) increase the electron density at positions 2 and 3, but diminish it on the key atom. Acceptors (cyano and methine) decrease the electron density at positions 2 and 3, but increase it on the key carbon atom. A carbonium ion produces effects of the same sign, by diminishing electron density on all the atoms of cyclopentadiene ring. Substituents of mixed type (formyl, etc.), by producing competing effects of opposite sign at the key atom, cause a slight change in shielding of the key carbon-13 nucleus.

In the current physics of elementary particles fairly complicated views are held on the spatial, charge, and temporal symmetry of their interactions, on the relation between the charge and space parities of particles and antiparticles. As illustration, a neutrino is regarded as a kind of screw with a left-hand thread, and an antineutrino as one with a right-hand thread. Such properties are represented in scientific literature by terms such as "chirality" and "helicity", which imply "handedness" and "twistedness".

Study of the properties and interactions of optically active compounds with asymmetric atoms has revealed many curious new analogies between the chemistry and the physics of elementary particles, which have sometimes already been explained but occasionally still await a strict interpretation based on quantum mechanics and group theory. An example of such a new fact is the interesting phenomenon (Fig. 12) discovered by Kursanov et al. [108] that, when a cyclopentadienyl ring contains a substituent with a symmetrical atom directly adjacent to the ring, the two α-carbon-13 atoms have identical n.m.r. spectra, and

Many other examples of this kind have recently been investigated by Reutov et al. [109] for several classes of organoelementary compounds. A series of papers by Kabachnik and his coworkers [110,111] have demonstrated the effects of the intermolecular interaction of enantiomers, which has become possible only because of the exceptional absolute sensitivity of n.m.r. and the excellent reproducibility of the results. A definite chemical shift in the singlet phosphorus-31 n.m.r. spectrum is observed for a solution of "left-hand" molecules of biologically active phosphoric depsipeptides in an optically inactive solvent (chloroform); exactly the same shift is observed, of course, for a solution of "right-hand" molecules. With the same number of left- and right-hand molecules present an n.m.r. singlet is still observed, but displaced. In general, i.e. in a left–right mixture, two n.m.r. lines are present, whose positions and intensities depend on the relative concentrations of the two forms, as shown in Fig. 14. Thus "homocontacts" and "cross contacts" of left and right molecules in an inert solvent are different,

and their mutual shielding is non-equivalent. A pair of left and right molecules associate to form a diastereomer, which is short-lived on the n.m.r. time scale ($\tau \leqslant 10^{-3}$ s). It is of fundamental importance to investigate not only the analogy of, but also the possible effect of the asymmetry of elementary particles in our world on, the asymmetry at molecular and biological levels.

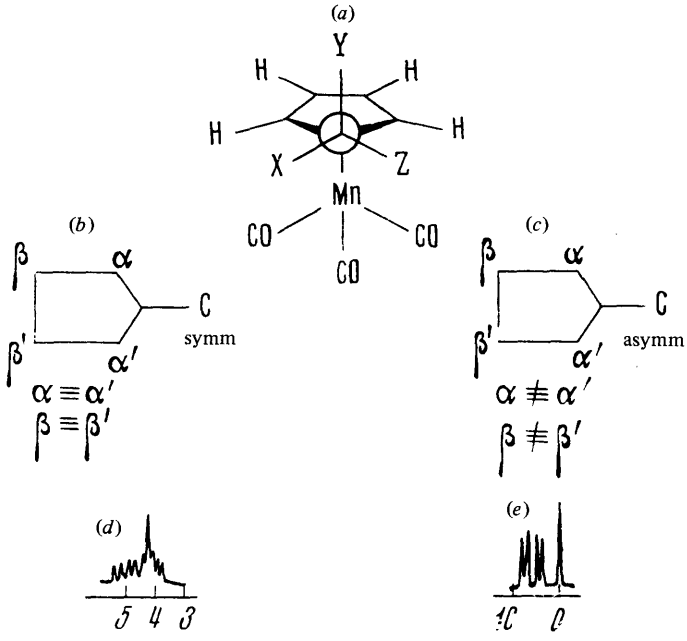

Figure 13. Increase in multiplicity of n.m.r. spectra of (*a*) cyclopentadienyltricarbonylmanganese under the influence of an asymmetric substituent[108,109]: (*b*) α- and β-carbon atoms chemically equivalent in pairs (giving a common n.m.r. signal) if the substituent is optically inactive; (*c*) all four carbon atoms in the substituted ring are chemically non-equivalent if the substituent is optically active; (*d*) ^{1}H n.m.r. spectrum; (*e*) ^{13}C n.m.r. spectrum.

Brief mention must be made of the extremely interesting work of Knunyants[112,113] on organofluorine compounds and of Andrianov[114-117] on organosilicon compounds. Comprehensive correlations between n.m.r. spectra and structure were obtained for both classes of compounds, and the chemical shifts of various fluorine-containing and silicon-containing functional groups were shown to be characteristic. Quantitative aspects of the effect of fluorine atoms on the carbon–mercury spin–spin interaction were obtained by Fourier carbon-13 n.m.r. spectroscopy. In molecules of the type R_2Hg, where R is a fluorine-containing substituent with sp^3 hybridisation of the α-carbon atom, only a small fraction of the observed spin interaction of the carbon-13 and mercury-199 nuclei is due to the usually prevalent Fermi contact mechanism.

A very peculiar reaction involving ring expansion in siloxanes has been discovered by means of n.m.r. spectroscopy. Furthermore, application of the method to organocyclosiloxanes led to a correct formulation of the converse problem, important for the method itself, which arises in interpreting the observed changes in chemical shifts and spin–spin interaction constants.

A clear and extremely important result at the level of the structure of complicated biomolecules has been obtained by Ovchinnikov et al.[118] working at the Shchemyakin Institute of Bio-organic Chemistry. Conformational rearrangements of the antibiotic valinomycin on complex formation with the potassium ion have been demonstrated by Fourier carbon-13 n.m.r. spectroscopy. Complex formation is accompanied by strong shifts (3–5.5 ppm) of the signals of the carbonyl groups to smaller magnetic fields, which is attributed both to the effect of hydrogen bonds and to the involvement of the carbonyl groups themselves in weak ion–dipole interaction retaining the potassium ion in the closed bud of valinomycin. Experiments finally confirmed a pattern of competition between intramolecular and intermolecular hydrogen bonds governing the bonding of ions in the central cavity of these beautiful, flowerlike cyclic molecules and their liberation on conformational opening of the bud, when the effect of the medium ruptures the intramolecular hydrogen bonds shown by double lines in Fig. 15*a*. These results are especially significant for the reason that the conformational rearrangements effect the transport of ions through cell membranes.

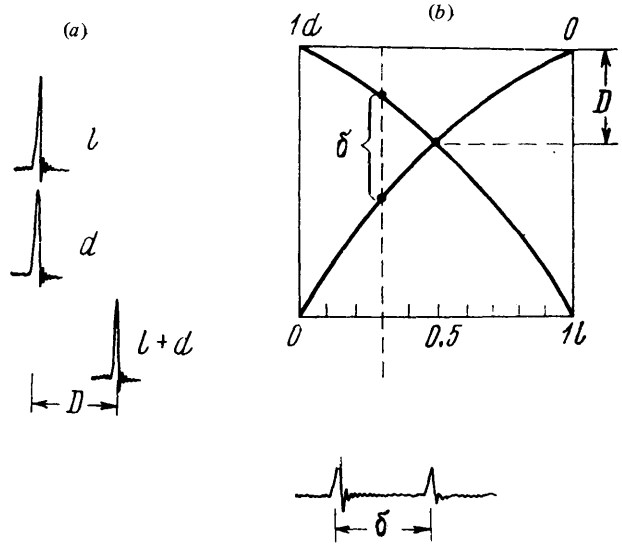

Figure 14. Statistically controlled diastereomeric association in solutions of enantiomers[110,111]: *a*) right-hand and left-hand molecules separately give a singlet n.m.r. signal with an identically coinciding chemical shift, which is displaced if they are mixed in equal quantities (deviation of chemical shift); *b*) with unequal concentrations of left-hand and right-hand molecules in solution the n.m.r. spectrum becomes a doublet, with the intensity ratio of the components equal to the concentration ratio.

Conditions of nuclear magnetic resonance are established by a strong and uniform external magnetic field, but in nuclear quadrupole resonance the three-dimensional quantisation of the magnetic moment of the nuclei is specified by intracrystalline electric field gradients which orient the nuclear quadrupole moments. The limited

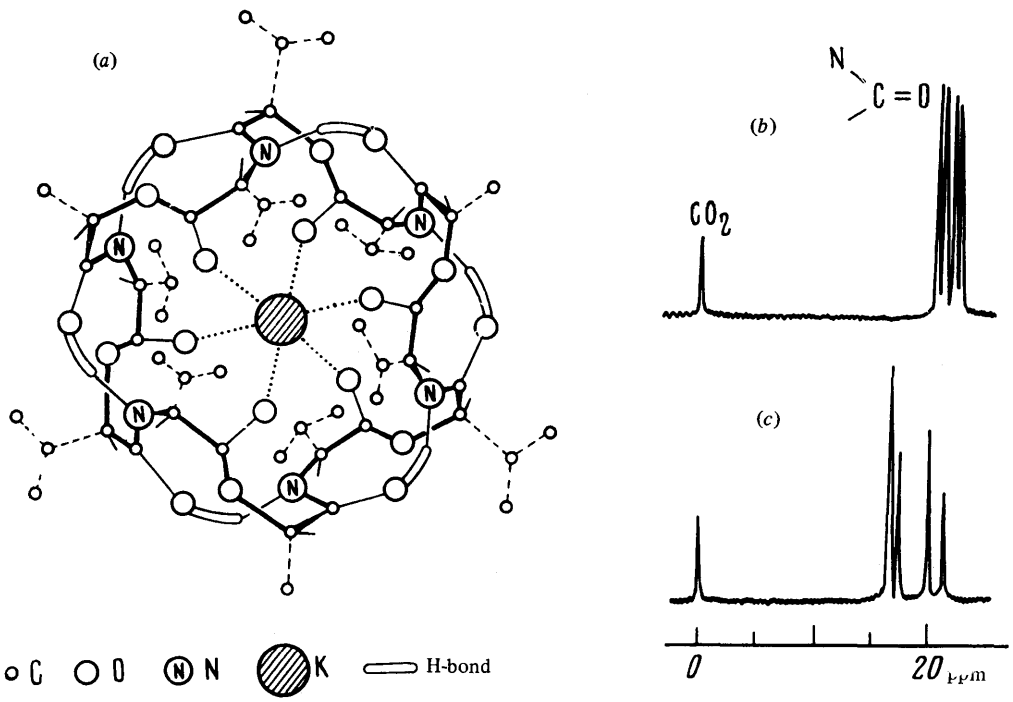

Figure 15. Observation of conformational rearrangement of valinomycin on complex formation with alkali-metal ions[118]: *a*) three-dimensional structure of potassium complex; *b*) position of n.m.r. signals of carbonyl groups in valinomycin; *c*) position in its potassium complex.

scope of the Review does not permit any detailed consideration of the work of Soviet scientists in applying nuclear quadrupole resonance to the study of the chemical structure of matter, although we have obtained the majority of the data on the chemical shifts of n.q.r. frequencies that have now accumulated in the world. Numerous correlations between n.q.r. frequencies and various σ-constants characterising the reactivity of molecules (such as the Hammett, Taft, etc. constants) have been established by the work of the Institute of Organoelementary Compounds[119,120], the Kazan chemical school of A.E. and B.A.Arbuzov[121], and also Voronkov[122]. Limitations have been revealed in the correlation approach, because several factors govern the relations between the electric field gradients on a given nucleus and the activity of the centres in different classes of reactions.

The applications of Mössbauer or γ-resonance spectroscopy to various fields of chemistry are universally associated primarily with the Institute of Chemical Physics. Investigations in this field were presented to the Annual General Meeting of the USSR Academy of Sciences in February 1966, and the lecture was subsequently published[122a], so that the present discussion will be confined to two or three significantly novel aspects. As early as 1962 the asymmetry of the γ-resonance spectra illustrated in Fig. 16 was discovered in the Institute. It permits detection and quantitative description of the anisotropy of bonds and vibrations of atoms in molecules and crystals from the type of spectra for isotropic polycrystalline powders, somewhat as the Debye method in X-ray diffraction gives the structure of single crystals from experiments on powders. During past years more than a hundred publications¶ have appeared on the above effect, which is referred in the world literature to Soviet scientists. A new effect of similar type was reported at the Institute in 1973, involving a difference between components of Mössbauer spectra not in peak area but in shape, whose study will permit characterisation of the anisotropic diffusion of molecular and supermolecular systems[133]. Use of emission γ-resonance spectroscopy, when the atoms are not in the stable form of absorbers but in the radioactive form of emitters of resonance γ-quanta, has opened up rich new possibilities for obtaining both structural and dynamic information.

Use of the iron-57 isotope as a Mössbauer label, with different spectra in all four forms—bivalent and tervalent, in high- and low-spin states—has shown convincingly[134] that the two classic coordination compounds familiar to all chemists since their student days of practical qualitative analysis—the beautiful Prussian Blue and Turnbull's Blue—are in fact the same compound (Prussian Blue), in which the high-spin outer-sphere ion is Fe^{3+}, while the low-spin inner-sphere iron is bivalent. However when these typical coordination compounds have been obtained, an electron escapes from the outer-sphere iron to the central ion of the complex, as illustrated by Fig. 17.

The first experiments by emission γ-resonance spectroscopy, when radioactive cobalt-57 was used as label

¶ Several interesting publications of recent years may be mentioned as example[123-132].

and the chemical state of iron-57 atoms formed by K-capture in the cobalt isotope was determined, supported the above conclusions. Subsequently, however, use was made of the fact that emission of a resonance γ-quantum of energy 14 keV by an excited iron-57 nucleus is preceded by the escape of another, harder quantum (123 keV–Fig. 18), and the time dependence of the form of the Mössbauer spectra of the hexacyanoferrate(II–III) complexes was studied. In this way it was possible to characterise an extremely unstable form of Turnbull's Blue at the instant of its formation[135], and to establish that the time of intramolecular electron transfer converting the complex into Prussian Blue was close to 10^{-8} s.

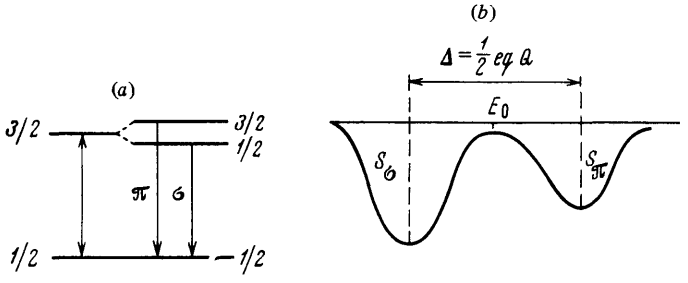

Figure 16. Illustration of effect of asymmetry of hyperfine structure of γ-resonance spectra due to anisotropy of motion of Mössbauer atoms: *a*) scheme of $\frac{3}{2} \rightarrow \frac{1}{2}$ transition in the quadrupole splitting of upper level (π-transition $\frac{3}{2} \rightarrow \frac{1}{2}$; σ-transition $\frac{1}{2} \rightarrow \frac{1}{2}$); *b*) asymmetry of Mössbauer quadrupole doublet for isotropic powdered specimen with different mean square amplitudes of vibration $\overline{x^2}$ and $\overline{z^2}$ perpendicular and parallel to the direction of the gradient q of the electric field in a molecule or in a crystal (s_σ and s_π are the areas of the peaks).

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As a method sensitive both to the electronic structure and to the motion of atoms and electrons, γ-resonance spectroscopy should undoubtedly in future occupy a prominent position in molecular biology for the study of numerous examples of the interrelation between the transport of electrons and changes in electronic states with particular mechanical movements. A most important problem in molecular biology is the mechanism of photoreception—the nature of the action of light on visual pigments and photoreceptor membranes—with which the "rhodopsin" project headed by Yu. A. Ovchinnikov is concerned. An extremely interesting result has recently been obtained in the Institute of Chemical Physics by collaboration between the Structure of Matter Department and N. M. Emanuel's department[136]. This was based entirely on the unique possibilities of simultaneously revealing both the electronstructural and the dynamic properties of a substance by means of γ-resonance spectroscopy. It has been established that the first stage of photolysis of the pigment—conversion of rhodopsin into prelumirhodopsin—is already accompanied not only by photoisomerisation of the chromophore (11-*cis*-retinal → 11-*trans*-retinal) but also by reversible conformational rearrangement of the whole photoreceptor membrane, which occurs even at extremely low temperatures (77°K) and leads to a sharp increase in the rate of spin–lattice relaxation.

The relative accuracy of γ-resonance spectroscopic measurements has no equal: fractional energy changes of the spectral lines of 10^{-15}–10^{-16} have already been recorded; this improves the relative accuracy of nuclear magnetic resonance by factors of 10^5–10^6. However, the energies of the transitions between two nuclear levels

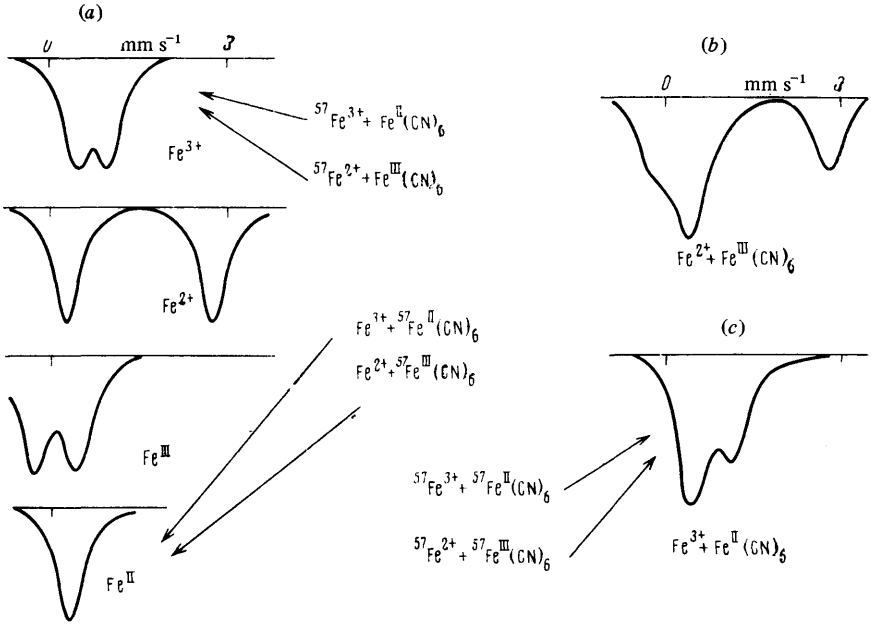

Figure 17. γ-Resonance spectra of hexacyanoferrate(II–III) complexes (only the spectra indicated by the arrows are observed): *a*) high-spin and low-spin forms of bivalent and tervalent iron; *b*) Fe^{2+} + Fe^{III} (Turnbull's Blue); *c*) Fe^{3+} + Fe^{II} (Prussian Blue).

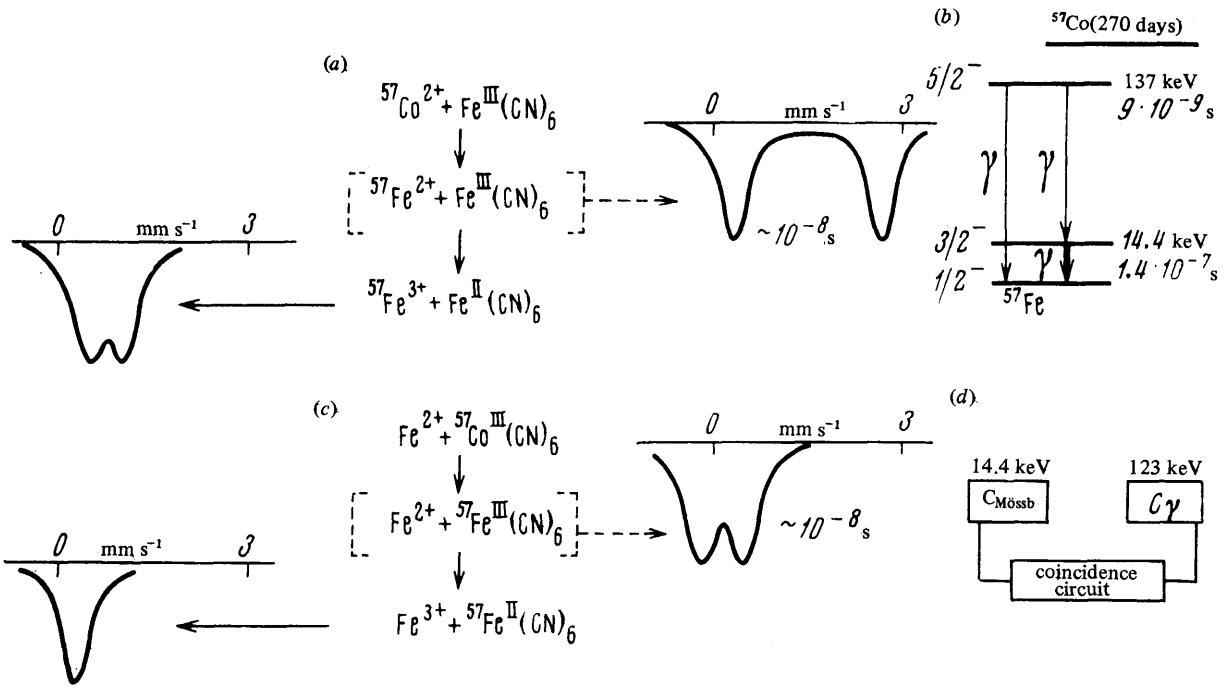

Figure 18. γ-Resonance emission spectra of systems formed by K-capture by cobalt-57 nuclei of: *a*) outer-sphere Co^{2+} with a hexacyanoferrate(III) anion—spectra integrated with time ($> 10^{-7}$ s) after the disintegration $^{57}Co \rightarrow {}^{57}Fe$); *b*) spectra of system (*a*) ~ 10^{-8} s after the disintegration; *c*) hexacyanocobaltate(III) anion with outer-sphere Fe^{2+} cation—spectra integrated with time ($> 10^{-7}$ s) after the disintegration; *d*) spectra of system (*c*) ~ 10^{-8} s after the disintegration.

used in the Mössbauer effect are reckoned in tens of electron-kilovolts, exceeding by almost a billion (10^{12}) the typical energies of n.m.r. transitions. Because of the scatter of local electric and magnetic fields and the presence of all kinds of defects, dislocations, etc., furthermore, the strongest non-uniform broadening of the spectral lines occurs when two different nuclei—an emitter and an absorber of γ-quanta—are involved in the resonance transition. Hitherto, therefore, it has not been possible to observe in Mössbauer spectra absolute line widths below 10^{-10} eV, which is wider than the best n.m.r. lines by a factor of 10^7. This fact played a decisive part in the unsuccessful plans of all kinds to produce a γ-ray laser, abandoned over a decade ago. During the past two or three years, however, fundamentally new ideas have appeared in papers by Soviet scientists—Kagan, Khokhlov, the present Reviewer, and others[137,138]—opening the way to produce γ-ray lasers both on lines of great natural width (i.e. on short-lived nuclei) with neutron pumping and by eliminating various forms of line broadening by combining the methods of γ-ray resonance spectroscopy and nuclear magnetic resonance. Furthermore, an original laser method has been suggested for separating nuclei excited to the Mössbauer levels necessary for stimulating γ-emission from the same nuclei in the ground state[139]. Work aimed at producing a γ-ray laser is of very great interest to physics, chemistry, and biology, for powerful beams of coherent radiation are apparently able to produce direct holographic three-dimensional images of molecules.

We have been considering above the use of hyperfine interactions between electrons and nuclei to study the structure of matter. Considerable successes have also attended quantitative observations of the interaction between electrons of outer and inner shells. The well known phenomenon of the photoeffect—the dislodgment of an inner or a valency electron by a quantum of definite energy—underlies X-ray electron or photoelectron spectroscopy, and the kinetic energy of the electron is measured in the most accurate β-spectrometer. The binding energy of an electron in chemically combined atoms is determined from the difference between the energy of the quantum and the kinetic energy. This quantity is a sensitive characteristic of the chemical bond: with its help we can use data on relative line intensities to construct diagrams of valency and inner electron levels, to determine the degree of oxidation of an element and the donor–acceptor character of a ligand in a complex, to solve many problems of the geometrical structure of a molecule, to estimate the effective charge on an atom, to make a quantitative analysis of elements and functional groups, and to study adsorbed molecules, catalysts, diffusion, the composition of the thinnest surface films, etc. Broad investigations in this field were begun in the Kurnakov Institute of General and Inorganic Chemistry at the end of 1970, and more than 500 simple

and complex inorganic compounds have been examined during the past three years. Some of the most interesting and important results[140] will be noted here.

Examination of specimens of a lunar regolith provided by Soviet automatic stations and by American cosmonauts has shown that the concentrations of elements at the surface of the particles differ appreciably and regularly from the bulk concentrations. A substantial part of the surface consists of metallic iron, coated with only an unusually thin layer of oxide or even in part not oxidised at all after a long time in the earth's atmosphere (Vinogradov, Zhavoronkov et al.[141,142]).

Study of a large number of isostructural series of complex compounds of platinum, palladium, rhodium, iridium, cobalt, and other transition metals has established sequences of ligands according to their ability to withdraw electron density from the central atom[140]. The sequence for acido-ligands is

$$F > NO_3 \gtrsim NO_2 \gtrsim CN \simeq \tfrac{1}{2}C_2O_4 \simeq NCS > Cl > Br \simeq SCN > I$$

the corresponding sequence for neutral ligands is

$$N_2 > CO \simeq C_2H_4 > C_2(C_6H_5)_2 > C_6H_5CN > NH_3 > C_5H_5N > R_2S > P(C_6H_5)_3$$

Buslaev et al.[143] have obtained schemes of molecular valency levels for oxo-anions and fluorides of non-transition elements in Groups II–V, and have established for the first time several regularities in the variation of energy levels of isoelectronic and isovalent series of compounds. These rules are supported by calculations[144]. Detailed consideration has been given to experimental and theoretical aspects of the determination of relative line intensities in an X-ray electron spectrum. A technique developed for the quantitative analysis of thin films on solid surfaces has been used to examine the surface characteristics of catalysts, semiconductors, certain protective coatings, etc.

Although electron spectroscopy for chemical analysis in its X-ray form (X-ray electron spectroscopy) has reached us from abroad, accurate chemical X-ray spectroscopy owes not only its fruitful application but also its actual origin to Soviet scientists. Chemical changes in the energy of X-ray lines, like the ionisation potentials of the inner electrons, are governed by the shielding effect of the outer electron shells on the inner shells. It was established as early as the 1920s that the energies of X-ray transitions are slightly dependent on the chemical bond, but only in the 1960s were methods first proposed, as a consequence of development of the appropriate quantum-chemical techniques in the Institutes of the USSR Academy of Sciences[77-83,145], for determining the effective atomic charges in molecules from the shifts in the lines of the X-ray emission spectrum. These methods are based on the principle that the magnitude of the shift is completely determined by the number and the character of the valency electrons belonging to the given atom. The effective charge on an atom in a compound is found from this relation and the measured shift of the X-ray line. At the present time the X-ray spectroscopic method for determining the effective charge on an atom is probably the most soundly based, and is widely used in Soviet and foreign laboratories. Measurement of the shift of the inner X-ray lines provides solutions in particular to the problems of the degree of oxidation of an element in a compound, the presence of non-equivalent atoms of the same element in a compound, and the coordination numbers of certain elements, and permits the study of several other characteristics of the geometrical structure of molecules.

Extremely important information on the electronic structure of chemical compounds (the ionisation energies of valency levels and the character of their wave functions) can be extracted from the energies and the relative intensities of X-ray transitions from valency levels and bands. For example, the relative intensities of the maxima in the K-spectrum of chlorine can be used to determine the ratio of the squares of the coefficients in the $3p$ orbitals of the chlorine atom in all the wave functions of the valency levels, and the energy position of the maxima to find the relative positions of the valency levels. Since the X-ray spectra of almost all the atoms in a compound can be studied, a fairly detailed picture of the electronic structure of the molecule is obtained. Work on the chemical X-ray spectroscopy of free molecules and isolated groups in crystals, semiconductors, and metals has been done in several Institutes of the USSR Academy of Sciences—the Kurnakov Institute of General and Inorganic Chemistry[146], the Institute of Inorganic Chemistry of the Siberian Division (Nikolaev et al.[147]), and the Institute of Metal Physics of the Ural Science Centre[148]—the Institute of Metal Physics of the Ukrainian SSR Academy of Sciences[149], etc.

The chemical bond has been investigated also by use of the fine structure of the edges of X-ray absorption spectra, which corresponds to electron transitions from inner levels to vacant levels of the discrete and continuous spectrum. These transitions can be used to construct a scheme of vacant levels and to determine the effective charge on the absorbing atom. The first method for such determination was developed in the Vernadskii Institute of Geochemistry and Analytical Chemistry and the Institute of the Mineralogy, Geochemistry, and Crystal Chemistry of the Rare Elements of the USSR Academy of Sciences[77-80], and was based on the dependence of the energy position of the discrete absorption lines and their relative intensity on the effective charge of the absorbing atom. This method stimulated the study of X-ray absorption spectra, and on its basis the problem of the relative intensities of the discrete spectrum and the origin of the continuous absorption spectrum was first posed and solved for the simplest model. Until the mid-1960s accurate chemical X-ray spectroscopy was confined to elements at the beginning and the middle of the periodic system. X-Ray methods for determining effective charges on atoms even of the heaviest elements were subsequently developed from work at the Konstantinov Leningrad Institute of Nuclear Physics of the USSR Academy of Sciences[81-83]. This new type of spectroscopy thereby acquired universal value.

Chemical X-ray spectroscopy provided a very clear demonstration of the particular inadequacy of formal ideas on the oxidation states of atoms. The determination of effective charges from X-ray emission and absorption spectra sometimes led to quite remarkable conclusions[77,78]. For example, whereas the effective charges in high-spin compounds of bivalent iron were only slightly less than the formal valency of the ion (2+), in the analogous compounds of tervalent iron these charges were not simply very far from the formal valency of the ion (3+) but, moreover, even smaller than for bivalent iron, about +1.2. The effective charges on iron in ferrocene and the ferricinium ion (where one electron has been removed) were almost identical (about +0.6). The effective charges of cations are in general always less than their formal valencies, while the charges on anions are numerically less than unity: in other words, Coulombic repulsion prevents the accommodation of more than one extra electron in an atom, after which only a redistribution of electrons

among different molecular orbitals takes place. In just the same way a large positive charge on an ion is balanced by electrons (which "leak" from other parts of the molecule) from other molecular orbitals. Therefore, as in the ferricinium ion it is not the central iron atom but the cyclopentadienyl ring which is ionised; in the ion $[Fe(H_2O)_6]^{3+}$, however, ligands (water molecules)—not the iron itself—lose three electrons. Although the calculation of effective atomic charges in molecules and the significance attributable to these quantities, in particular the volume in which the measured charge is concentrated, continue to be debated†, the positive side of the conclusions is undoubted: the electrostatic description of chemical bonds is decisively rejected even in high-spin compounds having a weak ligand field (which were the most reliable "refuge" of electrostatic concepts); the rightness and also in some measure validity of such an empirical generalisation as Pauling's principle of electrical neutrality are confirmed; and finally the need to apply the currently most popular and fruitful method of quantum chemistry—molecular orbital theory—to almost all chemical structures is convincingly demonstrated.

Modern structural chemistry makes use of radiation covering a range of more than thirty octaves (10^{10} of wavelengths, from fractions of an Ångström unit to decimetres). Different methods give, of course, complementary information, and only the combination of all methods will yield a consistent picture of the electronic structure of atoms and molecules. Owing to the impossibility of obtaining exact solutions to the Schrödinger equation for many-electron systems, chemists are compelled to use only approximate solutions. As a consequence, even in the most favourable case the complete wave function of a many-electron system—atom or molecule—can be sufficiently accurate only in certain of its regions: in other words, a wave function which may be entirely adequate e.g. for analysing the electronic spectrum of a molecule may prove completely unsuitable for describing the n.m.r., e.s.r., or γ-resonance spectrum of the same molecule.

The development of numerous spectroscopic methods enabling the various parts of many-electron systems to be "probed" has seriously tested theoretical methods of obtaining the wave functions of atoms and molecules. During the past decade this has greatly disturbed the coexistence of different approximate theories of the chemical bond, and one of them—the theory of molecular orbitals—has clearly tended to be preferred by research workers. This theory is based on the formation in a molecule of discrete states of individual electrons (molecular orbitals), defined by the self-consistent motion of the electrons in the field produced by the others and all the nuclei in the molecule. Thus the quantum-mechanical model of an atom—the theory of atomic orbitals—now represents the particular case in molecular-orbital theory in which the system contains only one atomic nucleus. Furthermore, the molecular-orbital theory involves the most general physical concepts on molecular structure, and the mathematics used is most suitable for making quantitative calculations on an electronic computer. All this is responsible for the dominant role of this theory in modern quantum chemistry.

One of the first to make wide use of the molecular orbital method and to popularise it in every way possible was Ya. K. Syrkin[150-152], founder of the Soviet school of quantum chemistry. He clearly demonstrated with numerous examples (including the effective charges on atoms in molecules[151]) the need to regard the properties of a molecule not as the simple sum of those of central ion and ligands but as involving all the intramolecular interactions, by no means reducible to small perturbations. Soviet scientists were the first to make systematic calculations by a form of the method which has since found widespread use in the so called zero differential overlap approximation (ZDO)[152,153], also to use the method to describe transition-metal complexes, including sandwich compounds[154,155], and to analyse the band structure of dielectrics and semiconductors[156].

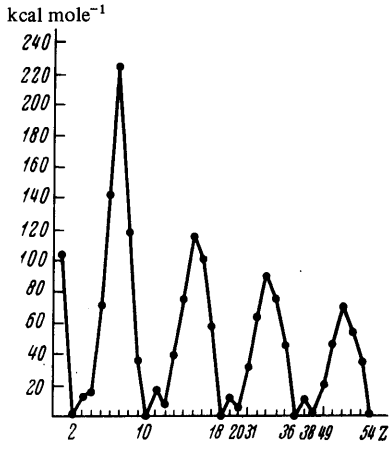

Figure 19. Stabilities (dissociation energies) of homonuclear diatomic molecules Z_2 for elements in the main groups of the first five periods of Mendeleev's system.

In conclusion let us consider briefly the periodicity of the chemical properties of the elements in the light of our modern knowledge of molecules. The molecular-orbital theory, which extends and generalises the atomic-orbital theory, regards the electronic structure of a molecule as resulting from the filling of discrete electron levels forming definitely repeated shells by virtue of the laws of quantum mechanics and the Pauli principle. Thus, just as periodic relations exist in the electronic structure of atoms, so also distinct periodic variations (though more complicated) are found in the electronic structure of molecules. A convincing example is the clear correlation of various properties of homonuclear diatomic molecules (e.g. the stability, i.e. the dissociation energy, of Z_2 in Fig. 19) with the position of the atom Z in the periodic system[157]. Here the sequence of molecular orbitals, bonding and antibonding in character, is almost invariant in Z_2 molecules for all atoms of a given period. The differing properties of these molecules depend on the relative numbers of bonding and antibonding electrons, which is ultimately determined by the total number of electrons

† The concept of the effective charges of atoms is most justified when such charges are compared in series of compounds of the same type, e.g. monosubstituted compounds or complexes of a given element with ligands having weak and strong fields respectively.

in the molecule, i.e. by the atomic number of the element Z. This is yet another of the innumerable confirmations expected by Mendeleev in the future superstructure and development of the periodic law.

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We have tried to trace the main line of research on the structure of matter from the establishment of Mendeleev's periodic law until the present time. These investigations provide the clearest evidence of the unity and indissolubility of the whole of modern natural science—primarily physics, chemistry, and biology—most closely linked with ideas on the structure of matter, from elementary particles to the most complicated molecules and cells. Indeed, the properties of elementary particles that have now been found and explained on the Mendeleev path of the development of physics and chemistry, interactions between nuclei and electron shells, have become the basis of methods correctly revealing the structure of molecules and the relation between this structure and their reactivity, i.e. the spatial rearrangement and movement of molecules, which means solving key problems both of theoretical chemistry and of future chemical industry, as well as understanding the molecular nature of the motion of biological materials. Contrary to the view sometimes held, the role of chemistry in this triad (physics, chemistry, biology) has by no means become subordinate, but is even central, for without chemistry a genuine union and mutual enrichment of the main natural sciences are impossible.

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Compounds of the Noble Gases

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The results of investigations of the physical and chemical properties of compounds of the noble gases and their structure, stability, and reactivity are given; the principal methods of synthesis are considered. Special attention is paid to the latest achievements in this field—to investigations of complexes, derivatives of xenon fluorides and oxo-acids, xenon hexafluoride, and the study of the electronic structure. Non-empirical methods of calculation on the bonding in noble gas compounds are discussed and their results are compared with experimental results obtained with the aid of photoelectronic and X-ray electronic spectroscopy. Possible practical uses of the compounds of the noble gases are considered on the basis of the material presented. There is a bibliography of 400 references.

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I. INTRODUCTION

The development of the new field of inorganic chemistry—compounds of the noble gases—which began not much more than ten years ago is still continuing, although the direction and nature of the investigations has undergone certain changes. Whereas in the first two years after the discovery of this new class of substances (1962–1964) there appeared many papers dealing with their preparation and preliminary study, subsequent years are distinguished by a broadening and simultaneous deepening of the investigations, by the isolation of a series of new, previously unknown compounds, and also by continuation on a more complete basis of the theoretical comprehension of new experimental results. A significant increase in the importance of the work of Soviet scientists is also characteristic for this period of time.

The studies of the first two years were reflected in a review[1] published in 1965. It is now opportune to systematise the many new experimental and theoretical results to create a complete picture of the present state of investigations of the compounds of the noble gases. The present review has this aim and deals with the literature available to the authors in January 1974.

During the years which have elapsed since the first review was published[1] there have appeared several publications[2-12] which treat in more or less detail the particular aspects of the problem being considered. Of these, we think that of Dyatkina[2] merits special attention, in which a detailed analysis is given of all investigations of the nature of the chemical bond in compounds of the noble gases, and also the reviews of Malm and Appelman[3], Holloway[4], and Jha[5]. Because of this, in the present review greater attention is paid to papers published after 1969.

For brevity and also with the aim of simplifying the exposition, the molecular constants and physical properties of the most studied compounds of xenon and krypton are given in Tables 3 and 5, and in the text are given only those data which require explanation or serve for subsequent discussion.

II. XENON COMPOUNDS

A. XENON FLUORIDES

1. The Fluorine–Xenon System

The fluorine–xenon system has been investigated[13] over a wide range of temperature and pressures. The processes taking place in this system are described by the following consecutive-concurrent reactions:

$$Xe + F_2 \rightleftarrows XeF_2;\ K_2 = [XeF_2]/[Xe][F_2];$$
$$XeF_2 + F_2 \rightleftarrows XeF_4;\ K_4 = [XeF_4]/[XeF_2][F_2];\ K_4^* = [XeF_4]/[Xe][F]^2;$$
$$XeF_4 + F_2 \rightleftarrows XeF_6;\ K_6 = [XeF_6]/[XeF_4][F_2].$$

Table 1 gives experimental and calculated (in parentheses) equilibrium constants.

The equilibrium constants showed[16] that XeF_2 and XeF_6 can be easily obtained in the pure form, whereas there are no conditions which would ensure that the XeF_4 concentration in the equilibrium mixture exceeds 91 vol.%. At an initial molar ratio of $Xe : F_2 \geq 1.4$ the equilibrium mixture consists almost solely of the excess of xenon and XeF_2. In every instance the equilibrium is reached rather rapidly above 250°C. The optimal conditions of synthesis of the pure xenon fluorides at various temperatures have been determined[17].

An investigation of equilibria in the fluorine–xenon system showed[13] that a xenon fluoride with the ratio $F:Xe > 6$ does not exist even under conditions of high pressures (500 atm, 250°C). Other work[18] agrees with this result and also refutes a previous report[19] of the synthesis of xenon octafluoride.

Table 1. Equilibrium constants of the reactions for the formation of xenon fluorides[13].

Equilibrium constant	25°	250°	300°	350°	400°	500°
K_2	$(1.23\cdot10^{13})$	$(8.8\cdot10^{4})$	$(1.02\cdot10^{4})$	(1670)	(360)	29.8
K_2[14]	$(7.23\cdot10^{12})$	—	$(7.74\cdot10^{3})$		(285±49)	—
K_4'[15]	$(1.65\cdot10^{24})$	$(1.1\cdot10^{8})$	$(1.49\cdot10^{6})$	$(4.14\cdot10^{4})$	$(1.98\cdot10^{3})$	(14.4)
K_4	$(1.35\cdot10^{11})$	1431	154.9	27.22	4.857	0.5020
K_6	$(8.2\cdot10^{5})$	0.9435	0.2112	0.05582	0.01822	—

The reaction rate in the fluorine–xenon system depends on the diameter of the reaction vessel and the state of its surface[16]. The reactions for the formation of the xenon fluorides are mainly heterogeneous and take place on the fluorinated walls of the reaction vessels or at the surface of certain metal fluorides, for example, CoF_3, NiF_2, or CaF_2. The catalytic influence of these fluorides was investigated[20] at 300–450°C and pressures of 1.5–2.0 atm and is tentatively explained by the formation of the complexes $XeF_6.CoF_3$, $XeF_6.NiF_2$, etc. The existence of such compounds was confirmed[21] by the investigation of interaction in XeF_6–metal fluoride systems: $XeF_6.2CrF_2$, $XeF_6.CoF_2$, and $XeF_6.2FeF_2$ were prepared. Slivnik and coworkers[22,23] investigated the catalytic influence of highly disperse nickel and magnesium fluorides on the reaction between xenon and fluorine (1 : 10) and found that at 120°C XeF_2 is almost the only product in the presence of MgF_2, whereas in the presence of NiF_2 the only reaction product is XeF_6 even at the molar ratio $F:Xe = 5$. Chromium, vanadium, and manganese fluorides also exert a catalytic influence[24].

The catalytic formation of XeF_2 on heated metals has been investigated[25]. This process is catalysed only by metals which form ionic fluorides, for example, Ni, Pd, Co, Cu, Al. Investigation of the adsorption of xenon in the presence of fluorine on nickel and palladium[26] suggested that the stage determining the rate of catalytic formation of XeF_2[25] is the desorption of XeF_2 from the metal surface.

2. Xenon Difluoride

a. Methods of Preparation

Most of the papers on the preparation of noble gas compounds belong to the first period of investigation[1]. No method new in principle has originated in recent years.

Almost pure XeF_2 can be obtained by the interaction of xenon and fluorine ($Xe:F_2 = 1.3–2.0$) in the temperature range 400–500°C at pressures of 0.5–27 atm.[27,28] XeF_2 can also be prepared in a cylindrical flow reactor filled with a nickel packing with a contact surface of 0.2 m^2, when heated to 600°C and at a total pressure of 650 mmHg.[29] XeF_2 is formed in good yield in a mixture of xenon and fluorine (1 : 1 by volume) subjected to a glow discharge[30]. The yield of XeF_2 increases with the rate of flow of the mixture through the reactor.

XeF_2 of high purity has been prepared photochemically[31–34]. Small quantities of XeF_2 can be obtained in quartz or Pyrex vessels by irradiation of mixtures of xenon and fluorine (600–1000 mmHg, $Xe:F_2 = 1:1$) with daylight. However, when the conversion reaches 60% the xenon difluoride begins to be contaminated with the tetrafluoride[33]. The irradiation of a mixture of xenon and fluorine with the light from a high-pressure mercury lamp is recommended[35,36] as a convenient method of obtaining pure XeF_2. The photochemical interaction of xenon with OF_2 leads to the formation of XeF_2.[31]

Xenon difluoride is obtained in 98% yield by the reaction of xenon with an excess of O_2F_2[37] at −118°C and O_4F_2.[38] The reaction of xenon with fluorine in the gaseous and condensed phases under the action of protons with energies of 10 MeV at temperatures from −78° to −180°C can be used for the synthesis of XeF_2.[39] XeF_2 is also formed by the reaction of xenon with fluorine in shock waves[40] at 1100°C.

b. Physical Properties of XeF_2

The vapour pressure of XeF_2 in the temperature range 0–115°C is expressed by the equation[41]

$$\lg P_{mmHg} = -3057.67/T - 1.23521 \lg T + 13{,}969736.$$

The density of liquid XeF_2 in the temperature range 115 to 90°C is given by the expression[42]:

$$\rho_{g\,cm^{-3}} = 3.641 - 3.96\cdot10^{-3}\,t.$$

The heat capacity of XeF_2 was measured[14] by an adiabatic method in the temperature range from −268° to 77°K.

The standard enthalpies of formation of XeF_2, and also XeF_4 and XeF_6, obtained by different methods[13,43–45] are somewhat different. Johnson and coworkers[45] consider the results of the calorimetric investigation of the reaction of solid XeF_n with phosphorus(III) fluoride to be the most reliable.

As an extension of the earlier[1] spectroscopic investigations, the infrared, Raman, and ultraviolet spectra of gaseous and solid XeF_2 have been studied. The high-resolution infrared spectrum of gaseous XeF_2 was investigated in the range of the ν_3 vibrations (544–574 cm^{-1}).[46] An analysis of the spectrum led to the following molecular constants: $\nu_0 = 560.101\ cm^{-1}$, $B_0 = 0.11350\ cm^{-1}$, $\alpha_3 = 3.31\times10^{-4}$, $X_{23} = -1.44\ cm^{-1}$. The B_0 found was used to calculate the bond length $r(Xe–F) = 1.997 \pm 0.0015$ Å.

The laser Raman spectrum of XeF_2 has been obtained and interpreted[47]. The very interesting band at 514.5 cm^{-1} has been assigned to the ν_1 symmetric stretching vibration. The agreement with the predicted $\nu_1 = 515\ cm^{-1}$ (from the composite band $\nu_1 + \nu_3$ at 1070 cm^{-1} in the infrared spectrum of XeF_3)[48] shows the very low anharmonicity of the vibrations of the XeF_2 molecule.

The investigation of the spectra of gaseous and solid (−193°C) XeF_2 in the far ultraviolet range (50–160 eV)[49] enabled information to be obtained about the excited electronic levels of the molecule and to assign the absorption lines in the range 61–73 eV on the basis of a semi-empirical calculation.

Radioelectronic[50,51] and photoelectronic spectroscopy[52–54] have played a large part in the study of the structure of noble gas compounds, especially XeF_2. The results for XeF_2 obtained by these methods are discussed in Chapter V.

NMR and EPR methods have also been used for studying XeF_2. In ^{19}F NMR the variation of the second moment of the rigid XeF_2 lattice with the external magnetic field has been measured [55]. The magnetic screening parameters do not agree with the results of semiempirical calculation [56]. The EPR of γ-irradiated XeF_2 were investigated at 77°K. [57] The spectrum obtained was assigned to the XeF radical; the parameters of the spin-hamiltonian of XeF in the XeF_2 and XeF_4 lattices [58] differ slightly. In connection with the EPR results it is interesting to note that the hypothetical formation of XeF in the gas phase [40, 59-61] has still not been confirmed experimentally [62]. A calculation by the SCF MO method showed that the $^2\Sigma^+$ and $^2\Pi$ states of XeF are repulsive and the XeF radical should not exist in the gas phase in the free state [63].

The deflection of an XeF_2 molecular beam in a heterogeneous electric field has been studied [64]. The results obtained confirmed the structure $D_{\infty h}$ for this molecule. The emission spectrum of a Xe + BF_3 (NaF, LiF) mixture in a microwave discharge [65] is characterised by the existence of two groups of bands of different intensity, assigned to XeF_2: 3510, 2635 and 3080, 2355 Å.

c. Chemical Properties

Behaviour of XeF_2 in Non-Aqueous Solvents

Xenon difluoride dissolves in BrF_3, [66] BrF_5, [67] HF, [68] IF_5, [69] SO_2, [69] and CH_3CN. [70] The solubility of XeF_2 in IF_5 reaches 1538 g per 1000 g IF_5. [71] Different opinions [72-74] have been expressed about the behaviour of XeF_2 in IF_5. The most complete picture of the interaction in the IF_5–XeF_2 system was obtained in investigating the equilibrium diagram [71,75] (Fig. 1). Fig. 1*b* shows the so-called "transitional" equilibrium diagram obtained at temperatures up to 80°C. At 80°C the irreversible conversion of the unstable solvates $XeF_2.nIF_5$ (n = 1.5–9) into $XeF_2.IF_5$ takes place. An attempt [76] to reproduce the earlier results [72-74] led to the production of only $XeF_2.IF_5$, which according to spectroscopic, Raman, and X-ray diffraction results is a molecular compound [76]. $XeF_2.IF_5$ is tetragonal with parameters a = 7.65, b = 10.94 Å, space group $I4/m$. The structure (Fig. 2) shows the existence of the discrete molecules XeF_2 ($D_{\infty h}$) and IF_5 (C_{4v}). [77]

The maximal solubility of XeF_2 in BrF_5 is 1893 g per 1000 g bromine pentafluoride [78]. Xenon difluoride dissolves readily in anhydrous HF; at −2°C the solubility is 6.38 moles XeF_2 per 1000 g HF and increases with the temperature. The enthalpy of dissolution is 2.5 kcal mole^{-1}. The investigation of the electrical conductivity of such solutions, their Raman spectra, and ^{19}F NMR led to a conclusion about the solubility of XeF_2, in molecular form, in HF. [68] The solubility of XeF_2 in 3HF.NOF is unusually high [79]: 73.25 wt.% at 16.8°C.

Xenon difluoride is slightly soluble in Mo and W hexafluorides. According to DTA results [80], the unstable compounds $XeF_2.MoF_6$ and $XeF_2.WF_6$ are formed in the WF_6–XeF_2 and MoF_6–XeF_2 systems.

The solubility of XeF_2 in acetonitrile at 0°C is 16.8 g and that at 21°C 32.0 g per 100 cm^3 solvent [70]. Xenon difluoride is oxidised at the boiling point of acetonitrile [69]. XeF_2 dissolves in dimethyl sulphoxide (DMSO) and pyridine but not in liquid ammonia [69]. XeF_2 forms the complex $XeF_2.2Bipy$ with bipyridyl [72].

The behaviour of XeF_2 in various solvents was investigated by infrared spectroscopy [81]. A shift in the frequency of the vibrations of the Xe–F bond into the longer-wave range with increase in the donor strength of the solvent was noted and this can be regarded as qualitative indication of the weakening of this bond.

The XeF_2–XeF_6 system has a simple eutectic [82].

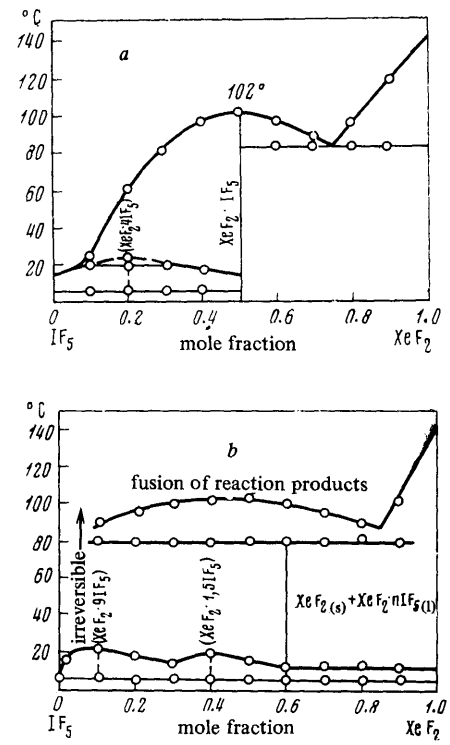

Figure 1. *a*) Equilibrium diagram of the IF_5–XeF_2 system; *b*) "transitional" equilibrium diagram of the IF_5–XeF_2 system.

Redox Reactions of XeF_2

It would seem that in redox fluorination reactions XeF_2 from both the thermodynamic and kinetic viewpoints does not compete with such powerful fluorinating agents as molecular fluorine, oxygen fluorides, certain halogen fluorides, etc. However, this "kinetic inertness" is the merit of XeF_2 and simplifies the practice of oxidising fluorinations.

DTA has shown [83] that at moderate temperatures XeF_2 reacts with many elements: with Mo at −11°, W (21°), Te (16°), S (27°), P (−10°), Ge (−12°), Si (16°), Nb (6°), Ta (22°), Sb (33°), Sn and Ti (28°), etc. In all these reactions higher fluorides of the corresponding elements are formed. XeF_2 reacts with elemental bromine and iodine with the formation of BrF_3 and IF_5. On the basis of the results of an investigation of the reactions of XeF_2, of the calculations of the free energies of the corresponding processes, and also of the relative reactivities of the halogen fluorides [84] a series for the relative fluorooxidising capability of XeF_2 has been compiled [83]:

$$ClF_3 > BrF_5 > IF_7 > ClF > BrF_3 > XeF_2 > IF_5 > BrF\ .$$

The high fluorinating activity of XeF_2 also appears in reactions with WO_3 (27°), U_3O_8 (67°), Nb_2O_5 (49°), V_2O_5 (26°), KBr (21°), KI (12°), KIO_3 (47°), and $NaBrO_3$ (41°), as a result of which higher fluorides, $KBrF_4$, KIF_6, and $NaBrO_2F_2$ are formed[88]. Solid XeF_2 reacts at 20°C with ICl and ICl_3 with the formation of IF_5.[85] Chromium(V) fluoride fluorinates XeF_2 to XeF_4 at 120°C, and at 60°C a mixture of $XeCr_2F_{10}$ and XeF_4 is formed[86].

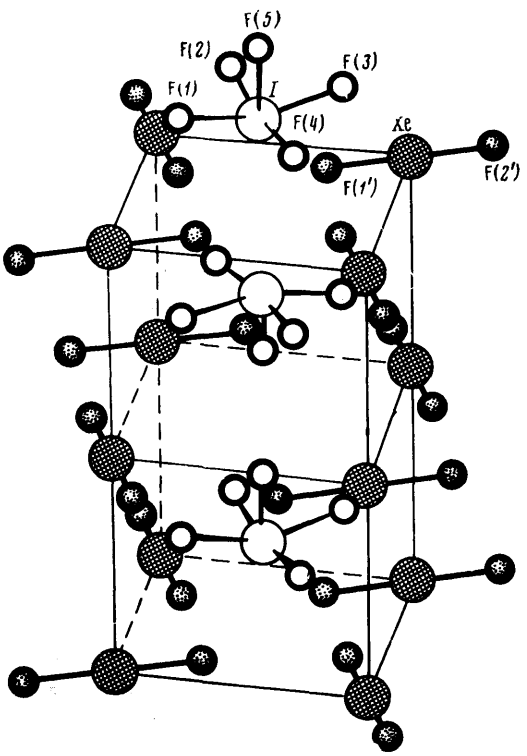

Figure 2. Crystal structure of $XeF_2.IF_5$.

A qualitative investigation of the oxidising power of xenon fluorides was carried out in the case of their interaction with UF_4.[87] The greatest rate of fluorination is observed with XeF_6.

Xenon difluoride is used as fluorinating agent for obtaining the higher fluorides of the rare-earth elements (r.e.e.). When mixtures of XeF_2 and TbF_3 are heated to 300–350°C, TbF_4 is formed[88,89]. The reaction of XeF_2 with the fluoro-complexes of tervalent r.e.e. can be used to obtain compounds of Ce^{IV}, Pr^{IV}, and Tb^{IV} of composition Cs_3LnF_7.[90]

The oxidising reactions of XeF_2 in solutions of non-aqueous solvents are interesting. In acetonitrile, the reactions of XeF_2 with I_2, SO_2, and SO_3 take place with the formation of IF_5, SO_2F_2, and $S_2O_6F_2$ respectively[67]. The reactions are catalysed appreciably by traces of HF and BF_3, which is probably linked with the formation of the cations XeF^+ and $Xe_2F_3^+$ in the solutions[67]. The catalytic influence of certain fluoro-acids on the formation of BrF_3 was investigated[83]; the rate constants observed are characterised by the catalytic activity of certain fluoro-acids in the reactions of XeF_2 with Br_2 in BrF_3 solutions (s^{-1}) at 19°C: 0.0081 (XeF_2), 0.016 ($XeF_2 + TaF_5$), and 0.045 ($XeF_2 + SbF_5$). The order of increase of the rate constants $BrF_3 < TaF_5 < SbF_5$ ($k_{BrF_3} : k_{TaF_5} : k_{SbF_5} = 1:2:6$) agrees with the relative acceptor capability of these fluorides[91]. The reaction of XeF_2 with the oxides of As, P, and Sb in BrF_3 leads to the formation of AsF_5, PF_5, and SbF_5.[66] In the presence of AsF_5, BF_3, PF_5, or TiF_4, xenon difluoride decomposes acetonitrile[92].

Solutions of XeF_2 in CCl_4 are stable up to the boiling point of CCl_4.[93] In the presence of traces of Group V element halides, XeF_2 reacts with CCl_4 with the formation of Freons, SiF_4, Xe, and Cl_2. The reaction of XeF_2 with $SiCl_4$, $TiCl_4$, and $SnCl_4$ leads to the formation of tetrafluorides[93]; when there is an excess of XeF_2 the compounds $2XeF_4.MF_4$ (M = Sn or Ti) are formed. $2XeF_2.ZrF_4$ and $2XeF_2.HfF_4$ are formed in the direct interaction of the fluorides[93].

In HF solutions xenon difluoride reacts with $Re_2(CO)_{10}$ with the formation of ReF_5.[94] Tungsten and molybdenum carbonyl fluorides can be obtained analogously[95]. Marshall and Peacock[96] reported the production of Re, Mo, Ru, and Os carbonyl fluorides by the reaction of XeF_2 with carbonyls and carbonyl chlorides of the corresponding metals. They also obtained the double carbonyl fluorides $Mo(CO)_3F_2.MoF_5$, $Re(CO)_5F.ReF_5$ of tungsten, osmium, iridium, and rhodium[97].

Reactions of XeF_2 in Aqueous Solutions

Xenon difluoride dissolves readily in water but the solutions are unstable[98]. The solubility of XeF_2 in the molecular form has been shown by the ultraviolet spectra[99] and electrical conductivity[100,101] of its aqueous solutions.

The hydrolysis of XeF_2 is a first-order reaction, the rate constant in pure water being 2.8×10^{-5} s^{-1} at 0° and 25×10^{-5} s^{-1} at 25°C.[102] The activation energy of hydrolysis is 18.4 kcal $mole^{-1}$.[103] The rate constant for the hydrolysis of XeF_2 in 0.01 M $HClO_4$ is 42×10^{-5} s^{-1} at 25°; the activation energy is 20.2 kcal $mole^{-1}$.[104] The rate of hydrolysis of XeF_2 in water is minimal in the range pH 4–9.[105] The hydrolysis is strongly catalysed by bases, the anions F^-, NO_3^-, HCO_3^-, CO_3^{2-}, $H_2PO_4^-$, HPO_4^{2-}, PO_4^{3-}, and by the cations Th^{4+}, Al^{3+}, La^{3+}, and Be^{2+}.[104,105] The rate of hydrolysis of XeF_2 also increases with the concentration of HF in the solution[106]. The results obtained in investigating the hydrolysis of XeF_2 in neutral aqueous solutions are explained[104] by the reactions:

$$XeF_2 + H_2O \rightarrow XeO + 2HF;\ XeO + H_2O \rightarrow$$

$$\rightarrow Xe + H_2O_2;\ H_2O_2 + XeF_2 \rightarrow Xe + 2HF + O_2,$$

which have also found experimental confirmation[104,107].

Aqueous solutions of XeF_2 exhibit a pronounced oxidising ability. The redox potential of the XeF_2/Xe couple in acidic medium $XeF_{2(aq)} + 2H^+_{(aq)} + 2e^- = Xe_{(g)} + 2HF_{(aq)}$ is estimated[3] to be 2.64 V ($\Delta G^\circ_{298}XeF_{2(aq)} = -20.35$ kcal $mole^{-1}$). Other results[108] obtained by use of the Powell and Latimer equation for aqueous solutions of non-electrolytes, give $E^\circ_{(XeF_2/Xe)} = 2.3$ V. The bromate ion was oxidised by XeF_2 in aqueous solutions, which enabled previously unknown perbromates to be synthesised, in particularly $RbBrO_4$.[109] Xenon difluoride also oxidises iodates and chlorates[110–112]. In alkaline solutions, XeF_2 oxidises astatides to perastatate[113], Np^V and Np^{VI} to Np^{VII}.[108,114]

Reactions of XeF_2 with Organic Compounds

The use of elemental fluorine in organic chemistry is very limited and requires a special technique [115]. The use of other fluorinating agents, such as HF, certain metal fluorides, or interhalogen compounds, while allowing fluoro-substituted compounds to be obtained, results in low yields and poor selectivity. Xenon fluorides, and XeF_2 in particular, have been investigated recently as promising fluorinating agents.

Xenon difluoride reacts with an excess of benzene in CCl_4 in the presence of small quantities of HF with the formation of fluorobenzene [116] (68% yield on the benzene); with substituted benzenes in CCl_4 or CH_2Cl_2 the corresponding fluorobenzenes are formed [117]. These investigations [116,117] showed that the use of XeF_2 gives a possibility of changing the Balz–Schiemann reaction for obtaining fluorinated aromatic compounds. The conversion is effected in a single stage, which is an advantage in comparison with the usual three-stage process [115].

An investigation of the reactions of XeF_2 with benzene and its derivatives by an EPR method allowed the formation of intermediate *para*-substituted radical-cations of the polyphenyls $R(C_6H_4)_2R^+$, where R is Cl, CH_3, F, or $F-C_6H_4-C_6H_4$, to be established [118]. On this basis it was concluded that XeF_2 initiates the generation of radical-cations, in particular from compounds with a relatively high oxidation potential. The results obtained are explained satisfactorily within the framework of a mechanism [119] which postulates the formation of an intermediate complex and a radical-cation.

Xenon difluoride reacts with 1,1-diphenylethylene in the presence of HF and CF_3CO_2H as catalysts with the formation of 1,2-difluoro-1,1-diphenylethanes (yield 65–95%). [120] Aromatic compounds are fluorinated not just in solutions; XeF_2 readily replaces hydrogen in benzene and its derivatives in the gas phase [121] at 100–200 °C. Pentafluorophenyl peroxide has been isolated [122] by the reaction of XeF_2 with pentafluorophenol in acetonitrile. Ethylene reacts with XeF_2 with the formation of 1,2-di- and 1,1,2-trifluoroethanes with yields of 35 and 20% respectively [123]. XeF_2 reacts with propene with the formation of a multicomponent mixture of volatile substances. Propyne resists the action of XeF_2; only after 100 days at room temperature is 2,2-difluoropropane formed (33% yield) [123].

In acetonitrile, XeF_2 reacts with certain organometallic compounds containing Si–Si, Si–H, Si–C (allyl), or Si–O bonds [124]. With chlorine-containing compounds the following substitutions take place:

$$2\,R_3SiCl + XeF_2 \rightarrow 2\,R_3SiF + Cl_2 + Xe\ [R = CH_3,\ C_2H_5,\ R_3 = C_6H_5(CH_3)_2]\ ,$$

$$R_3SiHCl \xrightarrow{XeF_2} R_3SiHF \xrightarrow{Cl_2} R_3SiClF \xrightarrow{XeF_2} R_3SiF_2\ [R_3 = C_6H_5(CH_3)]\ .$$

An effective oxyacylation of benzene is effected in the presence of XeF_2. [125] Oxyacylation was studied by the example of the reactions of benzene with toluic acid, benzoic acid and its nitro- and fluoro-derivatives; the corresponding phenyl benzoates are formed:

$$RCOOH + C_6H_6 + XeF_2 \rightarrow RCOOC_6H_5 + Xe + 2HF\ .$$

The activation energy of the oxybenzoylation of benzene in the presence of XeF_2 is 16 kcal mole^{-1}. [126] The yield of esters is 50–70%. In the absence of benzene the carboxylic acids in the RCOOH + XeF_2 + CCl_4 mixture undergoes decarboxylation with the formation of hydrocarbons and their fluoro-derivatives.

Xenon difluoride participates in solvolysis with alcohols; reaction with C_1–C_4 primary aliphatic alcohols leads to the formation of aldehydes [127]. The rate constants for the oxidation decrease with increase in the length of the carbon chain. The direct fluorination of pyridine by xenon difluoride in the gas phase at 100 °C leads to rapid polymerisation of pyridine [126]. In the fluorination of liquid pyridine, 2-, 2-, and 4-monofluoro-derivatives are formed in 10% yield (on XeF_2), which then are also polymerised. The fluorination of 2-fluoropyridine allows all the disubstituted products to be synthesised, mainly the 2,5-difluoro-isomer [128].

3. Xenon Tetrafluoride

The principal methods of synthesis of XeF_4 were described in the previous review [1]. Xenon tetrafluoride can be obtained by thermal, photochemical [33], and radiation [39] methods, and also by the action of a glow discharge. The synthesis of comparatively pure XeF_4 can be effected at 400 °C and a total pressure of the mixture of xenon and fluoride of 7 atm ($Xe : F_2 = 1 : 5$). [129] After an hour the yield of XeF_4 reaches 90%. The purification of XeF_4 from the impurities XeF_2 and XeF_6 is effected on metal fluorides, owing to the differing abilities of the xenon fluorides for complex formation [91,130]. XeF_4 is also purified effectively by gas–liquid chromatography [131–133]. This method is recommended as a preparative method for the synthesis of the pure individual fluorides of Xe and for their quantitative analysis [132,133].

Xenon tetrafluoride readily sublimes at room temperature. The vapour pressure over solid XeF_4 is represented by the equation [41]:

$$\lg P_{mmHg} = -3226.21/T - 0.43434\ \lg T + 12.301738\ \ (2-117^\circ)\ .$$

The density of supercooled liquid XeF_4 is described by the equation [42]:

$$\rho(g\ cm^{-3}) = 3.500 - 4.05\ 10^{-3}\ t\ \ (110-50^\circ)\ .$$

The heat capacity of XeF_4 has been measured [15] in the range 5–350 °K. The laser Raman spectrum [47] of gaseous XeF_4 has been interpreted and compared with the Raman spectrum of solid XeF_4. As a result of a study of the spectra of gaseous and solid (−193 °C) XeF_4 in the far ultraviolet range (50–160 eV) [49] information has been obtained about the excited electronic levels of this molecule and the absorption lines in the range 61–73 eV have been assigned on the basis of a semiempirical calculation.

Brundle and coworkers [53] investigated the photoelectronic spectrum of XeF_4 with a high resolution by use of HeI and HeII radiation. The electron-impact excitation method was also used for studying XeF_4. [134]

The ^{19}F NMR method was used to study the variation of the second moment of XeF_4 with temperature and the external magnetic field for a rigid lattice and for higher temperatures, when the molecular motion leads to some narrowing of the absorption lines [135]. The magnetic screening parameters found do not agree with the results of a semiempirical calculation [56]. The results of an investigation of the deflection of an XeF_4 molecular beam in a non-homogeneous electric field [64] confirmed that the structure of this molecule was D_{4h}.

Xenon tetrafluoride dissolves in anhydrous HF [68] and in liquid NOF.3HF. [79] The results of an investigation of the electrical conductivity of the XeF_4 solutions and of their ^{19}F NMR spectra show the solubility of XeF_4 in the molecular form in HF, [68] NOF.3HF, [79] and IF_5. [136] The results obtained by various investigators [69,137] for solutions of XeF_4 in IF_5 disagree. The most reliable results are those of Sladky and Bartlett [76], who found that specially

purified XeF_4 dissolves readily in IF_5 without any reaction even in the presence of AsF_5.

Xenon tetrafluoride reacts[69] with NH_3, AsF_3, CCl_2F–$CClF_2$, C_5H_5N, CH_3CN, and $(CH_3)_2SO$ with the formation of the same products as for XeF_2, but the oxidising properties of XeF_4 in these reactions is more clearly expressed. With perfluoropropene, XeF_4 forms perfluoropropane; 1,2-di and 1,1,2-tri-fluoroethane are formed with ethylene; cyclohexane is fluorinated to fluorocyclohexane. With aromatic compounds, XeF_4 takes part in substitutions[123]: benzene is fluorinated to fluorobenzene; toluene to *o*-, *m*-, and *p*-fluorotoluenes, fluorobenzene to the *o*-, *m*-, and *p*-difluorobenzenes, hexafluorobenzene to perfluorocyclohexane, perfluoro-1,4-cyclohexadiene, and perfluoro-1,3-cyclohexadiene. Unlike those of XeF_2, the reactions of XeF_4 take place in the absence of a catalyst[123].

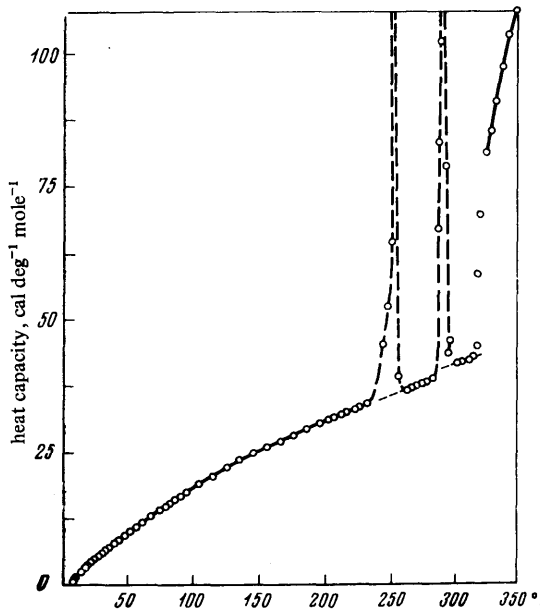

Figure 3. Temperature dependence of the molar heat capacity of xenon hexafluoride.

As a result of the hydrolysis of XeF_4, solutions of XeO_3 are obtained[98,138]:

$$3XeF_4 + 6H_2O \rightarrow XeO_3 + 2Xe + {}^3/_2O_2 + 12HF.$$

Owing to the extremely violent nature of the reaction, the hydrolysis was carried out[139,140] by the slow addition of water to XeF_4 cooled by liquid nitrogen followed by heating the "frozen" mixture.

An attempt to use XeF_4 for obtaining solutions of Pu^{VIII} from Pu^{VII} was unsuccessful[141]. Testing for sensitivity to shock and detonation stability showed that XeF_4 is not an explosion hazard[142]. However, it often explodes when mixed with substances of organic origin.

4. Xenon Hexafluoride

Xenon hexafluoride can be obtained by heating a mixture of xenon and fluorine (1 : 10 or 1 : 20) at 200–300 °C for 15–17 h and a total pressure of 30–50 atm.[17,143] XeF_4 is removed most effectively on sodium fluoride[1]. XeF_6 can also be obtained by a radiation method[39].

The density of XeF_6 was measured[144] over a wide range of temperatures. An equation was derived for the temperature dependence of the molar volume of XeF_6. The following analytical expressions were found[144] for the vapour pressure of XeF_6:

$$\lg P_{mmHg} = -3313.5/T + 12.5923, \quad \text{(from -19° to 18.65°C)};$$

$$\lg P_{mmHg} = -3093.9/T + 11.8397, \quad \text{(from 18.65° to 49.23°C)};$$

$$\lg P_{mmHg} = -6170.88/T - 23.67815 \lg T + 80.77778, \quad \text{(from 49.38° to 76.85°C)}.$$

The second virial coefficient is determined by the relation[144]: $B = -1.143 \times 10^8 T^{-2}$ cm^3 mole^{-1}. The relatively small B (−955 cm^3 mole^{-1} at 73 °C) shows the monomericity of XeF_6 in the gas phase; this agrees with the results of measurements of the vapour density of XeF_6 at 73 °C and 494 mmHg,[144] and at 25 °C and 15 mmHg.[13] Another picture is observed in liquid xenon hexafluoride. In the range from the melting point of XeF_6 (49.48°) to 100 °C the Raman spectra[145] and heat capacities[144] as well as the unusually high entropy of vaporisation at the boiling point clearly show either polymerisation or a high degree of association in the liquid.

Table 2. Crystalline modifications of XeF_6.[149]

Phase and temp. limits of existence, °C	Characteristics of the crystal lattice							
	a	*b*	*c*	angle, deg	*Z*	ρ_{calc}, g cm^{-3}	space group	structural element
Monoclinic, from 49.48 to 18.65	9.33	10.96	8.95	β 91.9	2	3.56	$P2_1/m$ or $P2_1$	2 tetrameric rings of XeF_5^+ groups and F^-
Orthorhombic from 18.65 to −19.35	17.01	12.04	8.57	—	16	3.71	$Pnma$	4 tetrameric rings of XeF_5^+ groups and F^-
Monoclinic below −19.35	16.80	23.93	16.95	α 90.7	64	3.825	$P2_1/b$	16 tetrameric rings of XeF_5^+ groups and F^-
Cubic from −180 to 49.48	25.06	—	—	—	144	3.73	$Fm3c$	24 tetrameric and 8 hexameric rings of XeF_5^+ groups and F^-

The heat capacity of XeF_6 was investigated[144] in the temperature range 5–350 °K. Fig. 3 shows the variation of the molar heat capacity of XeF_6 with temperature. The distinct maxima are due to phase transformations in the solid state. Investigations[146–151] of the crystal structure of XeF_6 made by X-ray diffraction and neutron diffraction methods, confirmed the polymorphism of this compound and the existence of four crystalline modifications (Table 2).

The structure of the cubic phase of XeF_4 has been studied in most detail[147,151]. An X-ray diffraction examination of a single crystal was made at 93 °K. The main structural elements are XeF_5^+ tetragonal pyramide, the five vertices of which are occupied by fluorine atoms. The pyramids are connected with one another by bridges of fluoride ions into tetrameric and hexameric rings (Fig. 4) which are found in the structure in right and left forms; there are for the hexameric rings an ordered, and for the tetrameric rings a disordered, alternation of enantiomorphic forms. The polymeric rings are three-dimensional and also have an almost spherical form.

The tetramer (Fig. 4*a*) is an eight-membered ring consisting of four XeF_5^+ ions and four F^- ions. In the XeF_5^+ ion the interatomic distances are (the F atoms at the vertices are denoted F*a*, and those in the basal plane F*b*): Xe–F*a* = 1.83 Å, Xe–F*b* (mean) = 1.84 Å, F*a*–F*b* (mean) = 2.29 Å, F*b*–F*b* (mean) = 2.54 Å. The mean angles are: F*a*–Xe–F*b* = 77.2°, F*b*–Xe–F*b* = 87.2°. The bridging F^- is 2.23 Å from one Xe and 2.60 Å from the other; the angle in the bridge is 120.7°.

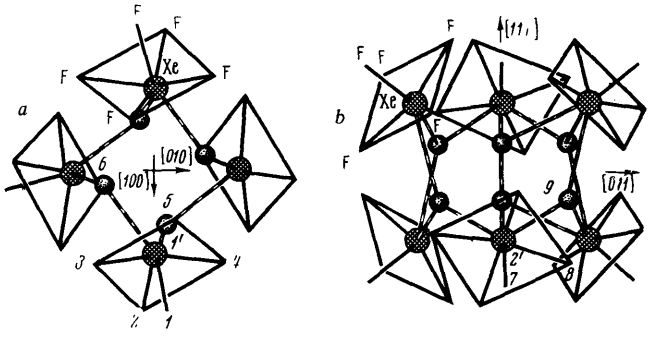

Figure 4. *a*) Structure of the tetrameric rings in the crystal lattice of xenon hexafluoride; *b*) structure of the hexameric rings in the XeF_6 crystal lattice.

The hexamer (Fig. 4*b*) is a twelve-membered ring of six XeF_5^+ ions and six F^- ions. In the XeF_5^+ the distances are: Xe–F*a* = 1.75 Å, Xe–F*b* = 1.88 Å, F*a*–F*b* = 2.33 Å, F*b*–F*b* = 2.62 Å. The angles are: F*a*–Xe–F*b* = 80.0°, F*b*–Xe–F*b* = 88.3°. The bridging F^- are 2.56 Å from each of the Xe; the angle in the bridge is 118.8°.

The polymeric nature of xenon hexafluoride in condensed phases does not allow the structure of the XeF_6 molecule to be found by investigations of, for example, crystal structure, as has been done for XeF_2 and XeF_4. The problem of the structure of XeF_6 is therefore still the subject of discussion and its solution must evidently be sought in an investigation of the gas phase, where the XeF_6 molecules are monomeric.

As even the first investigations of the vibrational spectra showed[1], XeF_6 differs from all the known hexafluorides and evidently exhibits a symmetry other than octahedral. Interest in the structure of XeF_6 has also been aroused by the fact that the first calculation made within the framework of the valence-bond theory predicted a non-octahedral structure for the then still hypothetical XeF_6 molecule, whereas in accordance with a semiempirical calculation by the MO method O_h symmetry is preferable for XeF_6.[1] In discussing these results, Dyatkina[2] suggested that the success of the valence-bond theory in this instance was only apparent, since certain arbitrary assumptions were made in the calculation.

In attempting to explain this difference and also the earlier experimental results, Goodman (see Holloway[5]) advanced a hypothesis according to which these results are completely compatible with the ground state O_h and a low-lying triplet state ^3T_u which can be thermally populated at room temperature. However, measurements of the magnetic susceptibility of XeF_6 showed[152,153] temperature-independent diamagnetism; this signifies that over the entire range of temperatures studied (that is, in the condensed phases) the ^3T_u state is not occupied. An investigation of the deflection of a molecular beam in a non-homogeneous magnetic field[154] led to the same conclusion extended to the gas phase.

An investigation of the deflection of a molecular beam of XeF_6 in a non-homogeneous electric field[64] showed that XeF_6 has a structure with a symmetry-forbidden dipole moment.

After the first electron diffraction investigations[155,156] which showed, as did theoretical results[157,158], that XeF_6 did not have octahedral symmetry, Gavin and Bartell[160] made a careful electron diffraction investigation of gaseous XeF_6 and thoroughly discussed the results in conjunction with the accumulated experimental and theoretical data[159,161].

The results of the investigations[160] seemed incompatible with a regular octahedral configuration for the XeF_6 molecule, in which there are independent normal vibrations. Some asymmetry of the radial distribution in the region of the Xe–F bonds shows the existence of non-equivalent bonds; the mean length of the Xe–F bond is 1.890 Å. The mean square amplitude of the vibrations for non-bonded fluorine atoms l(F...F) = 0.07 Å is somewhat less than l(Xe–F) = 0.08 Å. According to Bartell and Gavin[160,161], the electron diffraction results show either distortion of an octahedral configuration with displacement of the fluorine atoms towards a configuration with C_{3v} or (less probably) C_{2v} symmetry, or that in the XeF_6 molecule there exists an inversion motion (combination of deformation vibrations t_{1u} of very large amplitude and t_{1g}) with a minimum energy at the configuration with symmetry O_h. Theoretical consideration[159,161] showed that in the XeF_6 molecule there can exist conditions under which there appears a pseudo Jahn-Teller effect, brought about by distortion of the O_h configuration as a result of the deformation vibration of type t_{1u} (see Dyatkina[2]).

The results of early investigations of the vibrational spectra of XeF_6[1,162] were discussed by Glass[163] who drew the conclusion that the ground state of gaseous XeF_6 has symmetry O_h but unusual electronic properties affect the width of the bands.

On the basis of a simplified electronic model of XeF_6 derived to explain the "anomalies" of the electronic isomerism hypothesis, Goodman[164] concluded that gaseous XeF_6 at normal temperature is a mixture of three isomers differing in electronic states and geometric configurations (Fig. 5). In addition to the ground state $^1A_{1g}$ (O_h) in the lowest positions, there are also $^3A_{2u}$ (D_3d), and ^3Eu (D_3d) excited states, 450 and 1200 cm^{-1} respectively away from the ground state, due to the Jahn–Teller effect.

The results of an extensive spectroscopic investigation made by Claassen and coworkers[165] were interpreted in the spirit of Goodman's hypothesis. They measured the spectra of gaseous XeF_6 in the visible and ultraviolet ranges, the Raman spectra in the range from the boiling point of XeF_6 (76°C) to 150°C, the infrared spectrum and Raman spectrum in an argon matrix at 4°K, and also reproduced the earlier measurements[162] of the infrared spectrum of gaseous XeF_6.

According to Clarassen and coworkers[165], the temperature dependence of the spectra in the visible and ultraviolet regions confirms Goodman's hypothesis. Using results obtained at 298.1°, 323.6°, and 365.6°K, and the statistical weights of the three isomers calculated according to Goodman, three spectral curves were constructed

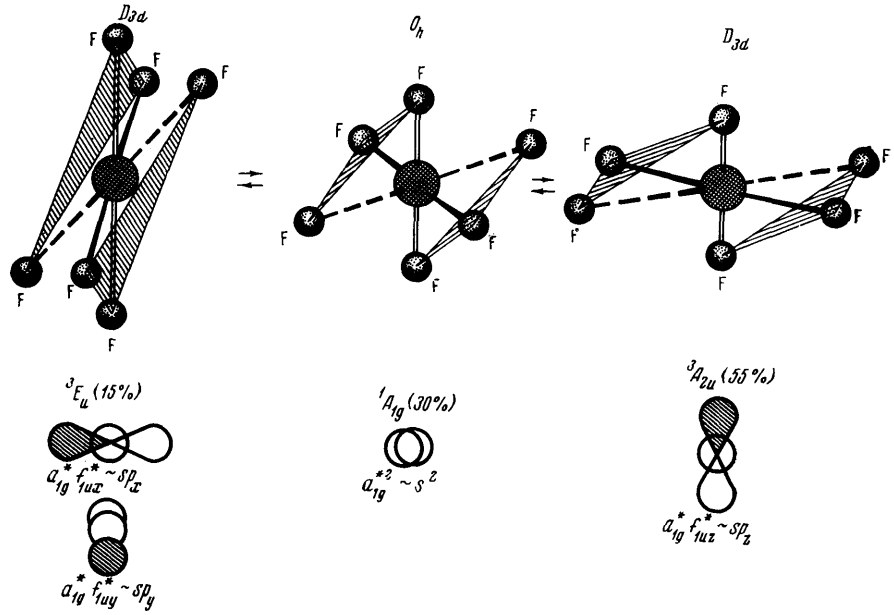

Figure 5. Electronic isomers of xenon hexafluoride; in parentheses, the statistical weights of the isomers.

in this way a spectrum measured at each of these temperatures was resolved into three temperature-independent spectra. The frequencies in these spectra were not assigned in this paper [165].

On the basis of the laser Raman spectra and their temperature dependence it was concluded that gaseous XeF_6 consists of two or more species, the relative concentration of which is a function of temperature. The interpretation of the infrared and Raman spectra, based on the hypothesis of electronic isomerism, led to a satisfactory (in the opinion of these investigators [165]) assignment of the bands to transitions in the isomers or between the isomers.

Mention has been made of the significant influence of preliminary heat treatment of the specimen on the infrared [165,166] and Raman [165] spectra of matrix-isolated XeF_6 molecules. The question of solid-state pseudorotation has been discussed [167].

The dependence of the second moment of polycrystalline XeF_6 on temperature and the external field has been studied by the ^{19}F NMR method [168]. The values found for the magnetic screening parameters are comparable with the corresponding values for UF_6, PuF_6, OsF_6, PtF_6, and MoF_6.

The solubility of XeF_6 in anhydrous HF also shows an anomaly in comparison with other hexafluorides [169]. At room temperature the solubility (moles per 1000 g HF) is: MoF_6 1.50, WF_6 3.14, UF_6 0.49, ReF_6 1.75, OsF_6 0.97, XeF_6 8.6. The results of the measurements of electrical conductivity and of the Raman spectra of solutions show that all the above hexafluorides except XeF_6 dissolve in the molecular form. The anomalously high electrical conductivity of XeF_6 in HF shows strong ionic dissociation in the solution. The solubility of XeF_6 in BrF_5 is ~11 moles per 1000 g BrF_5 at 25°C. [170]

Hydrolysis of XeF_6 takes place with the formation of xenon trioxide [98]:

$$XeF_6 + 3H_2O \rightarrow XeO_3 + 6HF.$$

Hydrolysis can be effected most simply and safely by using argon or helium as carrier [171,172] and also at liquid nitrogen temperature.

5. Complexes of Xenon Fluorides

After the years which have elapsed since the discovery of noble gas compounds, there have been considerable developments in investigations of the interaction of these compounds, especially xenon fluorides, with fluoro-acids and fluoro-bases.

The SbF_5–XeF_2 system has been investigated in detail [173]. Fig. 6 shows the equilibrium diagram of this system. The considerable supercooling (up to 100 deg) of the specimens in composition range 0.1–0.3 mole fraction XeF_2 is due [75] to the formation of XeF and XeF^+. The presence of an EPR spectrum of solutions of $XeF_2.2SbF_5$ in SbF_5 can be confirmation of the occurrence of this type of process [174].

The TaF_5–XeF_2, [175] NbF_5–XeF_2, [175] and VF_5–XeF_2 [176] binary systems have been investigated. In the TaF_5–XeF_2 system $XeF_2.TaF_5$ and $XeF_2.2TaF_5$ are formed, in the XeF_2–NbF_5 system only $XeF_2.2NbF_5$, and in the VF_5–XeF_2 system only $XeF_2.VF_5$. [176,177] The production of $XeF_2.NbF_5$ has also been reported [178].

The UF_6–XeF_2 system [179] consists of mixture with unrestricted mutual solubility of the components in the liquid state and with the crystallisation of $XeF_2.UF_6$ without formation of solid solutions. The degree of dissociation of $XeF_2.UF_6$ in the region of the melting point (120°C) does not exceed 20%. The pressure for the dissociation into constituent components is determined by the relation [180]:

$$\lg P_{mmHg} = 9.30 - 2171/T \quad (20\text{–}100°C).$$

The enthalpy of dissociation of $XeF_2.UF_6$ is independent of temperature (18.6 kcal mole^{-1}); the enthalpy of fusion is −3.5 kcal mole^{-1}.

$XeF_2.RuF_5$, $2XeF_2.RuF_5$, $XeF_2.2RuF_5$, $XeF_2.IrF_5$, $2XeF_2.IrF_5$, $XeF_2.2IrF_5$, $XeF_2.PtF_5$, $XeF_2.OsF_5$, $2XeF_2.OsF_5$, and $2XeF_2.AsF_5$ have been isolated[130] from solutions of XeF_2 and the noble metal pentafluoride in BrF_5. A report[34] of the formation of stable $XeF_2.AsF_5$ was not confirmed subsequently[130]. $XeF_2.OsF_5$ also decomposes[130] at 20°C; with the formation of osmium hexafluoride:

$$3(XeF_2 \cdot OsF_5) \rightarrow 2XeF_2 \cdot OsF_5 + 2OsF_6 + Xe.$$

Bartlett regards this reaction as an intermolecular reaction with the transfer of an electron and the intermediate formation of the XeF radical in the solid phase.

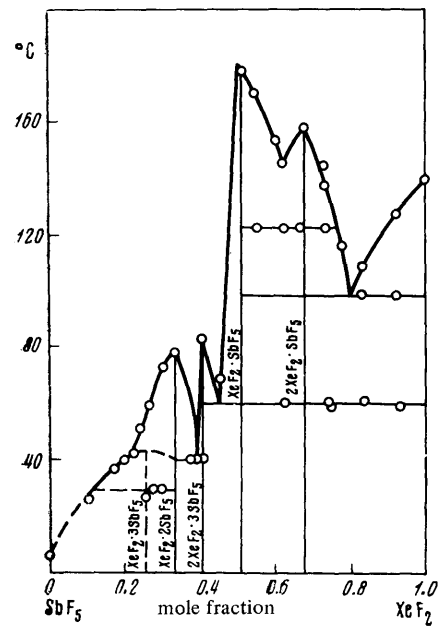

Figure 6. The equilibrium diagram of the SbF_5–XeF_2 system.

The reaction of XeF_2 with MnF_2 leads to the formation of the paramagnetic complex $XeMnF_6$ with an effective magnetic moment[181] of 3.86 μ_B, which shows that Mn is quadrivalent in the compound.

Xenon tetrafluoride reacts in BrF_3 solutions with PBr_5, As_2O_3, and Sb_2O_3 with the formation of the corresponding pentafluorides[182]. Only recently it was found reliably that XeF_4 reacts with fluoro-acids: $XeF_4.2SbF_5$[183] and $XeF_4.SbF_5$[184] are formed during the dissolution of XeF_4 in SbF_5 at 50°C.

When XeF_6 is reduced with uranium tetrafluoride, in addition to XeF_4 and UF_6, $XeF_6.UF_5$ is also obtained[185,186]. This compound can be made also by mixing XeF_6 and UF_5. The magnetic susceptibility of $XeF_6.UF_5$ obeys the Curie–Weiss law in the temperature range from −183° to 17°C, the Weiss constant being 55° and the effective magnetic moment 1.57 μ_B, which confirms that uranium is quinquevalent in the complex.

$XePtF_{11}$ and Xe_2PtF_{17} are formed[187] in the F_2–PtF_5–Xe system at a fluorine pressure of 80 atm and 180–220°C. The magnetic susceptibility of $XePtF_{11}$ obeys the Curie–Weiss law in the temperature range from −183° to 18°C; the Weiss constant is 35° and the effective magnetic moment of $XePtF_{11}$ is 1.97 μ_B.[187]

Under conditions most favourable for the formation of XeF_6, fluorination at 400°C of a mixture of AuF_3 and XeF_2 in the molar ratio 1:6 gave[188] a gold(V) complex $2XeF_6.AuF_5$; this shows that XeF_6 facilitates the stabilisation of the higher degrees of oxidation of the elements. $XeF_6.CrF_4$ was obtained[189] by the reaction of a considerable excess of XeF_6 with CrF_2 at 120°C. The oxidation of Cr^{II} to Cr^{IV} was confirmed by magnetic susceptibility measurements: the effective magnetic moment was 2.76 μ_B. The formation of $XeF_6.CrF_4$ by the reaction of XeF_6 with CrF_5 was also reported[189], although considering the known properties of XeF_6 and CrF_5, the reduction of Cr^V is difficult to explain.

In reactions with alkali metal fluorides[190], NOF,[191] and NO_2F[4,192] xenon hexafluoride acts as a fluoro-acid; in these reactions M_2XeF_8 (M = Cs, Rb, K, Na) and $MXeF_7$ (M = Cs or Rb), $2NOF.XeF_6$ and $NO_2F.XeF_6$ are formed. An X-ray diffraction investigation[193] of $2NOF.XeF_6$ showed the presence in the crystal lattice of the groups NO^+ and XeF_8^{2-}; $a = 8.914$, $b = 5.945$, $c = 12.83$ Å, $\rho_{calc} = 3.354$ g cm^{-3}, $Z = 4$, space group *Pnma*. Fig. 7 shows the structure of XeF_8^{2-}.

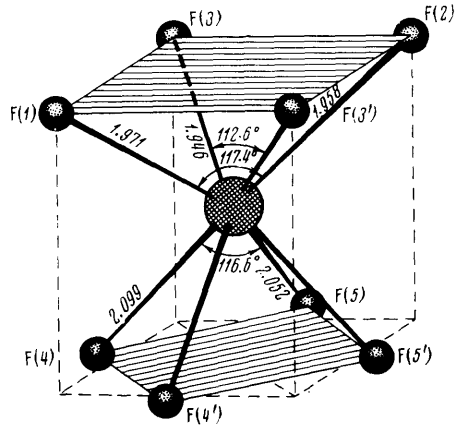

Figure 7. Structure of the XeF_8^{2-} anion in the $2NOF.XeF_6$ crystal lattice.

Reactions of the xenon fluorides in which they act as fluoro-bases (donors of fluoride ions) are interesting. Up till now the following complexes of xenon difluoride have been prepared: $2XeF_2.MF_4$ (M = Sn,[83] Ti,[83,194] Zr,[93] Pd,[195] Mn,[181]), $4XeF_2.PdF_4$,[195] $3XeF_2.PdF_4$,[195] $XeF_2.PdF_4$,[195] $XeF_2.2PdF_4$,[195] $XeF_2.MF_5$ (where M = As,[130] Sb,[173] Ta,[175,178] Nb,[178] V,[177] I,[71,76] Os,[130,178] Ir,[178] Pt,[130] Ru[130]), $XeF_2.2MF_5$ (M = Sb,[173] Ta, Nb,[175,178] Br,[78] Ir, Ru[130]), $2XeF_2.MF_5$ (M = As,[34,130] Sb,[173] Os,[130,178] Ir, Ru[130]), $XeF_2.MF_6$ (M = U,[179] Mo, W[80]), $XeF_2.XeF$,[196,197] $XeF_2.XeOF_4$;[198] xenon tetrafluoride: $XeF_4.SbF_5$,[184] $XeF_4.2SbF_5$;[183,184] xenon hexafluoride: $2XeF_6.MF_4$ (M = Ge,[199] Sn,[200] Pd[195]), $4XeF_6.MF_4$ (M = Ge,[199] Sn,[200] Pd,[195] Mn[201]), XeF_6MF_4 (M = Ge,[199] Pd,[195] Cr[189]), $XeF_6.MF_5$ (M = As,[91,200] Sb,[170] Ir,[190] Ta,[201] Ru,[91] Pt,[187] U[185]), and $2XeF_6.MF_5$ (M = P,[202] As,[91,202] V,[203] Ta,[201] Pt,[187] Au[188]); the ability of the xenon fluorides to supply fluoride ions decreases in the order[91]: $XeF_6 > XeF_2 > XeF_4$.

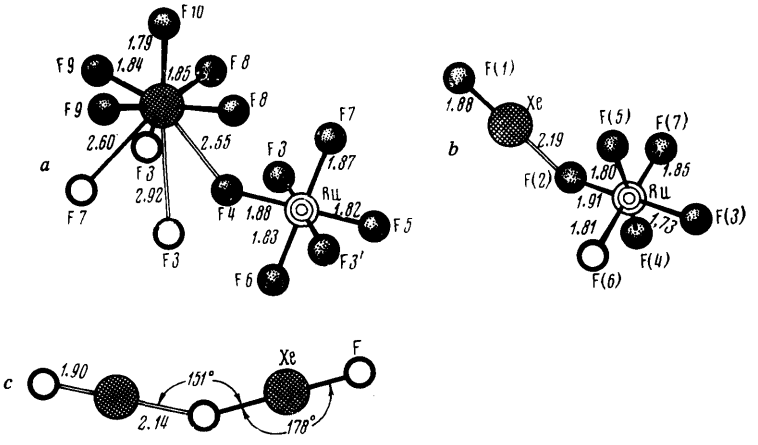

Figure 8. Crystal structure of the complexes of the xenon fluorides: *a*) $XeF_5^+RuF_6^-$; *c*) $Xe_2F_3^+$ in $2XeF_2.AsF_5$.

X-Ray diffraction and spectroscopic investigations of several xenon fluoro-complexes have enabled an understanding of their structure to be approached.

Peacock and coworkers [204] made an X-ray structural diffraction investigation of $XeF_2.2SbF_5$ and although they formally represented the complex in an ionic form ($XeF^+Sb_2F_{11}^-$) they attributed covalent character to the bonds in it. Bartlett and coworkers' X-ray diffraction investigation [205] of $2XeF_2.AsF_5$ led to the opposite conclusion: the structure of $2XeF_2.AsF_5$ is constructed from $Xe_2F_3^+$ cations and AsF_6^- anions. As Fig. 8 shows, the $Xe_2F_3^+$ cation has a planar V-shaped configuration with bridging fluorine atoms.

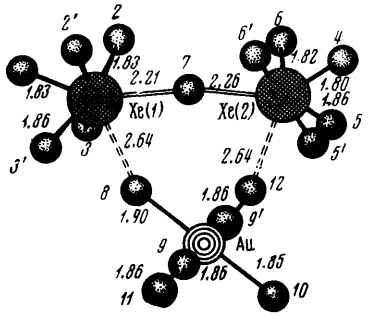

Figure 9. Crystal structure of $Xe_2F_{11}^+AuF_6^-$.

Bartlett and coworkers [130] investigated the Raman spectra of the compounds of XeF_2 with noble metal pentafluorides and calculated the normal vibrations of $XeF_2.IrF_5$ for strong and weak interactions of the XeF^+ and IrF_6^- ions. On the basis of a comparison of calculated and experimental frequencies for the ionic and bridging models they concluded it was possible to describe the compounds $XeF_2.MF_5$ and $XeF_2.2MF_5$ within the framework of the ionic model. An approximate calculation of $XeF_2.SbF_5$ using the frequencies of the Sb–F stretching vibrations of the $SbF_5SO_3F^-$ anion and the "frequency" formulae for a linear triatomic asymmetric molecule also showed that an ionic structure corresponds to the best agreement of the observed and calculated spectra [206]. Infringement of the selection rules for molecules with symmetry O_h, which is observed in the vibrational spectra of xenon fluoro-complexes cannot alter the correctness of ideas about the ionic structure of the compounds and is tentatively explained by a reduction in the symmetry of the anion in the crystal lattice [180,207]. X-Ray diffraction investigations confirmed the conclusion about the ionic structure of these substances.

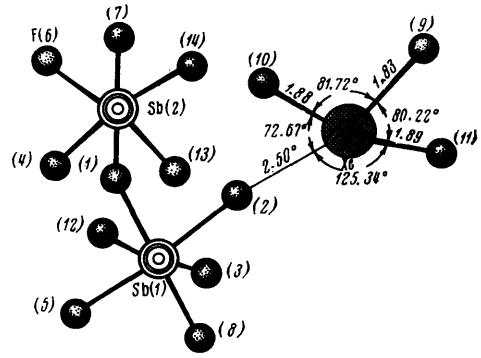

Figure 10. Crystal structure of $XeF_3^+Sb_2F_{11}^-$.

In addition to the molecular constants of the simple xenon compounds, Table 3 gives experimental values of the vibrational frequencies of the cations of certain fluoro-complexes of xenon. Table 4 gives the crystallographic properties of these compounds. Figs. 8–10 show the structures of typical compounds.

Table 3. Molecular constants of xenon compounds.

Compound, reference	Symmetry	Vibrational wavenumbers (Ref.208) and their assignment		Bond length, Å		Force constant	
				Xe–F	Xe–O	K_F^{**}	K_O^{**}
		ν_{Xe-F}^{**}	δ_F^{**}				
XeF_2[47] *	$D_{\infty h}$	Ram(g)—514,5 (ν_1); IR(g)—555 (ν_3)	Ram(g)—213,2 (2) (ν_2)	1.98		2.694	
XeF^+ $(XeF^+SbF_6^-)$[209–211]	$C_{\infty v}$	Ram(s) —615,617; IR(s) —615; Ram(s) —337,388 (Xe . . .F);	Ram(s) —141,180 (F—Xe . . .F)	1.84		3.68	
$XeF^+(XeF^+IrF_6^-)$[130]		Ram(s) —608,602		1.88		3.59	
$XeF^+(FXeOSO_2F)$[211]		Ram(s) —539,532,527	Ram(s) —239 (OXeF)	1.94	2.15	2.85	
$XeF^+(2XeF^+SnF_6^{2-})$[212]		IR(s) —585				3.35	
$Xe_2F_3^+$ $(Xe_2F_3^+SbF_6^-)$[209–211]	C_{2v}	Ram(s) —582.591,420 (Xe . . .F); IR(s) —617,584,572,440 (Xe . . .F)	Ram(s) —161,171,179,255 (F–Xe...F)	1.90			
XeF_4[47]	D_{4h}	Ram(g)—591,3 (ν_1); 524 (ν_5) IR(g) —586 (2) (ν_6)	Ram(g)—218 (ν_3); IR(g)—291 (ν_2); 161 (2) (ν_7)	1.94		2.829	
$XeF_3^+(XeF_3^+SbF_6^-)$[213]	C_{2v}	Ram(s) —645,613,569	Ram(s) —290,275 (F—Xe . . .F)	1.83—1.88			
		IR(g) —619 (f_{1u}); IR(s) —624 (f_{1u})					
	O_h	Ram(g)—613 (a_{1g}), 509 (e_g)	IR(s) —252 (f_{2u})	1.75—1.88			
XeF_6[165]	D_{3d} ($^3A_{2u}$)	IR(s) —630 (a_{2u}), 506 (e_u) Ram(g)—582 (a_{1g}), 509 (e_g)	IR(s) —302 (e_u), 326 (a_{2u}) Ram(g)—69 (e_g), 102 (a_{1g})				
	D_{3d} (^3E_u)	IR(g) —599 (a_{2u}), 520 (e_u) Ram(g)—582 (a_{1g}), 509 (e_g)	IR(s) —352 (a_{2u}), 365 (e_u)				
$XeF_5^+(XeF_5^+SbF_6^-)$[170]		IR(s) —582,550,420					
$XeF_5^+(XeF_5^+BF_4^-)$[184]	C_{4v}	Ram(s) —650—680,585—630,600—640, 640—670		1.80—1.85			
$Xe_2F_{11}^+(Xe_2F_{11}^+AuF_6^-)$[188]		Ram(s) —661,600,593,400	Ram(s) —356,290,111,58	1.80—1.86			
		form of spectrum	ν_{Xe-F}^{**}	ν_{Xe-O}^{**}	δ_F^{**}	δ_O^{**}				
$XeOF_2$[130,208]	C_{2v}	IR(s)	520.490	747	213(2)	(327)	1.95	1.76		
XeO_2F_2[214]	C_{2v}	IR(s)	585(ν_8)	848(ν_1).905(ν_6)	317(ν_9)	324(ν_7)	1.93	1.75		
		Ram(s)	537(ν_2)	850(ν_1).882(ν_6)	315(ν_9)224(ν_5) 205(ν_4)	350(ν_3)				
$XeO_2F^+(XeO_2F^+Sb_2F_{11}^-)$[215]		Ram(s)	595	865.924						
XeO_3F_2[216]	D_{3h}	Ram,IR(s)		894(2)(ν_5)	318(2)(ν_6); (190)(2)(ν_7)	361(2)(ν_8)	(1.91)	(1.73)	2.69	6.67
		Ram(s)	567.4(ν_2)							
		IR(s)	631.7(ν_3)	806.7(ν_1)	375.4(ν_4)				3.112	6.245
$XeOF_4$[47]	C_{4v}	IR,Ram(g)	609(2)(ν_7)	926.3(ν_1)	285.9(ν_3)219(ν_8)	362(2)(ν_8)				
			576.9(ν_2)		161(2)(ν_9)		1.90	1.71	2.964	6.672
		Ram(g)	543(ν_5)	225(ν_4)						
$XeF_2 \cdot XeOF_4$[198]		Ram(s)	494(XeF_2),573, 532	903	254,188,125	378				
$XeOF_3^+(XeOF_3^+SbF_6^-)$[213]	C_{2v}	Ram(s)	633,621,583	944		365.341 (O–Xe–F)	1.86	1.70		
XeO_3	C_{3v}	IR(g)		833(2)(ν_3).780(ν_1)		344(ν_2)317(2)(ν_4)		1.76		5.66
$XeO_3F^-(KXeO_3F)$[217]	C_{3v}	IR,Ram(s)	257(ν_3)	781(ν_1).822(2)(ν_4)	222(2)(ν_6) (O–Xe–F)	358(ν_2).315(2)(ν_5)	2.36	1.75—1.79		5.48
XeO_4[218,219]	T_d	IR(g)		879.2(3)(ν_3)		305.7(3)(ν_4)				6.28
		Ram(s)		867(3)(ν_3);767(ν_1)		303(3)(ν_1); 277(2)(ν_2)		1.736		6.40

Note. *The Raman spectra of the complexes of XeF_2 were investigated in Refs. 130, 206, 209, and 211; the infrared spectra in Refs. 206, 209, 210, and 220; **ν and δ are stretching and deformation vibrations respectively; K is the force constant of the main stretching vibration; the following abbreviations are used in the Table: IR(g) and IR(s), the infrared spectra of the gaseous and solid substances; Ram(g) and Ram(s) the Raman spectra of the gaseous and solid substances respectively. The numbers in parentheses show the degree of degeneracy of the vibrations.

From Table 3, clearly in compounds which contain the XeF^+ cation the frequency of the vibration of the Xe–F terminal bond is shifted to the long-wave part of the spectrum. This shift is explained with semiempirical calculation by the simple LCAO MO method[212], which led to the following series of energies of the xenon–fluorine bond (in kcal mole^{-1}): XeF^+ (~ 50) > XeF_2 (~ 30) > XeF (< 10); consequently for an ionic compound the frequency of the vibration of the Xe–F bond should be higher than for XeF_2, which is also observed experimentally. Since the frequency of the vibrations of the Xe–F bond depends directly on the strength of the fluoro-acid, it can serve as a criterion of the relative acceptor capability of fluoro-acids in reactions with XeF_2:[212]

$$(Sb_2F_{10}) > SbF_5 > (Ir_2F_{10}) > PtF_5 > IrF_5 > (Ta_2F_{10}) > RuF_5 > Ta_{\ldots} > (Nb_2F_{10}) > TiF_4 > SnF_4 > SO_2F > CF_3COO > IF_5.$$

Rüdiger and Meinert[226] showed the possibility of using the MO method in the Hückel approximation for bonding calculations on the complexes of XeF_2 and obtained satisfactory correspondence of the experimental and calculated results for the salts XeF^+ and $Xe_2F_3^+$.

Table 4. Some properties of the complexes of xenon fluorides.

Compound	Method of preparation	M.p., °C	Lattice (°C)	Characteristics							Structure	Reference
				a	*b*	*c*	angle β, deg	*Z*	ρ_{calc}, g cm^{-3}	space group		
$XeF_2 \cdot RuF_5$	XeF_2+RuF_5, 120°	110—111	monoclinic	7.991	11.086	7.250	90.68	4	3.78	$P2_1/n$	$XeF^+RuF_6^-$	221
$XeF_2 \cdot 2SbF_5$	XeF_2+SbF_5	79—80	monoclinic	8.07	9.55	7.33	105.8	2	3.69	$P2_1$	$XeF^+Sb_2F_{11}^-$	204
$XeF_2 \cdot IF_5$	XeF_2+IF_5	102	tetragonal	7.65	—	10.94	—	4	4.06	$I4/m$	$XeF_2 \cdot IF_5$	77
$XeF_2 \cdot XeF_4$	XeF_2+XeF_4		monoclinic	6.64	7.33	6.40	92.40	4	4.02	$P2_1/c$	$XeF_2 \cdot XeF_4$	197
$XeF_2 \cdot XeOF_4$	XeF_2+XeOF_4	29	tetragonal	7.56	—	11.36	—	4	—	$I4/m$	$XeF_2 \cdot XeOF_4$	198
		99—100	monoclinic (20)	15.443	8.678	20.888	90.13	12	—	$I2/a$		
$2XeF_2 \cdot AsF_5$	XeF_2+AsF_5 (in BrF_5)		trigonal (50)	8.68	—	10.70	—	3	—		$Xe_2F_3^+AsF_6^-$	198
$XeF_4 \cdot SbF_5$	$(XeF_4 \cdot 2SbF_5)+XeF_4$	109—113	monoclinic	5.50	15.50	8.95	102.9	4	3.81		$XeF_3^+SbF_6^-$	213
$XeF_4 \cdot 2SbF_5$	XeF_4+SbF_5	81—83	triclinic	8.237	9.984	8.004	112.59 (α)72.54 (γ)117.05	2	3.98	$P\bar{1}$	$XeF^+Sb_2F_{11}^-$	222
$XeF_6 \cdot RuF_5$	$(XeF_6 \cdot RuF_5)+F_2$, 350°C		orthorhombic	16.771	8.206	5.617	—	4	3.79	$Pnma$	$XeF_5^+RuF_6^-$	221
$XeF_6 \cdot PtF_5$	$Xe+F_2+PtF_5$, 200°	100	orthorhombic	8.16	16.81	5.73	—	4	4.52	$Pmns$	$XeF_5^+PtF_6^-$	223
$XeF_6 \cdot AsF_5$	XeF_6+AsF_5 (in BrF_5)	—	monoclinic	5.886	16.564	8.051	91.57	4	—	$P2_1/c$	$XeF_5^+AsF_6^-$	198
$XeF_6 \cdot UF_5$	XeF_6+UF_5	—	orthorhombic	9.39	19.86	8.41	—	8	4.70	$Pcca$		186
$2XeF_6 \cdot AsF_5$	XeF_6+AsF_5	—	monoclinic	15.63	8.96	8.37	91.5	4	—		$Xe_2F_{11}^+AsF_6^-$	198
$2XeF_6 \cdot AuF_5$	$XeF_2+AuF_3+F_2$, 400°	145—150	orthorhombic	9.115	8.542	15.726	—	4	4.24	$Pnma$	$Xe_2F_{11}^+AuF_6^-$	224
$2XeF_6 \cdot PdF_4$		—	orthorhombic	9.346	12.786	9.397	—	4	3.91	$Pca2_1$	$[XeF_5^+]_2[PdF_6^{2-}]$	225
		65	monoclinic (20)	15.436	6.846	17.241	93.12	4	—	$C2/c$		
$2XeF_6 \cdot XeF_2 \cdot 2AsF_5$	$XeF_6+AsF_5+XeF_2$, 85°		monoclinic (40)	16.82	7.00	15.40	95.30	4	—		$XeF_2 \cdot 2[XeF_5^+AsF_6^-]$	198

B. Oxygen-containing Compounds of Xenon

1. Xenon Oxide Fluorides

Xenon oxide tetrafluoride can be obtained by controlled hydrolysis of XeF_6 or by reaction of XeF_6 with silicon dioxide [1,98]; XeF_6 is removed on sodium fluoride.

At room temperature $XeOF_4$ is a colourless transparent liquid. The density of liquid $XeOF_4$ is given by the relation [227]:

$$\rho \text{ g cm}^{-3} = 3.168 - 0.0032\ t\ .$$

The similarity of the Raman spectra of $XeOF_4$ and of a solution of $XeOF_4$ in HF indicated [228] that $XeOF_4$ dissolves in molecular form in HF. A study of the change in the form of the peak of the Xe–O stretching vibration with dilution of the solution of $XeOF_4$ in HF suggested molecular association in liquid $XeOF_4$. [229]

The physical properties of $XeOF_4$ were studied rather thoroughly even at an early stage of the investigations [1] and are given in Table 5. The square pyramidal structure (Table 3) is confirmed by the microwave spectrum [233], according to which the Xe–O and Xe–F distances in the $XeOF_4$ molecule are respectively equal to 1.703 and 1.900 Å and the angle O–Xe–F is 91.8°. The results of an electron diffraction investigation [234] of gaseous $XeOF_4$ led to the following values: r(Xe–O) = 1.7109 Å, r(Xe–F) = 1.9010 Å, and the angle O–Xe–F = 91°. The agreement between the two methods is satisfactory.

The Raman spectra of gaseous [47] and liquid [235] $XeOF_4$ were obtained. The infrared and Raman spectra of $XeOF_4$ were interpreted [47] (Table 3).

The ^{17}O NMR spectrum of $XeOF_4$ [236] has the form of a triplet with an intense central peak of width 130 Hz and two symmetric side peaks of width 110 Hz. An analysis of the intensities showed that the side lines are due to the interaction of ^{17}O with ^{129}Xe and the main line to the interaction of ^{17}O with the remaining xenon isotopes. The ^{17}O chemical shift (relative to $H_2{}^{17}O$) is 313 p.p.m. The spin–spin coupling constant ($^{129}Xe-{}^{17}O$) is 629 Hz. Investigations of the ^{19}F NMR spectrum for $XeOF_4$ have continued [237,238]. The relaxation times were measured in the temperature range from −56° to 85°C and the presence of molecular association in liquid $XeOF_4$ was concluded. The high-resolution ^{19}F NMR spectrum [237] is characterised by an intense central line and a doublet with a spin–spin coupling ($^{129}Xe-{}^{19}F$) constant of 1124 Hz. The chemical shift at 25° is 100.27 p.p.m. (relative to CCl_3F). [237]

The interaction of $XeOF_4$ with alkali : metal fluorides leads to the formation of $3KF.XeOF_4$, $3RbF.XeOF_4$, and $CsF.XeOF_4$, [227] which decompose when heated. With NOF, $NOF.XeOF_4$ is formed [227]. With fluoro-acids, $XeOF_4$ forms the unstable $2XeOF_4.AsF_5$, [229] $2XeOF_4.VF_5$, [229] $XeOF_4.SbF_5$, [213,229] and $XeOF_4.2SbF_5$. [213,227] From the Raman spectrum [229], $2XeOF_4.VF_5$ is a molecular compound. The presence of ^{19}F NMR peaks and their position in the spectrum of solutions of $XeOF_4.2SbF_5$ in SbF_5 shows the presence in the solutions of the cation $XeOF_3^+$, in which the electron pair and the F atom occupy an equatorial position of the trigonal bipyramid and two other F atoms are located axially [215]. The chemical shifts at 5° are −195.1 p.p.m. ($F_{eq}-{}^{129}Xe$) and −147.1 p.p.m. ($F_{ax}-{}^{129}Xe$) relative to CCl_3F. The coupling constants ($^{129}Xe-{}^{19}F$) are 938 Hz (F_{eq}) and 434 Hz (F_{ax}). The ionic structure of $XeOF_4.SbF_5$ and $XeOF_4.2SbF_5$ is confirmed by their Raman spectra [213,215] and by X-ray diffraction investigations [213,222] (Tables 3 and 4).

Xenon dioxide difluoride XeO_2F_2 is formed in the interaction of XeO_3 with $XeOF_4$ or with XeF_6. [239] Removal of impurities is most effectively brought about by distillation. XeO_2F_2 forms colourless crystals which melt at 30.8°C to give a colourless liquid. XeO_2F_2 is more stable than XeO_3, but like XeO_3 is explosive; in moist air

Table 5. Physical properties of compounds of xenon and krypton.

Property	XeF_2	XeF_4	XeF_6	$XeOF_4$	XeO_3	KrF_2
Molecular weight	169.2968	207.2936	245.2904	223.2930	179.2982	121.7968
Melting point, °C	129.0 [41]	117.0 [41]	49.48 [144] 75.57(b.p.)	−46.2 [227]	—	(77) [10]
Vapour pressure, mmHg	4.55(25°) [41]	2.55(25°) [41] 95.28(77°)	28.9(25°) [144]	28(0°) [227]	—	31.0(0°) [10] 96(20°) [10]
Density, g cm^{-3}	4.32(25°) [42]		3.411(24.4°) [144] 3.229(50.3°)	3.11(22.5°) [227]	—	—
Critical parameters (Ref.42)						
temperature, °C	358	339	—	—	—	—
pressure, atm	92	69.5				
density, g cm^{-3}	1.14	1.10				
Solubility, moles per 1000 g						
H_2O	0.15(0°) [1,3]	XeO_3 is formed	XeO_3 is formed	XeO_3 is formed	>2 [1,3]	0.04(2°) [10]
HF	9.88(30°) [68]	0.18(20°) [68]	8.6(20°) [169]	—		16.0(20°) [230]
BrF_5	11.2(20°) [78]	—	~11(20°) [170]	—	—	16.5(20°) [10]
Electrical conductivity, Ω^{-1} cm^{-1}	—	—	$1.45\cdot10^{-6}$(50°) [3]	$1.03\cdot10^{-5}$(24°) [227]	—	—
Electrical conductivity in HF, Ω^{-1} cm^{-1}	—	—	$3.52\cdot10^{-3}$(0.02M) [1]	$1.0\cdot10^{-5}$(24°) [227]	—	—
Dielectric constant	—	—	4.10(55°) [1,3]	24.6 [217]	—	—
Thermodynamic properties:						
ΔH°_{298}(g), kcal $mole^{-1}$	−25.58 [45]	−49.28 [45]	−66.99 [45]	(−6) [3]	96 [1,2]	14.4 [231]
S°_{298}(g), cal deg^{-1} $mole^{-1}$	62.01 [208]	77.05 [208]	89.38 [208]	81.45 [208]	69.09 [208]	60.65 [232]
C°_{p298}(g), cal deg^{-1} $mole^{-1}$	12.94 [208]	21.45 [208]	30.15 [208]	24.87 [208]	14.89 [208]	12.96 [232]
ΔG°_{298}(g), kcal $mole^{-1}$	−17.54 [45]	−31.40 [45]	−38.46 [45]	—		22.1 [10]
$<D^\circ(Xe-F)>$, kcal $mole^{-1}$	31.62 [45]	31.15 [45]	29.94 [45]	—	(27) [1,3](Xe—O)	11.7 [231]
ΔH°_{298}(s), kcal $mole^{-1}$	−38.90 [45]	−63.84 [45]	−80.82 [45]	—	—	5.2 [10]
ΔG°_{298}(s), kcal $mole^{-1}$	−20.58 [45]	−34.77 [45]	−40.40 [45]	—	—	—
ΔH(fus.), kcal $mole^{-1}$			1.37 [144]	—	—	—
ΔH(subl.), kcal $mole^{-1}$	13.32 [41]	14.56 [41]	14.13 [45]	—	—	9.2 [10]
Crystal structure (Ref.1):						
—lattice	tetragonal	monoclinic			orthorhombic	tetragonal
—parameters: *a*, Å	4.315	5.050	cf. Table 2	—	6.183	6.533
b, Å		5.922	—	—	8.115	—
c, Å	6.990	5.771, β=99.6°	—	—	5.234	5.831
ρ_{calc}, g cm^{-3}	4.32(*Z*=2)	4.04(*Z*=2)	—		4.55 (*Z*=4)	3.24 (*Z*=2)
—space group	*I*4/*mmm*	$P2_1/n$	—	—	$P2_12_12_1$	—
—bond length, Å	2.00	1.951;1.954	—	—	1.74—1.77	—
Molar magnetic susceptibility (20°C) (Ref.1)						diamagnetic
Dipole moment (Refs.1,3)	−(40 −50)·10^{-6} 0.5	−50.6·10^{-6} <0.03	−76.9·10^{-6} [152] <0.03	— 0.65	—	—

The following abbreviations are used in the Table: (g) gaseous state of the substance, (s) solid (crystalline) state of the substance.

it is rapidly hydrolysed to XeO_3. When XeO_2F_2 reacts with XeF_6, $XeOF_4$ is formed [239]. The standard enthalpy of formation of XeO_2F_2 (g) [240] was estimated as 56 kcal $mole^{-1}$.

The Raman spectra of liquid and solid XeO_2F_2 and the infrared spectrum of solid XeO_2F_2 in an argon matrix at 4°K were investigated [214]. It was concluded that the XeO_2F_2 molecules are monomeric in the liquid and possibly the solid phases. According to the vibrational spectra, the XeO_2F_2 molecule has a pseudopyramidal structure of C_{2v} symmetry (Table 3). The normal vibrations of XeO_2F_2 and SO_2F_2, CrO_2F_2, and SeO_2F_2 were compared and it was shown that the frequencies of monotypical vibrations are arranged in a series in accordance with the mass of the central atom [214].

The molecular structure and symmetry of XeO_2F_2 were investigated by neutron diffraction on single crystals [241]. It was found that the XeO_2F_2 structure is orthorhombic, with parameters $a = 6.443$, $b = 6.288$, $c = 8.312$ Å, $Z = 4$, $\rho_{calc} = 4.10$ g cm^{-3}. The structure consists of dimeric layers of XeO_2F_2 molecules linked by weak Xe...O bridges.

The ^{19}F NMR spectrum for XeO_2F_2 and also that for XeO_2F_2–$XeOF_4$ mixtures (1 : 1) have been obtained [237]. The XeO_2F_2 spectrum is characterised by a single peak accompanied by a doublet from the spin–spin coupling ($^{19}F-^{129}Xe$) with constant 1178 Hz. The chemical shift is 105.10 p.p.m. in relation to CCl_3F. Throughout the entire range of temperatures studied (16–70°C) significant broadening of the lines was not observed.

The compound $XeO_2F_2.2SbF_5$ has been prepared [215]. The ^{19}F NMR spectrum of a solution of $XeO_2F_2.2SbF_5$ in SbF_5 shows the formation in the solution of the cation XeO_2F^+, the structure of which is analogous to the isoelectronic XeO_3—a trigonal bipyramid [215]. The chemical shift at 5° is −199.4 p.p.m. relative to CCl_3F; the spin–spin coupling constant ($^{129}Xe-^{19}F$) is 79.7 Hz. The presence of the XeO_2F^+ cation in $XeO_2F_2.2SbF_5$ is confirmed by the Raman spectrum [215] (Table 3).

Xenon trioxide difluoride XeO_3F_2 was isolated in the reaction of XeF_6 with Na_4XeO_6 at room temperature [242]; it was identified by the mass spectrum. The volatility of XeO_3F_2 is comparable with that of XeO_4 but less than that of XeO_2F_2. The infrared and Raman spectra of XeO_3F_2 in an argon matrix at 4°K were investigated [216] (Table 3).

Xenon dioxide tetrafluoride XeO_2F_4 is formed by the reaction [243]:

$$XeO_3F_2+XeF_6\rightarrow XeOF_4+XeO_2F_4\,.$$

Xenon oxide hexafluoride $XeOF_6$ could not be isolated but its compound $XeOF_5^+Sb_2F_{11}^-$ was obtained [184] by the reaction of $KrF^+Sb_2F_{11}^-$ with $XeOF_4$ at −10°C.

2. Xenon Trioxide

The behaviour of XeO_3 in aqueous solutions was discussed in detail by Malm and Appelman [3], and that in non-aqueous solutions by Jaselskis [11].

The method for obtaining pure aqueous solutions of XeO_3 [140] is the hydrolysis of XeF_6 with the subsequent precipitation of fluoride ion with magnesium oxide,

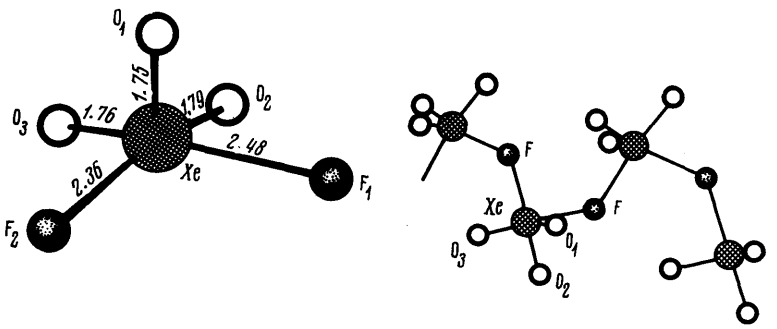

Figure 11. Structure of the XeO_3F^- anion in the $nK^+(XeO_3F^-)_n$ crystal lattice.

removal of Mg^{2+} ions by the action of zirconium phosphate and trace amounts of fluoride ions with the aid of ZrO_2.

Crystalline colourless XeO_3 can be obtained by the evaporation of aqueous solutions of XeO_3 at room temperature[244]; XeO_3 sublimes at 70°C and decomposes under these conditions; in amounts exceeding 20 mg gaseous XeO_3 partly explodes. According to other results[245], the thermal decomposition of XeO_3 starts at 40°C and proceeds without explosion. The properties of XeO_3 are given in Table 5.

The thermodynamic properties of aqueous XeO_3 have been studied[246]. The standard enthalpy of formation $\Delta H^\circ_{298}(XeO_3 \infty H_2O)$ is 99.94 kcal mole^{-1}. The value $\Delta G^\circ_{298}XeO_{3(aq)} = 120.8$ kcal mole^{-1} was used to calculate the redox potential of the couple XeO_3/Xe in acid medium and $HXeO_4^-/Xe$ in alkaline medium:

$$XeO_{3(aq)} + 6H^+_{(aq)} + 6e^- = Xe_{(g)} + 3H_2O,$$

$$HXeO_{4(aq)}^- + 3H_2O + 6e^- = Xe_{(g)} + 7OH^-,$$

equal respectively to 2.10 and 1.24 V.

The kinetics of decomposition of XeO_3 in a neutral aqueous solution has been studied[247]. The variation of the optical density of solutions of XeO_3 with time has been plotted. It has been shown that the decomposition of XeO_3 is described by a first-order equation up to high degrees of conversion. The rate constant is independent of the concentration of the solution in the range 1.01×10^{-3}–3.30×10^{-3} M. The Arrhenius relation has the form:

$$k = 10^{13,4\pm1,1} \cdot \exp(-28\,100 \pm 1900/RT).$$

The results of an investigation[247] of the kinetics of decomposition of XeO_3 in aqueous solutions can be regarded as a quantitative measure of the stability of these solutions As the pH is increased, the stability of the XeO_3 solutions falls[3]. γ-Radiolysis of the aqueous solutions of XeO_3 at room temperature leads to decomposition of XeO_3 into Xe and O_2.[248] The radiation-chemical yield increases with the XeO_3 concentration[249,250]. The possible mechanism of γ-radiolysis has been discussed[249,250].

Aqueous solutions of XeO_3 readily oxidise H_2O_2 to O_2,[251] Pu^{III} to Pu^{IV} in 2 M $HClO_4$,[252,253] Np^V to Np^{VI} in 2 M $HClO_4$,[254] Np^{VI} to Np^{VII} in 1 M KOH[255] and 10–11 M KOH.[108] Many organic compounds, for example, primary and secondary aliphatic alcohols,[256,257] benzyl alcohol,[257,258] benzaldehyde,[258] diphenylmethanol,[257] etc., are decomposed in aqueous solutions of XeO_3 with the formation of CO_2. XeO_3 reacts with t-butyl alcohol only in the presence of transition metal ions, with the formation of Bu^tOXeO_3K. $.Bu^tOH$.[259] In alkaline solutions XeO_3 epoxidises alkenes by electrophilic attack at the double bond[260]. Carboxylic acids are decomposed to CO_2.[261]

3. Xenates and Perxenates

The fluoroxenates $RbF.XeO_3$ and $CsF.XeO_3$ crystallise on the evaporation of a 0.5 M aqueous solution of XeO_3 (containing HF) after its neutralisation to pH 4 by the corresponding hydroxides[262]. $CsF.XeO_3$ can also be made by atmospheric hydrolysis of $CsF.XeF_6$[261] or $CsF.XeOF_4$.[227] Potassium fluoroxenate is formed in the evaporation of a mixture of a 0.5 M solution of XeO_3 and 1 M solution of KOH.[262] The fluoroxenates mentioned are comparatively stable; their decomposition starts to become appreciable above 260°C.[262] $CsCl.XeO_3$ can be obtained[263] by mixing aqueous solutions of XeO_3 and CsCl; unstable $CsBr.XeO_3$ has been isolated[262] from saturated solutions of CsBr at pH 9 and 0°C. The stability of the halogenoxenates falls with increase in the mass of the halogen[262]: $CsF.XeO_3 > CsCl.XeO_3 > CsBr.XeO_3$.

The halogenoxenates are much more stable than XeO_3, which does not agree with the view[227] that they are molecular compounds. Actually, X-ray diffraction investigations[264] showed that the crystal structure of $KF.XeO_3$ is constructed from infinite XeO_3 chains connected by bridging fluorine atoms in such a manner that each link acquires a negative charge, XeO_3F^-. As Fig. 11 shows, the anion has a polymeric structure and the links are connected by potassium ions. Consequently, the correct structural formula of potassium fluoroxenate is $nK^+(XeO_3F^-)_n$. The orthorhombic lattice of $KF.XeO_3$ has the parameters a = 7.354, b = 6.811, c = 8.815 Å, ρ_{calc} = 3.835 g cm^{-3}, Z = 4, space group $Pn2_1a$.[264] The ionic structure of the halogenoxenates has been confirmed by the results of an investigation[217] of the infrared and Raman spectra of $MXeO_3F$ (M = K, Rb, or Cs) and $MXeO_3Cl.MCl$ (M = Rb or Cs), which agree most satisfactorily with C_{3v} symmetry for XeO_3F^-.

Cs, Rb, K, and Na xenates of composition $MHXeO_4$ crystallise from solutions of XeO_3 when the corresponding hydroxides are added[265]. They are all stable up to 150 to 160°C, tend to detonate, and decompose slowly in aqueous solutions. An investigation[266] of the Raman spectra of aqueous 1.1 M solutions of $NaHXeO_4$ showed the presence of $HXeO_4^-$ in them.

In the ozonisation of aqueous solutions of XeO_3 and KOH the stable salt of sexivalent and octivalent xenon is isolated—$K_4XeO_6.2XeO_3$,[267] which tends to denotate and decomposes above 200°C by the reaction:

$$K_4XeO_6 \cdot 2XeO_3 \rightarrow K_4XeO_6 + 2Xe + 3O_2.$$

On the basis of the results of investigations of the thermal stability, infrared spectra, and an X-ray diffraction analysis of $K_4XeO_6.2XeO_3$, it was concluded[267] that in this

compound the XeO_3 molecules are coordinated (by means of two bridging oxygen atoms) to the central group—octahedral perxenate, in such a manner that $K_4Xe_3O_{12}$ is formed.

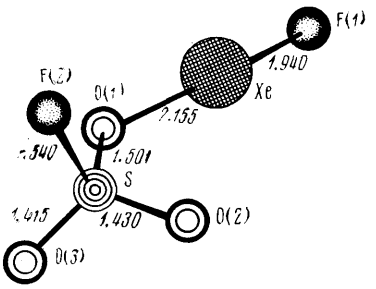

Figure 12. Molecular structure of $FXeOSO_2F$.

The salts of xenon(VIII), the perxenates, are formed in solutions of strong bases in the hydrolysis of XeF_6, the disproportionation of XeO_3, and in ozonation of XeO_3 solutions. Appelman thinks[268] that the ozonation of XeO_3 in 1–2 M alkali is the most effective. Some perxenates, for example, $Na_4XeO_6 . 2.5NaF$, can also be obtained, but in smaller yield, by the hydrolysis of XeF_4 in alkaline solutions[269]. An investigation of the Raman spectra of aqueous solutions of perxenates[266] shows the high concentration of symmetric, evidently octahedral, anions:

$$HXeO_6^{3-} + OH^- \rightleftarrows XeO_6^{4-} + H_2O.$$

Methods of making $Na_4XeO_6.nH_2O$ (n = 2, 4, or 6) of high purity have been developed[270], involving the hydrolysis of mixtures of XeF_4 and XeF_2 in alkaline solutions. The thermal stability of $Na_4XeO_6.6H_2O$ has been investigated[271]. The following parameters of its hexagonal lattice have been found[272] for Na_4XeO_6 by X-ray diffraction: a = 5.63, c = 16.00 Å. At the basis of the structure lies cubic close packing of O atoms with distribution of the Na and Xe atoms in octahedra; here the $Na_2XeO_6^{2-}$ layer lies parallel to the plane bc with distance between them 6.25 Å. Lithium perxenate of composition $Li_4XeO_6.nH_2O$ where $0.6 < n < 2$,[273] is less stable than sodium perxenate.

The rare-earth elements (r.e.e.) form dipole perxenates. In the general instance, the r.e.e. and yttrium form complex salts[270,274] $M_nLn_m(XeO_6)_l.xH_2O$, where M is an alkali metal, Ln is Ho, Eu, Dy, Pr, La, Nd, or Y, with $2 < x < 4$. Analogous compounds are obtained for Th^{IV}, U^{VI}, Np^{VI}, and Pu^{VI}.[275] The compound $3(UO_2)_2XeO_6 . 5Na_4XeO_6.nH_2O$, which is stable up to 100°C and is slowly hydrolysed in water, has also been synthesised. Np^{VI} perxenate decomposes spontaneously with the formation of Np^{VII}.[275] Americium perxenate $Am_4(XeO_6)_3.4OH_2O$ is precipitated from basic solutions of Am^{III}.[276] Cobalt[277], barium and strontium[278], copper, lead, silver, nickel, tin, and zinc[3] perxenates have also been obtained. Their properties have not been studied. In aqueous solutions the perxenates are strong oxidants[3].

4. Xenon Tetroxide

Xenon tetroxide XeO_4 is formed in the reaction of perxenates with sulphuric acid at room temperature, for example[1]:

$$Ba_2XeO_6 + 2H_2SO_4 \rightarrow XeO_4 + 2BaSO_4 + 2H_2O.$$

The standard enthalpy of formation of XeO_4 is 153.5 kcal $mole^{-1}$, which corresponds to a mean thermochemical bond energy of 21.1 kcal $mole^{-1}$.[279]

The molecular structure of gaseous XeO_4 has been determined by electron diffraction[280]; the tetrahedral configuration of the molecule (symmetry Td) has been confirmed; the interatomic distances are: r(Xe–O) = 1.736 Å, r(O...O) = 2.832 Å, and the mean square amplitudes of the vibrations are: l(Xe–O) = 0.046 Å, l(O...O) = 0.086 Å. The results obtained for the bond lengths led Gundersen and coworkers[280] to the conclusion that the bond between xenon and oxygen had considerable double bond character, although the amplitudes of the vibrations are more characteristic of a single bond.

The vibrational spectra of XeO_4 were investigated by Yeranos[281] (infrared spectrum), Huston and Claassen[218] (Raman spectrum), and McDowell and Asprey[219] (infrared and Raman). Table 3 gives the vibrational wavenumbers of XeO_4. The frequencies in the laser Raman spectra of gaseous and solid XeO_4 have been assigned[218] and with the aid of a force field Urey and Bradley calculated the force constants. Unlike most of the tetrahedral molecules and ions studied[282], in XeO_4 the force constant for the interaction of non-bonded atoms is negative (–0.18 mdyn $Å^{-1}$). McDowell and Asprey[219] studied the infrared and Raman spectra of gaseous XeO_4^{16} and XeO_4^{18} and showed the existence of a difference between the force fields of XeO_4 on the one hand and OsO_4,[283] and RuO_4[284] on the other. The negative sign of the coupling constant of non-bonded atoms shows, in complete agreement with Huston and Claassen's work[218], a significant difference between the nature of the bonds in XeO_4 and in the tetroxides of the noble metals.

5. Derivatives of Xenon Fluorides and Oxides

Xenon forms comparatively stable compounds only with the most electronegative elements—fluorine and oxygen. The concept of electronegativity played a positive part in the prediction of the possibility of the formation of compounds with groups more electronegative than fluorine and oxygen.

When XeF_2 reacts with stoichiometric amounts of fluorosulphonic or perchloric acids below –60°C colourless crystalline substances are formed: $FXeSO_3F$, $Xe(SO_3F)_2$, $FXeClO_4$, $Xe(ClO_4)_2$.[285,286] $FXeSO_3F$ melts at 36.6°C to a yellow-green liquid and decomposes on melting:

$$2FXeSO_3F \rightarrow XeF_2 + S_2O_6F_2 + Xe.$$

The reactions of $FXeSO_3F$ are accompanied by the release of xenon. The $FXeSO_3F$ structure consists of discrete $FXeOSO_2F$ molecules (Fig. 12), in which the Xe atom is coordinated linearly with F and O atoms of a distorted tetrahedral fluorosulpho-group[287]. $FXeSO_3F$ has an orthorhombic lattice with parameters a = 9.88, b = 10.00, c = 10.13 Å, Z = 8, ρ_{calc} = 3.30 g cm^{-3}, space group $Pbca$. $Xe(SO_3F)_2$ melts at 43–45° to a yellow liquid, which slowly decomposes[285,286]:

$$Xe(SO_3F)_2 \rightarrow S_2O_6F_2 + Xe.$$

Preliminary investigation[286] of the crystal structure of $Xe(SO_3F)_2$ showed that the crystals are monoclinic with $a = 7.94$, $b = 13.7$, $c = 6.84$ Å, $\beta = 96°$. $FXeClO_4$ melts sharply at 16.5°C with decomposition; $Xe(ClO_4)_2$ melts at 0°C. Xe, O_2, and Cl_2O_7 have been observed[286] in the decomposition products of $FXeClO_4$ and $Xe(ClO_4)_2$.

The reaction of XeF_2 with $HOTeF_5$ leads to the formation of $FXeOTeF_5$ and $Xe(OTeF_5)_2$.[288-291] These compounds decompose above 150°C with the formation of $F_5TeOTeF_5$. The compound $Xe(OTeF_5)_2$ is orthorhombic with the lattice parameters $a = 9.83$, $b = 8.73$, $c = 12.97$ Å, $Z = 4$, $\rho_{calc} = 3.64$ g cm^{-3}, space group *Cmca*.[289] Like the noble gas fluorides, $FXeOTeF_5$ acts as a fluoride-ion donor with the formation[288,292] of $[F_5TeOXe]^+[AsF_6^-]$, is a weaker fluorobase than XeF_6 and XeF_2, but a stronger one than XeF_4. When XeF_2 reacts with $HOSeF_5$, $FXeOSeF_5$ and $Xe(OSeF_5)_2$ are formed[293,294]; their properties are reminiscent of xenon pentafluoro-orthotellurates. The thermal decomposition of these compounds starts at 100°C and leads to the formation of $F_5SeOSeF_5$.

XeF_2 forms $FXeOC(O)CF_3$ and $Xe[OC(O)CF_3]_2$ with trifluoroacetic acid at −24°C; they are pale yellow solid substances which explode when heated above 25°C and detonate under impact[290,295,296]. In addition to the above compounds, the following have been obtained: $FXeOSO_2CF_3$ and $FXeOSO_2CH_3$,[286] and $F_5TeOXeOSeF_5$,[294] which exists in equilibrium with $Xe(OTeF_5)_2$ and $Xe(OSeF_5)_2$, $FXeOPOF_2$ and $Xe(OPOF_2)_2$ are formed by the reaction of XeF_2 with $P_2O_3F_4$ in trichlorofluoromethane at −40°C and are stable up to 20°C.[297]

Investigation of the infrared and Raman spectra of derivatives of XeF_2 in oxo-acids[286-293] gave certain information about the nature of the bonds in the compounds obtained. Comparison of the vibrational frequencies of the Xe–F bond in these compounds and in XeF_2 led to the conclusion that the bonds of the Xe atoms with the ligands in all the compounds are similar[286]. This agrees with the results of the X-ray diffraction investigation of $FXeOSO_2F$:[287] the length of the Xe–F terminal bond in $FXeOSO_2F$ (1.94 Å) is close to the Xe–F distances in XeF_2 (2.01 Å), $Xe_2F_3^+$ (1.90 Å), $FXeFRuF_5$ (1.88 Å), and $FXeFSb_2F_{10}$ (1.84 Å).

The compounds listed are thermodynamically and thermally unstable. There are two points of view concerning the mechanism of their decomposition: according to one of these[286] the decomposition proceeds through the intermediate formation of the free radicals SO_3F and XeF; according to the other[298], the decomposition of $FXeOSO_2F$ takes place through the intermediate formation of XeF_2 and SO_3. Recently published results of experimental investigations of certain products of the reactions of XeF_2 with oxo-acids show the formation of rather stable free radicals during the course of their decomposition. Thus, in the EPR spectra of the yellow solutions of $FXeOPOF_2$ in CCl_4 a line of width 67 G with *g*-factor of 2.0067 is found[297]. This fact, just like the nature of the ultraviolet spectra of such solutions[297], has been interpreted as a sign of the formation of free radicals (evidently, PO_2F_2) in the decomposition of $FXeOPOF_2$ and $Xe(OPOF_2)_2$. The EPR method was also used for studying[294] the intermediate products of the photochemical decomposition of $Xe(OTeF_5)_2$ and $Xe(OSeF_5)_2$; the investigation was made in the solid state and in hexafluoroethane at −150°C. Lines with half-width 10.2 G, *g*-factor 2.00 were observed in the spectra of both solid substances. The appearance of the EPR signals is explained[294] by the formation of the free radicals $OSeF_5$ and $OTeF_5$.

The interaction of $FXeSO_3F$ with AsF_5, SbF_5, and RuF_5 did not lead, as expected[286], to the formation of salts containing the cation $(XeSO_3F)^+$; however, the complex $[(FXe)_2O_2S(O)F]^+[AsF_6]^-$, which decomposes above 60°C, was obtained[286] by the reaction of $FXeSO_3F$ with XeF_2 and AsF_5. An analysis of the Raman spectra of $[(FXe)_2O_2S(O)F]^+[AsF_6]^-$ and $[(FXe)_2F]^+[AsF_6]^-$ showed similar Xe–F bonds in these cations and confirmed the structure given[286].

Xenon tetrafluoride and hexafluoride are also capable of the formation of compounds with oxo-acids[299]. $FXeOSO_2F$ and $Xe(OSO_2F)_2$ are formed in the reaction of XeF_4 with $HOSO_2F$ in the temperature range from −22° to 5°C; under analogous conditions XeF_6 forms the colourless crystalline substance F_5XeOSO_2F, which melts above 73°C with decomposition[298]. The results of the measurement of the ^{19}F NMR spectrum of F_5XeOSO_2F, in HSO_3F at −60° show the existence in the solutions of the cation F_5Xe^+ ($FXeF_4^+$).[298] The data of the NMR spectrum: chemical shift (relative to HSO_3F) −188 p.p.m. (F_{ax}) and −68.9 p.p.m. (F_{eq}), (^{129}Xe–^{19}F) coupling constants 1377 Hz (F_{ax}) and 170 Hz (F_{eq}), agree with the results of earlier investigations[215] of the ^{19}F NMR for XeF_5^+. The ionic structure of F_5XeSO_3F is also confirmed by the Raman spectrum[298], the intense polarised bands at 650 and 595 cm^{-1} in which were assigned[300] to ν(Xe–F) and $\nu_{sym}(XeF_4)$ in XeF_5^+.

C. Other Xenon Compounds

Xenon dichloride $XeCl_2$ can be obtained: (a) by passing a high-frequency discharge (25 MHz, 150–350 mA) through a mixture of xenon, fluorine, and $SiCl_4$ or CCl_4 at −78°C.[300] It is suggested that the XeF_2 formed initially undergoes an exchange reaction with the halogen from the $SiCl_4$ (or CCl_4) with the formation of $XeCl_2$. It was shown later that an exchange reaction actually occurs in solutions of XeF_2 in CCl_4 under the action of ultraviolet radiation[301]; (b) by the action of a microwave discharge in a mixture of xenon and chlorine in the molar ratio 25:1 with subsequent rapid withdrawal of the reaction products into a zone cooled to 4°K;[302] (c) in the β-decay reaction[303]: $^{129}ICl_2^- \rightarrow {}^{129}XeCl_2$; (d) by the reaction of xenon with chlorine at high pressure and room temperature for several days[304] (Malm and Appelman think[3] that under the experimental conditions[304] unstable clathrates of xenon are formed, and not $XeCl_2$).

Xenon dichloride is a colourless crystalline substance which can be stored in sealed glass ampoules for long periods, which sublimes under reduced pressure at room temperature and decomposes in a high vacuum or when heated to 80°C.[300] The calculated standard enthalpy of formation ΔH°_{298} $XeCl_2$ (g) is 27 kcal mole^{-1},[286], which corresponds to a thermochemical bond energy of 15 to 16 kcal mole^{-1}.

In the infrared[302] and Raman[305] spectra of matrix-isolated $XeCl_2$ at 4°K bands with maxima at 319 and 253 cm^{-1} respectively are observed. These experimental wavenumbers agree with those calculated for a linear symmetric molecule (symmetry $D_{\infty h}$). The force constant of the Xe–Cl bond is 1.34 mdyn Å^{-1}.[304] The Mössbauer effect in solid $XeCl_2$ at 4.2°K was investigated[303]. The quadrupole splitting is 28.20 mm s^{-1}, the isomer shift 0.17 mm s^{-1} (relative to atomic xenon). The formal charge on each chlorine atom is 0.5.

Xenon tetrachloride $XeCl_4$ was identified by the Mössbauer spectrum as the product of the β-decomposition of ^{129}I introduced into $KICl_4$: $^{129}ICl_4^- \rightarrow {}^{129}XeCl_4$.[303] The quadrupole splitting in $XeCl_4$ is 25.62 mm s^{-1}, the isomer

shift 0.25 mm s^{-1}. The results of the investigation confirm the square planar configuration for $XeCl_4$. The charge on the central xenon atom in $XeCl_4$ is 1.9.

The negative ion $XeCl^-$ is formed as a result of the occurrence in the gas phase at a pressure of 10^{-4} mmHg of the ion-molecular reaction $Xe + CoCl^-$.[306] The energy of the dissociation of $XeCl^-$ into Xe and Cl^- is less than 10 kcal $mole^{-1}$.

Xenon dibromide $XeBr_2$, which is formed in the β-decay of ^{129}I in $KIBr_2$, was identified from the Mössbauer spectrum[307]. The outer ones of the three intense, sharply resolved lines are regarded as an $XeBr_2$ doublet with quadrupole splitting 22.2 mm s^{-1}. The formal charge on the bromine atoms in $XeBr_2$ is 0.41.[307]

Attempts to synthesise xenon chloride fluorides were unsuccessful[308,309]. The existence of $FXeBF_2$[310] has not yet been confirmed. The stable ion CH_3Xe^+ is formed in the interaction of xenon with CH_3FH^+ in the gas phase[311].

D. Radiochemistry of Xenon Compounds

The synthesis of xenon fluorides containing ^{133m}Xe or other radioactive isotopes can be effected from the elements by traditional methods, and also by the irradiation of xenon fluorides with neutral fluxes in a nuclear reactor[1,3]. The xenon fluorides are then used for obtaining oxygen compounds of xenon[274]. The retention of radioactive xenon in the initial XeF_2 and XeF_4 when they are irradiated in neutron fluxes (10^{12}–10^{13} n cm^{-2} s^{-1}) reaches 98% in XeF_4 and 93% in XeF_2,[312] that of radioactive fluorine is 100% in XeF_2 and 90% in XeF_4.[313] In the isomeric transformation of ^{135m}Xe in XeF_2 in organic solvents, ^{133}Xe is released in the elemental state to the extent of 95%.[314] The effectiveness of such processes for XeF_4 in aqueous solutions of XeO_3 is 50%.[315]

The distribution of iodine among the chemical species in the process of capture of an electron $^{125}Xe \rightarrow {}^{125}I$ in H_2O, XeF_2, and XeF_4 has been studied. It has been found that 95% of the ^{125}I is found in the form IO_4^- and 5% in the form IO_3^-. These investigations[316] allowed a method to be developed for obtaining ^{125}I without a carrier, which enabled preparations in the form of NaI with a specific activity exceeding 100 mC ml^{-1} to be obtained. The irradiation with an integral neutron flux of 2.5×10^{19}–5.1×10^{19} of a matrix target, for which XeF_2 was used, leads to the formation of a final product with a yield of 26–43 mC per g XeF_2.[317]

The chemical changes in the β-decay of iodine isotopes in the composition in iodates and periodates are regarded as an effective method of investigating the processes of formation of the xenon fluorides[318]. For example, the yield of chemically bound xenon in the decay of the isotopes ^{131}I, ^{133}I, ^{135}I in periodates reaches 45–85% in crystals and 70% in H_2O, 0.001 M H_2SO_4, and 1 M HNO_3.[319,320] The yield of combined xenon in the decay of isotopes in the alkali metal iodates varies from 10% (Cs, Rb, K) to 43.8% (Na) and 62.2% (Li) in 0.001 M H_2SO_4 and amounts to only 0.3% (K, Na) in 2 M NaOH.[321] An analysis of the results obtained allowed a complex relation to be found between the yield of chemically bound xenon and the valence of the iodine in the compounds, the state of these compounds (solution or crystal), the nature of the cation, the conditions of storage, the presence or absence of carriers, etc.[319–321] XeO_3 is formed in these processes. Xenon trioxide is also the only form of combined xenon in the β-decay of ^{131}I in I_2O_5 (yield 27%) and HIO_4 (yield 44%).[322] The processes for the formation of oxygen compounds of xenon in the β-decay of iodine and some of their properties have been discussed[323,324]. It has also been shown that XeO_3 is formed in aqueous solutions in the β-decay of ^{131}Xe in the composition of $C_6H_5IO_2$.[325] Several methods have been proposed for the separation of radioactive XeO_3 from the parent compounds by use of ion-exchange and thin-layer chromatography[326–329].

The possibility of the formation of xenon compounds under natural conditions as a result of the occurrence of nuclear processes has been examined[330]. The Szillard–Chalmers effect in dissolved XeO_3 has been investigated[331]. The retention of radioactive xenon amounts to 3%. It was found that the factor of enrichment of the xenon radioactive isotopes in the gas phase varies with the period of irradiation. Investigations[332,333] of processes of β-decay of ^{131}I or ^{133}I in C_6H_5I, $(C_6H_5)_2ICIO_4$, and other iodonium salts showed the formation of chemically bound xenon in an involatile form and it was concluded that $C_6H_5Xe^+$ is formed. The yield of onium compounds depends on the nature of the anion present, and the stabilising ability in relation to $C_6H_5Xe^+$ decreases in the order:

$$ClO_4^- > BF_4^- > SO_4^{2-} > NO_3^- > Cl^-.$$

III. KRYPTON COMPOUNDS†

Krypton difluoride is formed by the action of an electric discharge (15–20 mA, 3000–4000 V) on a mixture of krypton and fluorine with the molar ratio 1.1 : 1 at a total pressure of 20 mmHg.[230] The variation of the yield of KrF_2 with the parameters of the electric discharge, the pressures of krypton and fluorine, and the geometry and the temperatures of the walls of the discharge tube was investigated[334]. The synthesis of KrF_2 in an electric discharge can also be brought about in a metallic reactor at a wall temperature of −196°C, pressure of the gas mixture 4–20 mmHg, molar ratio $F_2 : Kr = 5 : 1$, current 20–30 mA, potential 500–1000 V.[335]

Gaseous krypton and fluorine react readily, with the formation of KrF_2 under the action of protons with energies of 10 MeV or α-particles with energies of 40 MeV at −140°C.[39] The radiation-chemical yield is 1.0–1.5, depending upon the temperature. A photochemical reaction is effected in the $Kr–F_2$ and $Kr–OF_2$ systems at room temperature[336]: the yield of KrF_2 in these experiments is insignificant.

At room temperature krypton difluoride is a colourless crystalline substance; it sublimes below 0°C. The vapour pressure in the temperature range from −30° to +25°C is described by the equation[337]:

$$\lg P_{mmHg} = 8.814 - 2000/T.$$

The physical properties of KrF_2 are given in Table 5.

The kinetics of thermal decomposition of gaseous KrF_2 were studied in the temperature range 20–100°C and at KrF_2 pressures of 5–70 mmHg.[338] The variation of the homogeneous decomposition of KrF_2 with temperature (60–100°C) is expressed by the equation:

$$k_{(hom)} = 2 \cdot 10^{13} \exp(-23\,800/RT)\,s^{-1}.$$

In the general instance, the activation energy of the thermal decomposition of KrF_2 varies from 10.2 kcal $mole^{-1}$ (20°C) to 23.8 kcal $mole^{-1}$ (60–100°C).

†See Prusakov and Sokolov's review[10] for a more detailed account of the papers published up to 1971.

The ions KrF^+ and Kr^+ with appearance potentials of 13.21 ± 0.25 and 13.71 ± 0.20 eV respectively have been observed[335] in the mass spectrum of KrF_2. The emission spectrum of KrF_2 in the ultraviolet range has been investigated[65]. The infrared and Raman spectra of gaseous KrF_2 have been obtained and interpreted[339] and have confirmed that the symmetry of this molecule is $D_{\infty}h$. The force constants were found to be: f_r = 2.46, f_{rr} = −0.20, f_{α} = 0.21 mdyn Å^{-1}. The negative force constant for the interaction between the bonds f_{rr} = −0.20 mdyn Å^{-1} and also the absence of Fermi resonance between the frequencies ν_1 and $2\nu_2$ were discussed[339–342]. The asymmetric stretching vibration ν_3 in the infrared spectrum of $^{86}KrF_2$ was studied[343] further with a resolution of 0.08 cm^{-1}. Two alternative assignments were proposed and two corresponding sets of constants were obtained. The most probable, in the opinion of Murchison and coworkers[343], set gives ν_0 = 589.889, B_0 = 0.126 26, B' = 0.125 75, D_0 = D' = 7.8 × 10^{-8} cm. Hence r(Kr–F) = 1.875 ± 0.002 Å (or 1.876 ± 0.002 Å). The spectrum of solid KrF_2 (400 to 1000 cm^{-1})[170] at 77 °K is characterised by sharply expressed maxima at 520, 536, and 573 cm^{-1}. It has been suggested that KrF_2 is polymerised in the solid state. The band at 573 cm^{-1} is assigned to the Kr–F (ν_3) stretching vibration of the monomeric molecule, the remaining bands to the polymeric species of KrF_2. Electron diffraction investigations of gaseous KrF_2 confirmed the linear symmetry structure of the molecule[344]. The mean interatomic distances are r(Kr–F) = 1.889 and r(F...F) = 3.781 Å.

The ^{19}F NMR spectrum of KrF_2 in anhydrous HF was investigated[230]. The two fluorine atoms in KrF_2 were found to be equivalent. Exchange by the fluorine atoms between HF and KrF_2 was not noted even at 25 °C. From the Mössbauer spectrum of $^{83}KrF_2$ the quadrupole coupling constant was found to be 130 mm s^{-1} and the ratio of the quadrupole moments of the excited and ground states (1.70), and the isomeric shift (in relation to atomic krypton) (1.50 mm s^{-1}) were found[345]. The formal charge on the krypton atom in KrF_2 is 1.06. High-resolution photoelectronic spectra were obtained for KrF_2 in He–I and He–II radiation[346,347].

The BrF_5–KrF_2 system was studied by the DTA method[348]. The complexes $KrF_2.SbF_5$, $KrF_2.2SbF_5$, $KrF_2.TaF_5$, $KrF_2.2TaF_5$, $KrF_2.2NbF_5$, $2KrF_2.SnF_4$, and $2KrF_2.TiF_4$ have been isolated[10,337] from solutions of KrF_2 in anhydrous HF and BrF_5. The stability of the complexes of KrF_2 in non-aqueous solvents is much lower than that in the solid state, owing to the chemical reaction of these compounds with the solvents. Investigations of the infrared spectra[10] enabled ionic structures to be suggested for these compounds which were also confirmed by measurements of the Raman spectra of $KrF_2.2SbF_5$, $KrF_2.TaF_5$, $KrF_2.2TaF_5$, $KrF_2.2NbF_5$, and BrF_5 at −196 °C.[349] The stretching vibration Kr–F (KrF^+) in the Raman spectra[349] is characterised by doublet and even triplet absorption bands 620 and 623 cm^{-1} in $KrF^+Sb_2F_{11}^-$, 599 and 604 cm^{-1} in $KrF^+TaF_6^-$, 600 and 609 cm^{-1} in $KrF^+Nb_2F_{11}^-$, and 597, 605, and 613 cm^{-1} in $KrF^+Nb_2F_{11}^-$. The stretching vibration Kr–F in KrF^+ corresponds to the band at 622 cm^{-1} in the infrared spectrum[170] of $KrF^+SbF_6^-$.

$2KrF_2.SbF_5$ was synthesised in BrF_5 solutions at −40 °C; it is stable at the synthesis temperature[350] and decomposes in a dynamic vacuum at −30 °C with the formation of $KrF_2.SbF_5$, which is stable at room temperature. The Raman spectra of these compounds were investigated[349]. The bands at 627 and 619 cm^{-1} in $KrF_2.SbF_5$ were assigned to the KrF^+ vibration; the bands at 595 and 607 cm^{-1} in $2KrF_2.SbF_5$ to the principal stretching vibrations of the $Kr_2F_3^+$ cation. Gillespie and Schrobilgen[351] obtained $KrF_2.MF_5$ (M = As, Pt), $2KrF_2.AsF_5$, and $(KrF_3^+MF_6^-)_n KrF_2$ (M = As, Sb) and confirmed the existence of $KrF_2.SbF_5$ and $2KrF_2.SbF_5$. The compound $KrF_2.PtF_5$ was prepared by the reaction of KrF_2 and PtF_6 at 0 °C. The Raman spectra of these compounds were studied[351] and the ^{19}F NMR in $KrF_2.SbF_5$ at −40 °C and in $2KrF_2.SbF_5$ at −66 °C was measured in anhydrous HF and BrF_5. The results show the existence of the cations KrF^+ and $Kr_2F_3^+$ in the solutions. In the NMR spectrum of $KrF^+SbF_6^-$ a singlet line with a chemical shift of 22.6 p.p.m. relative to CCl_3F (−55.6 p.p.m. for KrF_2 in HF) is observed. The NMR spectrum of a solution of KrF_2 and SbF_5 with molar ratio 2:1 is assigned to the AX_2 type, which suggests a

Table 6. Change in free energy (enthalpy) in the reactions of certain gaseous inorganic fluorides.

Initial substance	$-\Delta G^0_{298}$ EF_n ($-\Delta H^0_{298}$) kcal mole^{-1}	Reaction product	$-\Delta G^0_{298}$ EF_{n+2} ($-\Delta H^0_{298}$) kcal mole^{-1}	$-\Delta G_{298}EF_{n+2}$($-\Delta H_{298}$), kcal mole^{-1}								
				F_2	$OF_2^{(2)}$(to O_2)	$O_2F_2^{(2)}$	N_2F_2 (to N_2)	XeF_2	XeF_4 (to XeF_2)	XeF_6 (to XeF_4)	KrF_2	RuF_6^* (to RuF_5)
ClF	13.8 (13.9)	ClF_3	29.5 (37.8)	15.7	(19.5)	28.4	50.7	—1.8	1.8	8.6	37.8	(32.9)
ClF_3	29.5 (37.8)	ClF_5	35.8 (57.7)	6.3	(15.5)	19.0	41.3	—11.2	—7.6	—0.8	28.4	(28.9)
BrF_3	55.2 (64.8)	BrF_5	84.4 (106.2)	29.2	(37.0)	41.9	64.2	11.7	15.3	22.1	51.3	(50.4)
XeF_2	17.5 (25 6)	XeF_4	31.4 (49.3)	13.9	(19.3)	26.6	48.9	—	—	6.8	36.0	(32.7)
XeF_4	31.4 (49.3)	XeF_6	38.5 (66.7)	7.1	(13.0)	19.8	42.1	—	—	—	29.2	(26.4)
UF_4	424.6 (443.4)	UF_5	458.7 (485.2)	34.1	(39.6)	40.5	51.6	25.4	27.1	30.6	45.1	(46.3)
UF_5	458.7 (485.2)	UF_6	492.0 (511.0)	33.3	(23.6)	39.7	50.8	24.6	26.0	29.8	44.3	(30.3)
UF_4	424.6 (443.4)	UF_6	492.0 (511.0)	67.4	(63.2)	80.2	102.4	49.9	53.2	60.4	89.5	(76.6)
N_2F_4[1]	—18.7 (2)	NF_3	21.4 (31.6)	61.5	(56.8)	74.2	96.5	44.0	47.6	54.4	83.6	(70.2)
NOF	12.1 (15.8)	NOF_3	(32)	(16.2)	(11.8)	(20.9)	(41.8)	(—9.4)	(—7.5)	(—1.2)	(30.6)	(25.2)
Rn	—	RnF_2	(57.4*)	(57.4)	(53.0)	(62.1)	(92.4)	(31.8)	(33.7)	(40.0)	(71.8)	(66.4)

Notes. (1) The reaction of N_2F_4 proceeds through the formation of NF_2 radicals, for which the addition of fluorine with formation of NF_3 is energetically more favourable.

(2) In the reactions of OF_2 the radicals OF and F participate, in those of O_2F_2, the radicals O_2F and F.

(3) The relatively low fluoro-oxidising ability of N_2F_2 (according to the experimental results) is due to kinetic restraints.

*Estimated values.

V-shaped structure for $Kr_2F_3^+$ with fluorine bridging atom[351]. The ^{19}F chemical shifts are −19.0 p.p.m. (A) and −73.6 p.p.m. (X_2). The coupling constant ($^{19}F_A-^{19}F_X$) is 351 Hz, close to that found for $Xe_2F_3^+$ (308 Hz).[351] In the Raman spectrum of $Kr_2F_3^+$, bands are observed at 603 and 594 cm^{-1}, 555 and 456 cm^{-1}; the results are interpreted[351] in terms of the asymmetric structure $FKr^+...FKrF$.

$XeF_6.SbF_5$ was isolated from a solution of KrF_2, SbF_5, and XeF_6 (1 : 1 : 1) in BrF_5 at 0°C, showing that the donor properties of XeF_6 are stronger than those of KrF_2; this is also confirmed by XeF_6 replacing KrF_2 in its complexes[170]. Xenon difluoride is also a better fluoride-ion donor than KrF_2. The molecular complex $KrF_2.XeF_6$ has also been obtained[170]; it is a colourless crystalline substance with m.p. 41°C and a vapour pressure of 11 mmHg at 20°C. The molecular nature of the complex was established by measurements of the infrared spectrum.

Taken together, the properties of KrF_2 suggest that KrF_2 as a fluoro-oxidant surpasses such strong fluorinating agents as F_2, oxygen fluorides, and halogen fluorides, and is only slightly worse than atomic fluorine (see Table 6). The complexes of KrF_2 are also strong oxidants. For example, in solutions of bromine pentafluoride KrF^+ ($KrF_2.nSbF_5$) readily oxidises IF_5 to IF_6^+, $XeOF_4$ to $XeOF_5^+$,[184] and BrF_5 to BrF_6^+.[351]

Previous papers (cf. Neiding[1]) have discussed the preparation and study of krypton tetrafluoride, and also the formation during its low-temperature hydrolysis of kryptic acid and its barium salt. These results were not confirmed subsequently. Furthermore, mass-spectrometric measurements and investigations of the vibrational spectra and ^{19}F NMR spectra of the products of the reaction of krypton with fluorine in a glow discharge showed that the identification of the reaction product as krypton tetrafluoride is erroneous.

Mössbauer spectroscopy was used to observe the chemically bound states of krypton[352] formed during electron capture in ^{83}Kr. The Mössbauer spectra of ^{83}Kr in solid matrices are characterised by broad lines, which suggests a different degree of chemical bonding[345,352,353]. In an investigation[353] of the products of the β-decay of ^{83m}Br in $KBrO_3$ a resonance line 2 mm s^{-1} broad is observed in the spectrum and is assigned to the bond of ^{83m}Kr with oxygen. These results were confirmed by measurements of the Mössbauer spectra of the products of the β-decay of ^{83}Se ($^{83}Se \rightarrow {}^{83}Br \rightarrow {}^{83}Kr$) in Se, SeO_2, and $(NH_4)_2SeO_4$.[354]

IV. RADON COMPOUNDS

The preparation and identification of radon compounds is extremely difficult owing to the high activity of the most stable radon isotope ^{222}Rn ($\tau_{1/2}$ = 3.8 d.) Therefore information about radon compounds is only qualitative.

It has been reported[355] that radon is oxidised in aqueous solutions by certain oxidants, in particular H_2O_2, $KMnO_4$, and $K_2S_2O_8$. Subsequent investigations[356] showed that under the conditions of the experiment[355] the radon is held mechanically in the solid phase. The formation of significant amounts of oxygen-containing compounds of radon is also not observed[357] in the α-decay of ^{226}Ra.

Vasilescu[358] estimated $\Delta H^\circ_{298}RnF_n$ (g). After some refining of these values, the following quantities are obtained: $\Delta H^\circ_{298}RnF_2$ (g) = −57.4 kcal $mole^{-1}$ (mean energy of the Rn–F bond 46.5 kcal $mole^{-1}$), $\Delta H^\circ_{298}RnF_4$ (g) = −81.1 kcal $mole^{-1}$ (39.1), $\Delta H^\circ_{298}RnF_6$ (g) = −98.5 kcal $mole^{-1}$ (35.2).

Radon fluorides are formed in the reaction of elemental radon with ClF_3, KrF_2, and XeF_n at room temperature[359], with O_2F_2 at −100°C, or under the action of α-radiation in liquid fluorine or solid ClF_3 at −196°.[359] The products of these reactions were not identified. Radon fluoride of a definite composition is isolated by distillation with XeF_6 from the reaction products of mixtures of xenon and radon with fluorine at 300°C and 100 atm.[359] The formation of RnF_2 and RnF_4 has also been reported[360].

The oxidation of gamma amounts of radon was effected in BrF_3, BrF_5, and ClF_3 solutions[361]. The formation of RnF_2 was suggested. Radon can also be oxidised by the action of ClF, ClF_5, BrF, IF_7, or NiF_6^{2-} (in HF) in the temperature range from −195° to +25°C.[362] Experiments on the electrolysis of solutions of oxidised radon in BrF_3 (potential difference 18–50 V, current 50 mA) showed that the Rn is concentrated only in the near-cathode region without reduction. On this basis the existence in the solutions of the cations RnF^+ or Rn^{2+} (products of the dissociation of RnF_2) was suggested. The coprecipitation of radon fluoride with the molecular compound of XeF_2 and IF_5 was studied[363] to find the chemical composition of the radon in BrF_3–IF_5 solutions. The results show that the most probable product of the reaction Rn + XeF_2 (XeF_4) is RnF_2. Involatile radon compounds are formed in the reaction of radon with ClF_2SbF_6, BrF_2SbF_6, $BrF_4Sb_2F_{11}$, $If_4(SbF_6)_3$, or BrF_2BiF_6 at 25°C.[364] $KBrF_4$, $CsBrF_6$, $KClF_4$, $RbClF_4$, and BrF_2TaF_6 are less effective. It is suggested that the reaction leads to the formation of complexes of the type $RnF^+MF_6^-$ or $RnF^+M_2F_{11}^-$ and radon difluoride[364].

Vasilescu[358] discussed the possibility of obtaining various compounds of radon and their expected stability. Stein[365] discussed problems of radon chemistry in detail.

V. ELECTRONIC STRUCTURE OF COMPOUNDS OF THE NOBLE GASES

In her extremely thorough critical review[2] Dyatkina examined the main theoretical studies in this field published in the period 1963–1968 and compared the theoretical with the experimental results. Dyatkina came to the general conclusion "that the main reason for the formation of these compounds is the establishment of delocalised molecular orbitals and the specific characteristics of the molecular orbitals—their energies and atomic orbital coefficients—determine the properties of the molecules".[2]

Without any pretension to the completeness and depth of exposition present in Dyatkina's review[2] we will examine the most recent theoretical publications on the compounds of the noble gases.

First let us briefly examine the attempt of Mitchell[366–369] to prove by use of the valence bond method the significant role of the atomic *d*-orbitals (5*d* for Xe, 4*d* for Kr) in the formation of bonds in the halides of these elements. Mitchell calculated the excitation energy of three valence states of the Xe atom in hybridisations with participation of the 5*s*-, 5*p*-, and 5*d*-orbitals and with the aid of the method of Hartley, Lennard-Jones, and Pople evaluated the energies of the valence structures Hal–Xe–Hal, $Hal-Xe^+Hal^-$, and $Hal^-Xe^{2+}Hal^-$ (the first structure is based on the assumption of the hybridisation of the 5*s*- and $5d_{z^2}$-orbitals of Xe) for XeF_2 and $XeCl_2$.[368] The first structure seemed the most stable and on this basis Mitchell concluded that the 5*d*-orbitals of Xe participate in the formation of XeF_2 and $XeCl_2$, assuming that the high excitation energy is compensated by the gain in the bond

energy. Somewhat later, Catton and Mitchell[368] made a refined calculation of XeF_2 by the valence bond method and found that the structures based on the participation of the Xe $5d_{z^2}$-orbitals contribute ~ 69% to the complete wave function, whereas the contribution of the resonance structures which include only the $5p_z$-orbital totals only ~ 16%. Developing these ideas, the same investigators[369] calculated the energies of various valence structures in KrF_2, XeF_2, $XeCl_2$, and also in the hypothetical molecules ArF_2, $ArCl_2$, and $KrCl_2$. The calculations showed that in every instance (except ArF_2) the minimal energies are exhibited by the structure Hal–X–Hal. On this basis Catton and Mitchell concluded that the greater part is played by a valence scheme based on the promotion of p-electrons to a d-AO and the hybridisation of pd-AO; here the high excitation energy in the free atoms is compensated by the influence of the ligands on the AO atoms, greater for the fluorides than for the chlorides. The role of the Hal–X–Hal structure increases, according to the calculation, in the order Ar < Kr < Xe. Finally, in the most recent paper in this series[367] Mitchell has suggested the participation of the Xe $4f$- and $6s$-orbitals in the formation of xenon hexafluoride and he related the participation of the $4f$-orbitals to Bartell and Gavin's views (discussed above) on the structure of XeF_6.

Table 7. Correlation of the calculated[373] and experimental[53,374] values of the ionisation potentials of XeF_n (in eV).

XeF_2			XeF_4			XeF_6		
MO	$-0,92\varepsilon$	vertical IP	MO	$-0,92\varepsilon$	vertical IP	MO	$-0,92\varepsilon$	vertical IP
$10\ \sigma_g$	11.79	13.65	$10\ a_{1g}$	11.7	13.1	$8\ a_{1g}$	10.8	12.5
$5\ \pi_u$	12.51	12.42*	$5\ a_{1g}$	13.9	13.4	$5\ e_g$	17.2	15.2
		12.89	$5\ b_{1g}$	15.2	14.5	$1\ t_{1g}$	17.6	16.0
$3\ \pi_g$	14.71	14.35	$1\ a_{2g}$	15.8	15.1	$7\ t_{2u}$	18.0	(16.5)
		15.60*	$7\ e_u$	16.2	(15.4)	$1\ t_{2u}$	18.1	(17.4)
$4\ \pi_u$	15.92	16.00	$1\ b_{2u}$	16.5	15.8	$3\ t_{2g}$	18.8	17.7
$6\ \sigma_u$	16.93	17.35	$3\ e_g$	16.6	(16.0)	$6\ t_{1u}$	22.3	20.0
$9\ \sigma_g$	25.24	22.5	$3\ b_{2g}$	16.8	16.3	$7\ a_{1g}$	29.2	21.0
			$4\ a_{2u}$	19.0	17.9			
			$6\ e_u$	19.6	18.4			
			$9\ a_{1g}$	27.4	19.8			

*Doublet structure, due to spin–orbital coupling.

Before turning to the consideration of non-empirical calculations, we note the method proposed by Andreev for the determination of the conformation of the molecules of XeF_2, KrF_2,[370] and XeF_4[371] by the combined use of the theory of the interaction of bonding and unshared electron pairs and the maximal overlap criterion. The same investigator[372] considered the electronic structure of XeF_3 and XeF_3^+, having used the Wolfsberg–Helmholz method with allowance only for $p\sigma$-AO. According to the calculation, the most stable configuration for XeF_3 has C_{2v} symmetry, but for XeF_3^+ there are alternatives in the choice of a stable geometry—D_{3h} or C_{2v} are the most probable.

Basch and coworkers[373] made non-empirical calculations for XeF_2, XeF_4, and XeF_6, using Roothaan's complete SCF MO method with a basis set of gaussian functions including the $1s$-, $2s$-, $3s$-, $4s$-, $5s$-, $2p$-, $3p$-, $4p$-, $5p$-, $3d$-, and $4d$-AO of xenon, and the $1s$-, $2s$-, and $2p$-AO of fluorine (all the AO were checked by calculation of the orbital and total bond energies). The total and orbital energies were calculated and the composition of the valence MO was found. An analysis of the populations after Mulliken was made for the individual AO and the overlap populations were also found.

The photoelectron spectra of XeF_2 were investigated almost simultaneously by Brundle and coworkers[374] and by Brehm and coworkers[52]. The ionisation potentials found in the two studies agree and differ little from those obtained by the photon collision method[54] and by photoionisation mass spectrometry[44]. The photoelectron spectra of XeF_4 and XeF_6, investigated by Brundle and coworkers[53], led to ionisation potentials close to those found by photoionisation mass-spectrometry[44]. The assignment, proposed on the basis of these results[53,373,374], of the vertical ionisation potentials to ionisation from MO_5 and a comparison of the experimental results with the calculated orbital energies multiplied by 0.92 (a factor introduced by Brundle and coworkers[53] to correct for the approximations of the Koopmans theorem) are given in Table 7. Fig. 13 gives the corresponding correlation diagram.

The effective charges on the xenon atoms were evaluated in the calculation[373] and are +1.304, +2.455, and +3.458 for XeF_2, XeF_4, and XeF_6 for a comparatively constant charge on the fluorine atoms (−0.652, −0.614, and −0.576). Between the calculated effective charges and the quantities estimated on the basis of EPR[58] and NMR[375,376] investigations, Mössbauer spectra[303], and X-ray electronic spectra[50,51] there are significant differences; the reasons for these have been discussed[58].

Basch and coworkers[373] used the results of their non-empirical calculation of the xenon fluorides for a detailed interpretation of the electronic spectra of XeF_2 and XeF_4 on the basis of the experimental results of Jortner and coworkers (cf. Dyatkina's review[2]). They also calculated and tabulated certain one-electron properties of the molecules of the xenon fluorides: the mean values of magnetic screening tensor of the xenon and fluorine nuclei, the quadrupole moments of XeF_2 and XeF_4, the components of the field gradient at the xenon and fluorine nuclei[373].

A regular octahedral structure was chosen for XeF_6 in the calculation[373]. Such an approximation must reflect on the accuracy of the results obtained since in reality the XeF_6 molecule does not maintain strictly O_h symmetry. Unfortunately, later investigations of the electronic structure of XeF_6 made by the wave scattering method with statistical allowance for the exchange interactions[377] was also based on the adoption of O_h symmetry for this molecule. In this work[377] the orbital energies were calculated within the framework of the ideas of half-occupied spin-orbitals, since Koopmans' theorem is inapplicable in a statistical calculation of exchange interactions. When the factor 0.92 is not used, the results of the calculations by scattered waves method[377] give better agreement with experiment.

Three non-empirical calculations were made[378–380] for the krypton fluorides (KrF_2, KrF, and KrF^+). The calculations for KrF and KrF^+ were made by the SCF MO method with a large basis set of functions of the Slater type[380]. The potential curve for KrF was calculated by assuming the ground state $^2\Sigma^+$ (in agreement with EPR results[381]), and that for KrF^+ the state $^1\Sigma^+$. The curve for KrF, like that for XeF, is repulsive, since these molecules can exist in the gas phase solely owing to van-der-Waals interaction. The dissociation energy found for the molecular ion KrF^+ was $D_0 = 1.90$ eV, which agrees with the experimental $D_0 \geq 1.58$ eV.[382] The calculated spectroscopic constants of KrF^+ are also in good agreement

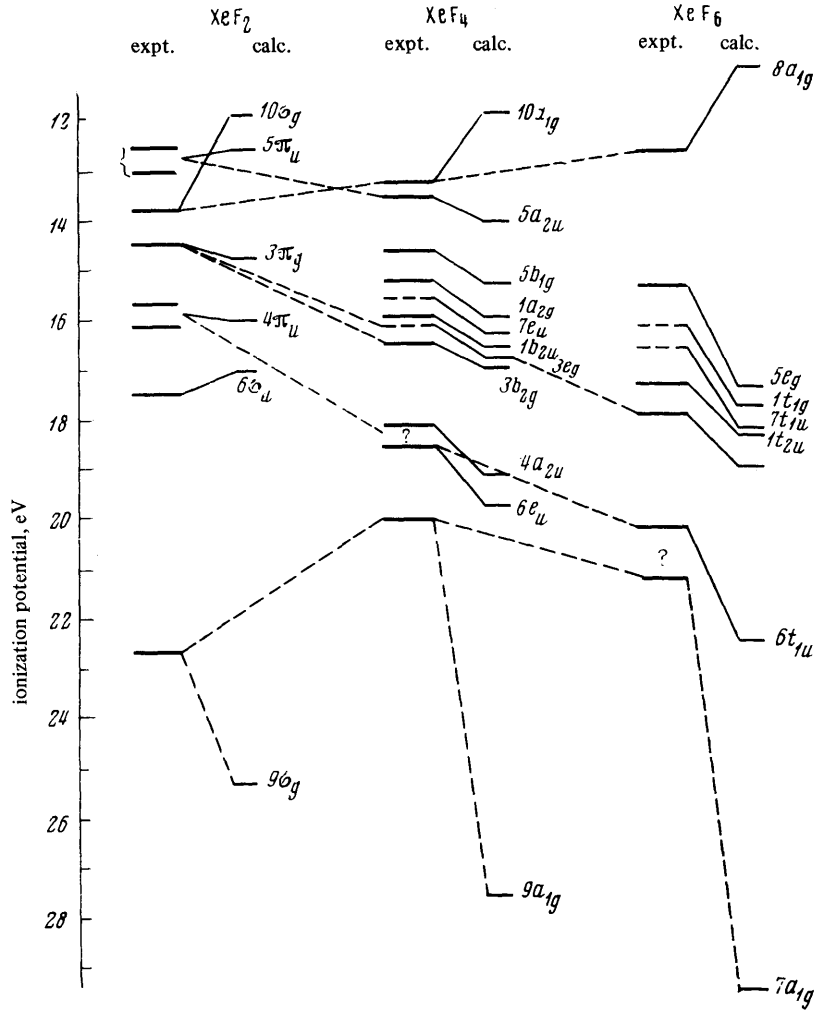

Figure 13. Diagram of the molecular orbitals of xenon fluorides.

with experiment, in particular the theoretical wavenumber of the stretching vibration (621 cm^{-1}) is close to that found from the Raman spectrum for $KrF^+Sb_2F_{11}^-$.[184]

Concerning the problem of the role of the "higher" AO's in the formation of bonds in noble gas compound (the role of the polarisation functions (4*d* and 4*f* for Kr and 3*d* and 4*f* for F) has been evaluated[380]. In KrF the inclusion of the polarisation functions decreases the total energy by only 0.0044 a.u., in KrF^+ by 0.0388 a.u. In the first non-empirical calculation for KrF_2, the main aim of which was the explanation of the role of the 4*d*-orbitals of Kr, the SCF MO method was used with a minimal set of Slater-type functions[378]. From the results of this work there follows the need for the inclusion in the basis of the Kr 4*d*-functions, but a calculation made with a broadened basis set[379] showed insufficient justification for this assertion.

Bagus and coworkers[379] made a complete calculation of KrF_2 by the SCF MO method using an extended basis set of Slater-type functions with allowance for configuration interaction. The potential curve found with 993-configuration wave function corresponds to the bound state of KrF_2 in relation to three atoms infinitely removed from one another. The calculated Kr–F distance, found to be 1.907 Å, and the dissociation energy, 0.39 eV, are comparable with the experimental results (respectively 1.88 ± 0.01 Å and 1.013 eV). On the potential curve there is a barrier at r(Kr–F) = 2.42 Å of height 0.22 eV in relation to the total energy of the disconnected atoms. The electric field gradient at the Kr nucleus near to the minimum of the potential curve is close to the value calculated by the SCF method for the Kr^+ ion and falls rapidly to zero close to the maximum of the potential curve. These results show that the Kr–F bond is ionic at the equilibrium distance and covalent at greater distances, which agrees with Coulson's views[340].

To investigate the role of the polarisation functions (4*d* and 4*f* Kr, 3*d* and 4*f* F), a series of calculations was

made[379] with various basis sets and it was shown that the role of the Kr 4*d*-AO is significantly less than that found from the previous calculation[378]. A compilation of the theoretical results[378,379] with high-resolution photoelectron spectra of KrF_2,[346,383] are given in Table 8 and Fig. 14 (on which results for XeF_2 are given for comparison).

Table 8.

MO	-0.92ε (Ref.378)	-0.92ε (Ref.379)	Vertical IP (Refs.346, 383)	MO	-0.92ε (Ref.378)	-0.92ε (Ref.379)	Vertical IP (Refs.346, 383)
$8\sigma_g$	7.9	14.71	13.90	$3\pi_u$	15.0	19.36	16.92
$4\pi_u$	10.5	15.43	13.34* 13.47	$5\sigma_u$	16.1	20.85	17.7
$2\pi_g$	12.6	17.64	14.37	$7\sigma_g$	29.0	33.75	23.0

*Doublet due to spin–orbital coupling.

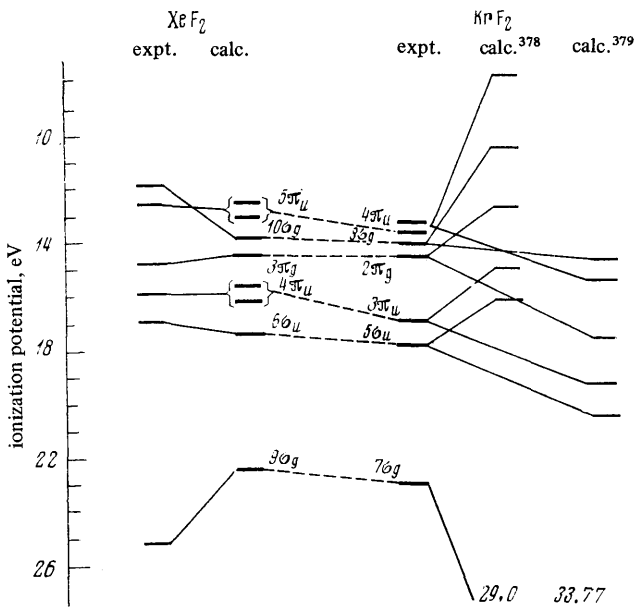

Figure 14. Diagram of the molecular orbitals of the lower fluorides of xenon and krypton.

The xenon oxide fluorides have been examined theoretically in only one paper, published comparatively recently[383]. The electronic structures of $XeOF_2$, XeO_2F_2, and $XeOF_4$ were calculated within the framework of the semiempirical modified Wolfsberg–Helmholz method. The results obtained by Gillespie using the method of localised electron pairs (see Dyatkina[2]) formed the basis of a comparison of the electronic and geometric structures of the oxide fluorides. The energies and populations of the MO were found on the basis of the nodal structure of the upper occupied MO and the geometric structure of the xenon oxide fluorides was predicted.

According to the prediction, the $XeOF_2$ molecule should have C_{2v} symmetry with an O–Xe–F angle less than 90°. For XeO_2F_2 the O–Xe–O angle should be less than 120°, and the F–Xe–F angle (at the side of both O atoms) less than 180°. For $XeOF_4$, C_{4v} symmetry was obtained with O–Xe–F angle greater than 90°. In all three molecules the Xe–O bond should be shorter than Xe–F.

When Hsu and coworkers' paper[383] appeared experimental results were known only for $XeOF_4$. They[383] cited only Martins and Wilson's study of the microwave spectrum[233] and did not consider a later electron diffraction investigation[234]. As for XeO_2F_2, a detailed electron diffraction investigation of this molecule appeared recently[241]. Theoretical calculations give qualitative agreement with experimental results for both XeO_2F_2 and $XeOF_4$. For the former the O–Xe–O angle is 105.7° and the Fe–X–F angle is 174.7°; the Xe–O and Xe–F distances are 1.714 and 1.889 Å respectively[241]; in the second instance the O–Xe–F angle is 91.9° and the Xe–O and Xe–F bonds are respectively 1.711 and 1.901 Å.[234]

VI. POSSIBILITY OF THE EXISTENCE OF COMPOUNDS OF THE NOBLE GASES LIGHTER THAN KRYPTON

An approximate evaluation of the possibility of obtaining some compounds of argon and their stability led Ferreria[384] to a conclusion about the similarity in stability of the Ar–F and Kr–F bonds and even of the greater stability of the Ar–O bond compared with Kr–O. However, an estimate of the enthalpy of formation of the hypothetical $ArF_2(g)$, made by extrapolation of the values of ΔH°_{298} along the series (RnF_2)–XeF_2–KrF_2–$[ArF_2]$ and on the basis of the ionisation potentials of the noble gases, leads to a negative bond energy in ArF_2. Some calculations show the possibility of the existence of HeF_2;[385] the results of other theoretical calculations[386,387], made by the SCF LCAO MO and valence bond methods show that for all forms of the geometry of HeF_2 an unstable repulsive state is characteristic. The potential curves for the processes of formation of HeF^+ and HeF, NeF, NeF_2, and NeO also do not have a minimum[388].

Liebman and Allen[389] undertook calculations for ArF^+ and ArO by the SCF LCAO MO method and showed that the $^1\Sigma\sigma^2\pi^4\pi^{*4}$ state should be rather stable and be characterised by the equilibrium distance r_e = 1.8 Å and dissociation energy $De \simeq 70$ kcal mole^{-1}. On the basis of these results they suggested the possibility of the synthesis of $ArF^+PtF_6^-$ by the reaction of argon with fluorine in the presence of platinum hexafluoride. Berkowitz and Chupka[390] reported that ArF^+ ($^1\Sigma\pi^4$) is formed in the ion-molecular reactions $F_2^+ + Ar$ and $Ar^+ + F_2$. On the basis of a simple analysis of the exothermic reaction

$$F_2^+ + Ar \rightarrow ArF^+ + F$$

they concluded that $D_0(ArF^+) \geqslant 38$ kcal mole^{-1}. Analogous reactions of F_2^+ with neon and helium were not observed even at high collison energies. Liebman and Allen[391] used the SCF LCAO MO method to calculate the potential curves for the lowest electronic states of HeF^+, NeF^+, HeN^+, and NeN^+ and made an analysis of the possibility of the synthesis and stability of these cations. Unlike earlier investigations[388], these calculations showed the rather high stability of the states $^1\Sigma\pi^4$ HeF^+ (r_e = 1.33 Å, $De \simeq$ 33 kcal mole^{-1}) and $^1\Sigma\pi^{*4}$ NaF^+ (re = 1.65 Å, $De \simeq$ 30 kcal mole^{-1}). It was suggested[391] that the stabilisation of these states can be effected by bonding in $HeF^+SbF_6^-$ and $NeF^+SbF_6^-$ by the reaction of He and Ne with fluorine (in the presence of SbF_5 or PtF_6) at high temperatures and pressures. Liebman and Allen[392] also showed that although

some of the states HeN^+, NeN^+, HeO^+, ArO^+, and NeO^+ are sufficiently stable and should be observed in ion-molecular reactions, the existence of the corresponding crystalline salts is improbable. On the basis of an SCF LCAO MO calculation of the potential surfaces of HeB^+, NeB^+, and ArB^+ the same investigators[393] concluded that the bound states of these ions were absent unlike the $^1\Sigma$ XeB^+ state, the bond energy of which is estimated to be 10–20 kcal $mole^{-1}$.

VII. POSSIBLE USES OF COMPOUNDS OF THE NOBLE GASES

The interest of the wide circle of investigators in the chemistry of the noble gases is not limited to the theoretical value of this problem. The considerable experimental and theoretical material on the compounds of the noble gases which has now accumulated allows the question of their practical use to be examined.

The investigation of the compounds of the noble gases is of prime importance in connection with the need for solving one of the most important problems of the protection of the environment—the collection of radioactive krypton and xenon—the gaseous products fission of uranium in nuclear reactors. The electrical power of atomic power stations now amounts to ~ 3% of the total power of all power stations. However, even in the next decade the position will change radically and the fraction of atomic power stations to the total production of electric energy will increase considerably. The development of atomic energy is responsible for the need for the reprocessing of large amounts of spent fuel elements of nuclear reactors. In the operation of nuclear reactors and the chemical reprocessing of irradiated nuclear fuel the removal of gaseous fission products is very complex, especially ^{85}Kr (half-life 10.76 years) and ^{133}Xe (9.27 days). This problem is still more complicated because of the future development of fast neutron reactors owing to the increased yield of fission products.

The successful development of noble gas chemistry opens new pathways for the utilisation of radioactive noble gases—in the form of their chemical compounds. The first success has already been achieved. This, it was shown recently[394] that when it reacts with O_2SbF_6 xenon is bonded in the solid involatile compound $XeF^+Sb_2F_{11}^-$. In five experiments with ^{133}Xe on a column of dia. 5.5 × length 65 mm. packed with O_2SbF_6 almost 100% bonding of the xenon from the air at 23–25°C was achieved (^{133}Xe from 2 to 10 mC $litre^{-1}$ mean flow rate 13 ml min^{-1}). It has been proposed to use the analogous reaction with radon for purifying the atmosphere in uranium mines[394]. The oxidation of radon and xenon can be effected also with the aid of K_3NiF_6, K_2NiF_6, Cs_2CoF_6, K_3CuF_6, $CsAgF_4$, Cs_2AgF_6, etc.[395–397] Radioactive xenon and radon are oxidised at 25°C by the action of N_2FSbF_6, but $N_2F_3Sb_2F_{11}$ oxidises only radon at 25–100°C.[398]

The most complex tasks in the problem of the removal of radioactive noble gases is the bonding of ^{85}Kr, since krypton forms only compounds that are comparatively unstable under ordinary conditions, their stability decreasing still further under the action of ionising radiations. In addition, the problems of the chemical bonding of krypton is further complicated by the high oxidising ability of krypton compounds, which is due to the need for obtaining inorganic fluoro-oxidants capable of oxidising krypton. Stein[394] notes that the replacement of the O_2^+ cations in O_2SbF_6 by a cation of greater oxidising ability can yield reagents capable of spontaneous reaction with krypton with the formation of $KrF^+Sb_2F_{11}^-$. On the basis of theoretical calculations[395] salts with the N_2F^+ cation can be regarded as potential oxidants for bonding ^{85}Kr.

Hence the problem of the chemical removal of radioactive xenon and krypton is closely connected with the fluoro-oxidising properties of the compounds of these elements. Naturally, use of the compounds of the noble gases as fluoro-oxidants is of independent interest. Table 6 gives the values of ΔG_{298} (ΔH_{298}) of the reactions of certain inorganic fluoro-oxidants with halogen fluorides, uranium tetrafluoride, nitrogen compounds, and radon. Comparison of the calculated and known experimental results suggests that the reactivity of the fluoro-oxidants correlates with their dissociation energies ($EF_n - EF_{n-} + 2F$) and on this basis the fluoro-oxidants can be arranged in the following series:

$$KrF_2 > O_2F_2 > RuF_6 > F_2 \approx N_2F_2 > XeF_6 > ClF_5 \approx XeF_4 > XeF_2.$$

Complexes of inorganic fluorides, the fluoro-oxidising ability of which is somewhat greater than that of the initial compounds, can also be regarded as potential fluoro-oxidants.

The noble gas fluorides and oxides of the noble gases are powerful oxidants in aqueous solutions of acids and bases. The redox potentials of the xenon compounds[3] are given below:

$$\begin{array}{ll} \text{acid} & Xe \xrightarrow{2{,}12\,V} XeO_{3(aq)} \xrightarrow{2.36\,V} H_4XeO_6 \\ & \quad \big\downarrow 2{,}36\,V\,(2{,}64) \\ & \quad XeF_{2(aq)} \\ \text{base} & Xe \xrightarrow{1.26\,V} HXeO_4^- \xrightarrow{0.95\,V} HXeO_6^{3-}. \end{array}$$

The oxidising ability of these compounds is not less than that of ozone. XeO_3 can also find a use as an effective oxidant in organic solvents[11].

The use of labelled xenon compounds is of importance for medical-biological investigations. Rapid methods for making periodates and perbromates labelled with short-lived isotopes[391–321] can be successfully developed on the basis of XeF_2. Methods of isolating ^{125}I without a carrier have been developed[316]. In view of their involatility, radon compounds can find a use in radiation therapy instead of gaseous radon[1].

The possibility of using XeF_2 and XeF_4 as photolytic sources of atomic fluorine for $F + H_2$ chemical lasers has been examined[399,400]. The use of xenon fluorides as initiators of polymerisations and in gas-filled incandescent lamps is known (cf. Jha[5]).

The study of the possibility of using noble gas compounds for practical purposes has only just begun, but already there is no doubt about the future possibilities of these compounds.

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The Electronic Structure of Conjugated Systems in Terms of the Pariser-Parr-Pole Approximation

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The potentialities of the π-electron approximation for the description of the electronic structures of conjugated molecules are analysed and two modern schemes for the parametrisation of the model Pariser-Parr-Pople π-electron Hamiltonian are considered. The application of this theory in the calculation of the properties of the ground state (bond lengths and angles, heats of formation, and dipole moments) and excited states (the energies of singlet and triplet excitations, oscillator strengths, and ionisation potentials) is also discussed.
The bibliography includes 80 references.

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I. INTRODUCTION

Molecules with Saturated and Unsaturated Bonds

The theory of the electronic structures of conjugated molecules constitutes the most extensively studied field in quantum chemistry. The reasons for this are in many respects related to the fact that the absorption spectra of such compounds occur in the optical and ultraviolet regions, which are very readily susceptible to experimental study, and also to the fact that the properties of such molecules are determined by a comparatively small proportion of their electrons. These electrons, called π-electrons, form a closed autonomous group, which impart to conjugated molecules all their specific properties.

The purely chemical definition of conjugated compounds is self-evident; they include molecules with multiple bonds and contain atoms with "unsaturated valences". They are characterised by enhanced reactivity, the transmission of influences through several atoms, and a marked influence of substituents on the geometrical structure (bond lengths and angles).

We shall attempt to specify more precisely from the standpoint of electronic structure the factors on which the differences between the properties of compounds with saturated and unsaturated bonds depend. For a qualitative interpretation of the cuases of these differences, one may confine the treatment to a one-electron computational scheme. Organic molecules are usually many-electron systems and therefore in the calculation it is necessary to take into account a large number of atomic orbitals (AO). As a result, in terms of the one-electron approximation there arise numerous energy levels, which are combined into groups (bands). The state of each band is characterised by some one property, for example symmetry and type of atomic orbitals, from which one-electron functions called molecular orbitals (MO) are made up.

In molecules with saturated bonds the bands are either completely filled with electrons (two electrons with opposite spins in each molecular orbital) or are vacant, while in molecules with unsaturated bonds there are bands partly filled with electrons. As a rule, each molecular orbital is a linear combination of the atomic orbitals of all the atoms in the molecule (the LCAO-MO approximation), i.e. there is delocalisation over the entire molecule. It is then found that the wave functions (MO) corresponding to the completely filled band can be subjected to a specific unitary transformation such that the new one-electron functions assume a distinct localised character. In particular, the new orbitals can be made largely localised at individual bonds in the molecule (with two electrons having opposite spins in each new orbital)[1].

In molecules with unsaturated bonds it is also possible to localise electrons at individual ("double") bonds when the so called π-electrons are considered. However, the interaction of two electrons of one such bond (proportional to the resonance bond integral) will be almost the same as the interaction between adjacent double bonds, because the resonance integrals for "single" and "double" bonds are almost the same. In molecules with saturated bonds the resonance integral is several times greater (in absolute magnitude) than the resonance integrals for electrons in adjacent bonds, so that in these compounds the steric localisation of electrons is accompanied by "energy" localisation: the interaction between bonds only slightly alters their energy. This implies that in molecules with saturated bonds the approximation of non-interacting bonds constitutes a satisfactory zeroth approximation, while in molecules with unsaturated bonds the introduction of functions localised at the bonds is as a rule ineffective and it is better to employ delocalised functions immediately.

In the language of the solid state theory systems with unfilled bands are metals. If the number of atoms in the saturated molecule is increased regularly, we obtain a system where the structure of the energy bands is analogous to the structure of the energy bands in a dielectric (for example, paraffins and diamond). On the other hand, an increase in the size of the π-electron system, for example on passing from condensed aromatic molecules

to graphite, leads to a system with an unfilled energy band, which is characteristic of metals. Admittedly one-dimensional π-electron systems (macro-molecules with conjugated bonds) are always semiconductors, but this is related to a specific phenomenon—the Mott "metal—dielectric" transition (described in detail in the review of Ovchinnikov et al.[2]).

Numerous studies on the theory of molecules with π-electrons have been published. This reflects the major role which compounds with conjugated bonds play in chemistry, biology, and chemical physics. Furthermore, the effectiveness of various methods for calculations on molecules of other classes is tested on conjugated systems. Molecules with conjugated bonds form a relatively small fraction of the total number of molecular systems and for this reason the theory of the structure of conjugated systems is of great heuristic value.

Significant advances have been made in the modern theory of conjugated systems in the qualitative and quantitative explanation of molecular properties.

Various characteristics of conjugated molecules are calculated with a relative error of about 10%, which reflects the comparatively high predictive power of the theory. Nevertheless, the errors, which in individual cases can exceed 10%, make it necessary to seek new ways for improving the theory. Owing to the enormous difficulties of the many-electron problem, the theory of conjugated systems is essentially semiempirical. Therefore various schemes and methods, differing in the procedures for the introduction of empirical parameters and in the degree of approximation of the methods of calculation are quite admissible in this theory and are indeed used. In all such studies a satisfactory agreement with experiment is as a rule achieved. Their analysis makes it possible to identify the most significant and general features of different computational schemes. It is found that the general and most important aspects of these schemes are very similar, which is an advantage of the theory as a whole.

Apart from studies where individual molecular properties are calculated, which is probably the main task of the theory, studies which justify the empirical and semi-empirical relations used to calculate specific molecular properties are very important for the development of the theory.

The aim of the present review is to outline the present state of the semiempirical theory of conjugated systems from the standpoint of general principles without going into the details of various computational methods. We are interested primarily in problems such as the internal logical self-consistency of the theory, the accuracy of the prediction of various experimental data and properties, and the possibility of improving the methods for the calculation of these data and properties.

II. THE π-ELECTRON APPROXIMATION FOR CONJUGATED SYSTEMS

Molecules with conjugated bonds are as a rule planar. The atoms supplying $2p_z$ electrons to the general π-electron systems have nuclei located in a single plane (the xy plane). The σ-bonds between the atoms of the molecule are also located in this plane and form the so-called σ-skeleton of the conjugated molecule. The electrons of the σ-skeleton occupy completely filled bands and therefore the corresponding one-electron functions may be localised at the interatomic bonds.

All the $2p_z$ orbitals are orthogonal with respect to all the one-electron functions of the σ-bonds. This orthogonality is the main reason why the electrons of the molecule can be divided into those of the σ-skeleton and π-electrons. Furthermore it is found that π-electrons are more weakly bound to the molecule than σ-electrons, so that almost all the observed properties of molecules with conjugated bonds are determined by π-electrons. These postulates form part of the basis of the theory of conjugated systems considered here, which explains molecular properties in terms of an explicit consideration of π-electrons alone. This is the so-called π-electron approximation.

We shall quote only one group of experimental data, which confirm directly the validity of the π-electron approximation. In the theory of conjugated hydrocarbons in the π-electron approximation there is a theorem that the optical spectra of the cation and anion derived from the same molecule are identical. This theorem is valid when full account is taken of the interaction between the electrons[3]. The experimental data presented in Fig. 1 demonstrate a striking similarity of the absorption spectra, which constitutes a direct confirmation of the theoretical conclusions.

Fig. 1 shows that certain absorption band maxima are displaced relative to one another by about 10% of the transition energies. We believe that these values demonstrate directly the limit of the accuracy with which it is possible to carry out calculations in terms of the modern theory employing the π-electron approximation. Examination of π-electrons alone when considering molecular properties greatly facilitates the theoretical analysis, since the number of π-electrons is several times smaller than the total number of electrons in the molecule. The presence of other electrons in the molecule (the electrons of the σ-skeleton) is taken into account implicitly. It alters the π-electron interaction, which is described by an effective model Hamiltonian. The parameters of this Hamiltonian depend on the properties of the σ-skeleton, i.e. on the σ-electrons.

For a quantum-mechanical description of a π-electron system, it is natural to employ the set of the atomic $2p_z$ functions as the basis functions. These $2p_z$ functions are non-orthogonal, which leads to considerable technical difficulties in calculations. Therefore it is natural to construct from the $2p_z$ functions an orthogonal basis set $\varphi_p(r)$ using the linear transformation

$$\varphi_p(r) = \sum_{i=1}^{M} U_{pi}\, 2p_{z_i}(r) \quad (p = 1, 2, \ldots M),$$

where M is the number of $2p_z$ functions or the dimension of the new basis set of the functions $\varphi_p(\bar{r})$. Löwdin[5] discovered the transformation U_{pi}, in which each of the functions $\varphi_p(r)$ consists largely of $2p_z$ functions of the atom p and contains only a slight admixture of the $2p_z$ functions of other atoms. Thus the functions $\varphi_p(r)$ are not only orthogonal (and normalised) but are also localised at the atoms. The slight delocalisation of these functions leads to effects associated with the mutual influence of the atoms.

We shall consider in greater detail the transition to an orthogonalised basis† set. This is done most naturally

† The idea of the treatment described below was communicated to the authors by M. V. Bazilevskii.

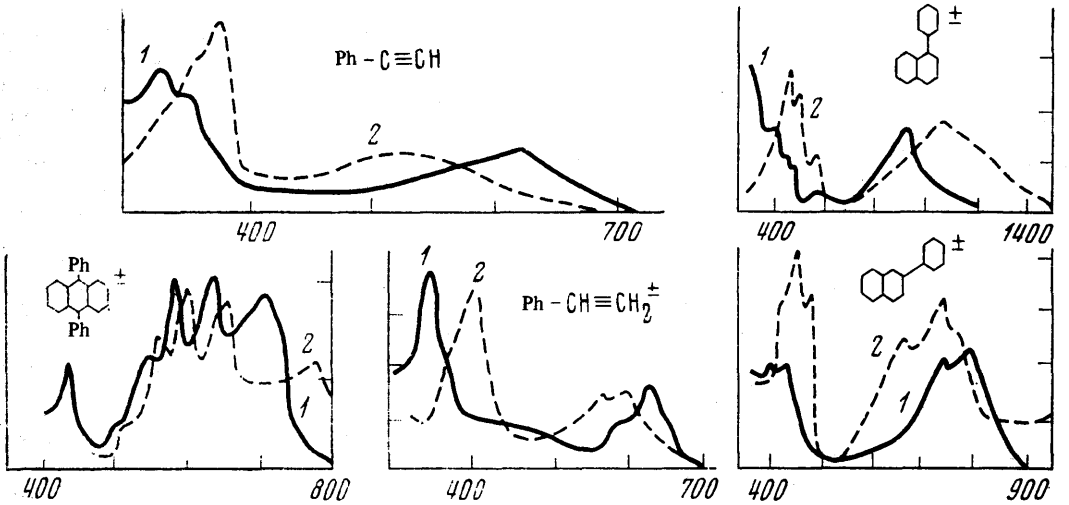


Figure 1. Experimental absorption spectra of the anions (curves *1*) and cations (curves *2*) of certain conjugated hydrocarbons[4].

by solving the standard quantum-chemical eigenvalue problem:

$$\hat{H}\psi = e\psi,$$

where $\hat{H}$ is a Hamiltonian or Fockian and ψ is the row-matrix of the molecular orbitals $\{\psi_1, \psi_2, \ldots\}$, which can be expressed in terms of the non-orthogonal atomic orbitals χ_i specified by the row-matrix $\{\chi_1, \chi_2, \ldots\}$ and the required coefficient matrix C (the LCAO-MO approximation):

$$\psi = \chi C, \quad \psi_l = \sum_{k=1}^{M} \chi_k c_{kl},$$

where c_{ki} are the elements of the matrix C.

We now introduce the overlap integral matrix

$$\chi^{+}\chi = \begin{bmatrix} \chi_1^* \\ \chi_2^* \\ \vdots \end{bmatrix} (\chi_1, \chi_2 \ldots) = S.$$

The row- and column-matrices are multiplied in accordance with the usual rules of matrix multiplication and integration with respect to coordinates is carried out; the asterisk (*) denotes a complex conjugate. The elements of the matrix S, for example, are of the form

$$S_{ij} = \int \chi_i^*(\mathbf{r})\chi_j(\mathbf{r})\,d\mathbf{r}.$$

We now reformulate our equation for eigenvalues as follows:

$$\hat{H}\chi C = \chi C e,$$

the left-hand side of the equation is multiplied by χ^{+}, and the matrix equation

$$HC = SCe$$

is obtained. Here $\chi^{+}\hat{H}\chi$ is the matrix $\hat{H}$ in the non-orthogonal basis set. The solution of the last matrix equation constitutes the familiar problem of double diagonalisation (of the matrices H and S). It would appear that, by multiplying the left-hand side of the equation by S^{-1} and obtaining thereby the equation

$$(S^{-1}H)C = Ce,$$

we reduce the problem to the diagonalisation of a single matrix $S^{-1}H$. However, this matrix is generally speaking asymmetric‡: its transposition (designated by the symbol ~)

$$\widetilde{(S^{-1}H)} = \tilde{H}\tilde{S}^{-1} = H\,S^{-1}$$

yields another matrix, namely

$$H\,S^{-1} \neq S^{-1}H.$$

At the same time it is known that the diagonalisation of an asymmetric matrix is difficult and requires special computer programs, which are difficult to devise.

Therefore the double diagonalisation problem will be solved in a different way. We reformulate our matrix equation as follows:

$$HS^{-1/2}S^{1/2}C = S^{1/2}S^{1/2}Ce,$$

multiply its left-hand side by $S^{-1/2}$, and obtain the equation

$$\bar{H}\cdot\bar{C} = \bar{C}e,$$

where $\bar{C} = S^{1/2}C$ and $\bar{H} = S^{-1/2}HS^{-1/2}$. The matrix $\bar{H}$ is symmetrical and therefore its diagonalisation is carried out with the aid of standard programs.

In order to obtain $\bar{H}$, it is necessary to calculate first the matrix $S^{-1/2}$. In qualitative studies one employs the method of expansion with respect to the non-diagonal part of S:

$$S = I + S',$$

where I is a unit matrix and S' the non-diagonal part of S.

---

‡ In all subsequent treatment it is assumed that all the atomic orbitals are real and therefore the matrices S and H are symmetrical and real.

Then

$$S^{-1/2} = (I + S')^{-1/2} = I - \frac{1}{2}S' + \frac{3}{8}S'S' - \ldots .$$

In computer calculations it is necessary to proceed in a different way. Initially S is diagonalised with the aid of a standard program, which yields S_{diag} and the transformation matrix $V(\tilde{V} = V^{-1})$:

$$S_{diag} = V^{-1}SV.$$

Suppose that S_{diag} is of the form

$$S_{diag} = \begin{pmatrix} a & & 0 \\ & b & \\ & & f \\ 0 & & & \ddots \end{pmatrix}.$$

Then it is easy to show that (a, b, f, ... are positive numbers)

$$S_{diag}^{1/2} = \begin{pmatrix} \sqrt{a} & & & 0 \\ & \sqrt{b} & & \\ & & \sqrt{f} & \\ 0 & & & \ddots \end{pmatrix}, \quad S_{diag}^{-1/2} = \begin{pmatrix} \frac{1}{\sqrt{a}} & & & 0 \\ & \frac{1}{\sqrt{b}} & & \\ & & \frac{1}{\sqrt{f}} & \\ 0 & & & \ddots \end{pmatrix}.$$

After calculating $S^{-1/2}$ in terms of the diagonal representation, we return to the non-diagonal representation with the aid of the matrix V and obtain the required expression for $S^{-1/2}$:

$$S^{-1/2} = VS_{diag}^{-1/2}V^{-1}.$$

In the diagonalisation of the matrix $\bar{H}$ we also find the coefficient matrix $\bar{C} = S^{1/2}C$. Hence we obtain $C = S^{-1/2}\bar{C}$.

We now express the wave function ψ in terms of $\bar{C}$:

$$\psi = \chi C = \chi S^{-1/2}S^{1/2}C = \lambda\bar{C},$$

where

$$\lambda = \chi S^{-1/2},$$

so that we arrive at a new orthogonalised basis set $\lambda = \{\lambda_1, \lambda_2, \ldots\}$. In fact

$$\lambda^+\lambda = S^{-1/2}\chi^+\chi S^{-1/2} = S^{-1/2}SS^{-1/2} = I.$$

We may also note that $\bar{H}$ is the matrix of the operator $\hat{H}$ in the basis set λ: $\bar{H} = \lambda^+H\lambda$. The functions λ_p are our required basis functions $\varphi_p(\mathbf{r})$ and the functions χ_i are the initial $2p_z$ functions.

1. The Effective Model Hamiltonian for π-electrons

The effective π-electron Hamiltonian can be formulated in terms of secondary quantisation:

$$H = \sum_{p,q,\eta} H_{pq}c_{p\eta}^+c_{q\eta} + \sum_{pqrt}\sum_{\rho\eta} \langle pq\,|\,rt\rangle c_{p\eta}^+c_{q\eta}c_{r\rho}^+c_{t\rho}. \qquad (1)$$

Any π-electron can be located in one of the basis states $\varphi_p(\mathbf{r})$ with projection of the spin η on the specified axis ($\eta = \pm 1/2$). The operators $c_{p\eta}^+(c_{p\eta})$ are called the operators of the generation (annihilation) of the π-electron in this state. These operators satisfy the transposition relations

$$c_{p\eta}^+c_{p'\eta'} + c_{p'\eta'}c_{p\eta}^+ = \delta_{pp'}\delta_{\eta\eta'},$$

$$c_{p\eta}c_{p'\eta'} + c_{p'\eta'}c_{p\eta} = c_{p\eta}^+c_{p'\eta'}^+ + c_{p'\eta'}^+c_{p\eta}^+ = 0.$$

The secondary quantisation representation makes it possible to avoid cumbersome steps involving Slater determinants made up of spin-orbitals. The Slater determinants, which ensure that the Pauli principle is observed for the wavefunction in terms of the coordinate representation are replaced by products of the operators $c_{p\eta}^+$, which operate in a special space. The Pauli principle (the antisymmetry of the wavefunction on transposition of two particles) holds automatically by virtue of the transposition relations for the operators $c_{p\eta}^+$ and $c_{p\eta}$.

We shall now consider briefly the essential feature of secondary quantisation in order to lift the "veil of incomprehensibility" from this concept, which is increasingly used in the literature on quantum chemistry. Secondary quantisation is introduced in quantum chemistry essentially when a one-electron wavefunction (molecular orbital) is expanded in terms of a basis set made up of atomic functions (the LCAO-MO approximation):

$$\psi(\mathbf{r}) = \sum_p c_p\varphi_p(\mathbf{r}).$$

One may say that the quantum-mechanical state $\psi(\mathbf{r})$ is yet again ("secondarily") "quantised" with respect to the states $\varphi_p(\mathbf{r})$. It is then possible to employ a matrix representation [all the operators are matrices with respect to the basis set $\varphi_p(\mathbf{r})$ with the wave functions expressed in the form of Slater determinants made up of the spin-orbitals $\varphi_p(\mathbf{r})\eta$] ($\eta$ is a spin function) or one can employ the secondary quantisation "representation" introduced by V. A. Fok (W. A. Fock), in which one again employs matrices made up of operators with respect to the basis set $\varphi_p(\mathbf{r})$ in which the expansion coefficients c_p are now regarded as operators, This makes it possible to employ simpler computational procedures without Slater determinants.

In the present review the secondary quantisation representation will be rarely used, mainly for the formulation of the Hamiltonian and other operators. Attention will be concentrated on the analysis of the matrix elements which are usually parametrised in semiempirical theories and which should be calculated, in accordance with general rules, in terms of the orthogonalised basis set $\varphi_p(\mathbf{r})$.

The parameters of Hamiltonian (1)

$$H_{pq} \text{ and } \langle pq\,|\,rt\rangle \qquad (2)$$

correspond to the one-particle and two-particle terms in the π-electron Hamiltonian in the coordinate representation

$$H_\pi = \sum_i \hat{H}(\mathbf{r}_i) + \sum_{i<j}\frac{1}{|\mathbf{r}_i - \mathbf{r}_j|}. \qquad (3)$$

Here $\hat{H}(\mathbf{r}_i)$ is the one-particle operator of the ith λ-electron, describing its kinetic energy and attraction to the σ-skeleton. The second term in Eqn. (3) is the two-particle operator of the Coulombic repulsion of π-electrons. The hamiltonians (1) and (3) are formally linked by relations of the type

$$H_{pq} = \int \varphi_p^*(\mathbf{r}_i)\,\hat{H}(\mathbf{r}_i)\,\varphi_q(\mathbf{r}_i)\,d\mathbf{r}_i,$$

$$\langle pq\,|\,rt\rangle = \iint \frac{\varphi_p^*(\mathbf{r}_1)\,\varphi_q(\mathbf{r}_1)\,\varphi_r^*(\mathbf{r}_2)\,\varphi_t(\mathbf{r}_2)}{|\mathbf{r}_1 - \mathbf{r}_2|}\,d\mathbf{r}_1\,d\mathbf{r}_2. \qquad (4)$$

These relations usually serve as a basis for the determination of the parameters (2).

As a result of the slight delocalisation of the functions $\varphi_p(\mathbf{r})$, the parameters (2) or (4) depend not only on the atomic indices indicated in formulae (2) or (4) but also on the indices for other atoms. Analysis of Eqns. (4) carried out by Fischer-Hjalmars[6] made it possible to

localise in the parameters (2) and (4) the contributions due to atoms with other indices, for example indices differing from p, q, r, and t. Such separation makes it possible to develop ideas on the mechanism of the mutual influence of atoms and to understand the changes in parameters on passing from one molecule to another. These ideas are important because the correct values of the parameters (2) cannot as yet be calculated theoretically. These parameters are determined from a comparison with experimental data and Eqns. (4) make it possible to reduce to a minimum the elements of arbitrary choice in the selection of the empirical values of the parameters.

The fundamental formulae relating the matrix elements in the orthogonal (φ_p) and non-orthogonal, atomic (χ_p) basis sets are obtained with the aid of the relation

$$\varphi = \chi S^{-1/2},$$

with which we are already familiar, and the series expansion of the matrix $S^{-1/2}$, which was also discussed above. Namely it was found that

$$H_{pq}^{(\varphi)} = H_{pq}^{(\chi)} + O(S^3) \ (p \text{ and } q \text{ are adjacent}),$$

$$H_{pq}^{(\varphi)} = O(S^3) \ (p \text{ and } q \text{ are not adjacent}),$$

$$H_{pp}^{(\varphi)} = H_{pp}^{(\chi)} - \sum_q S_{pq} H_{pq}^{(\chi)} + O(S^3),$$

(q are adjacent to p),

$$\langle pq \mid rs \rangle^{(\varphi)} = \delta_{pq}\delta_{rs} \langle pp \mid rr \rangle^{(\chi)} + O(S^3) .$$

In these formulae the left-hand side represents the matrix element in the basis set φ_p and the right-hand side represents the element in the basis set χ_p; the symbol $O(S^3)$ denotes terms of the order of S_{ij}^3 or a higher power of S_{ij}—the overlap integral for neighbouring atoms. These formulae are used below in a discussion of the difference between spectroscopic and thermochemical parameters (Section III, 2) and partly in devising one of the parametrisation schemes (Section IV, 1). The diagonal matrix elements $H_{pp}^{(\varphi)}$ and $H_{pp}^{(\chi)}$ differ by terms of the order of S_{pq}^2 (q are neighbours of p). These differences have been shown by M. V. Bazilevskii (see Section III, 2) to be important in the calculation of heats of formation and in the construction of potential energy surfaces.

2. The Pariser–Parr–Pople (PPP) Approximation and Method

Goeppert-Mayer and Sklar[7] calculated all the parameters (4) for benzene with the aid of Slater $2p_z$ functions and refined the concept of the σ-skeleton, having proposed special formulae for the parameters H_{pq}. As a result, a qualitatively correct description of the absorption spectrum of benzene was obtained in terms of the self-consistent field (SCF) approximation[7]. This was a major success of the theory and indicated the validity of the π-electron approximation.

Subsequently Pariser, Parr, and Pople[8] proposed other rules for the determination of the parameters (2) using partly the approximation of Geoppert-Mayer and Sklar for the σ-skeleton. The most significant feature in the new rules was the rejection of formulae of type (4) for the calculation of the parameters (2), which were now determined empirically. Next the approximation of zero differential overlapping (ZDO) was introduced which greatly reduced the number of non-zero parameters in the Hamiltonian. In the ZDO approximation $H_{pq} \neq 0$ only for neighbouring p and q or for $p = q$; $H_{pq} = 0$ for the other p and q and $\langle pq \mid rt \rangle = \langle pp \mid tt \rangle \delta_{pq}\delta_{rt}$. For the orthogonal functions $\varphi_p(r)$ the ZDO approximation is reasonable, since all the rejected integrals are indeed small.

In calculations on the ground state, the LCAO-MO SCF approximation was used[9]. For example, the ground state of benzene was described by a single Slater determinant of molecular spin-orbitals or by a single configuration. Pariser et al.[8] showed that in the description of excited states of conjugated molecules it is necessary to employ a superposition of all singly excited configurations and not just one excited configuration, as in the method of Goeppert-Mayer and Sklar. Because of the high symmetry of benzene (D_{6h}), it was possible to obtain simple formulae for the energies of the first electronic transitions in terms of combinations of the parameters $H_{p,\,p+1} = \beta$§ and $\langle pp \mid qq \rangle = \gamma_{pq}$. These energies are given by formulae of the type[8]

$$\begin{aligned}
\Delta E(^1B_{2u}) &= -2\beta + \tfrac{1}{6}(\gamma_{12} - 3\gamma_{13} + 2\gamma_{14}),\\
\Delta E(^1B_{1u}) &= -2\beta + \tfrac{1}{6}(2\gamma_{11} - 5\gamma_{12} + 7\gamma_{13} - 4\gamma_{14}),\\
\Delta E(^1E_{1u}) &= -2\beta + \tfrac{1}{6}(\gamma_{11} + 4\gamma_{12} - 4\gamma_{13} - \gamma_{14}),\\
\Delta E(^3B_{1u}) &= -2\beta + \tfrac{1}{6}(-2\gamma_{11} + 3\gamma_{12} - \gamma_{13}) \text{ etc.}
\end{aligned} \qquad (5)$$

Simple formulae were also obtained for the energies of ethylene. Comparison of these energies with experimental data (absorption spectra) led to numerical values of the parameters for these molecules and to the formulation of a system of rules for the determination of the parameters of other molecules, including molecules with heteroatoms[8]. The entire system of concepts concerning the parametrisation of the π-electron Hamiltonian and the degree of approximation in calculations on the states of the system (one configuration for the ground state and superposition of singly excited configurations for the excited state) has been called the "Pariser–Parr–Pople approximation" (the PPP approximation or method).

In most cases the theory of the electronic structure of conjugated systems in terms of the π-electron approximation uses the PPP Hamiltonian

$$H = \sum_{p,q,\eta} h_{pq} c_{p\eta}^{+} c_{q\eta} + \sum_{p,q} \sum_{\eta,\rho} \gamma_{pq} c_{p\eta}^{+} c_{p\eta} c_{q\rho}^{+} c_{q\rho} . \qquad (6)$$

The methods for the calculation of molecular properties using Hamiltonian (6) can differ from the PPP method by the procedures employed in the estimation of the parameters. In calculations on conjugated systems one uses nowadays methods which differ in the extent to which account is taken of the π-electron interaction, from the Hückel approximation in which all the parameters $\gamma_{pq} = 0$ up to different versions of the many-configuration approximation using several or all possible configurations.

3. The Information Contained in the Effective Parameters of the Model π-electron Hamiltonian

The PPP Hamiltonian (6) is a model or effective π-electron Hamiltonian. Having postulated that all the properties of a conjugated molecule are described by π-electrons alone, we have greatly simplified the problem of the calculation of molecular properties. If all the electrons in the molecule were considered, we would have found that σ-electrons and atomic orbitals other than those of the $2p_z$ type have a relatively small influence on the

§ The $2p_z$ atomic orbitals are numbered consecutively around the ring formed by carbon atoms.

properties of the π-electron system. Nevertheless these electrons and orbitals make a finite contribution to the observed properties. Therefore the semiempirical theory can yield the observed values when π-electrons alone are considered explicitly only in the case where the parameters of Hamiltonian (6) take into account the neglected electrons and states.

As a result the parameters of the Hamiltonian differ somewhat from the values calculated by Eqns. (4). These differences can be reduced to a minimum by a special choice of the functions $\varphi_p(\mathbf{r})$. However, some differences always remain. This is a consequence (or manifestation) of many-electron correlations.

The contribution of σ-electrons to the π-electron Hamiltonian has been examined by Fischer[10] for a simple model of a conjugated molecule. The effect of the neglected electrons and atomic orbitals on the effective Hamiltonian has been considered by Freed[11]. The problem of the calculation of the parameters of the effective π-electron Hamiltonian by more accurate formulae than Eqns. (4) (taking into account the effects of electronic correlation and the influence of the σ-skeleton), which was raised in these investigations[10,11], remains very complex and has still not been solved. However, it is known that equations of type (4), based on physical intuition, yield in the main the correct idea about the parameters of the effective Hamiltonian [when a successful choice of the functions $\varphi_p(\mathbf{r})$] is made. Since these parameters can be determined from a comparison with experiment, it is always possible to estimate the accuracy of formulae of type (4). Analyses of this kind have been carried out[12,13].

The unreal nature of the π-electron Hamiltonian is enhanced by the fact that, in terms of the ZDO approximation, a number of parameters are neglected. There are simplified versions of the PPP method with short-range action of π-electrons[14,15], in which only the parameters γ_{pp} and $\gamma_{pp\pm1}$ remain (for electrons at the same atom and at adjacent atoms) (see also Ovchinnikov[16]). In this case it is hardly possible to calculate these parameters, which are determined only by an empirical procedure.

Yet another aspect of the unreal nature of the Hamiltonian is associated with the degree of its approximation used in the calculation of the observed properties. If the electronic transition energies are calculated in terms of the PPP approximation, then one set of the Hamiltonian parameters must be used to recover the experimental values. If a calculation involving a larger number of configurations than in the PPP method is carried out, then the parameters which reproduce the experimental values differ from those of the first set. Clearly it is impossible to take into account these differences and to estimate the changes in the parameters. Nevertheless this is difficult to tolerate and for this reason several schemes have been proposed for the calculation of the parameters (mainly for the PPP method), which are partly based on equations of type (4); to some extent simple formulae for the interpolation of empirical values of the parameters are also employed. Parameters which correctly reproduce the experimental electronic transition energies, ionisation potentials, etc. are obtained as a result. This approach is characteristic of a semiempirical theory, in contrast to *ab initio* calculations based solely on formulae of type (4).

Yet another aspect of the problem of the separation of σ- and π-electrons and the derivation of the model Hamiltonian has been examined from the standpoint of summetry in terms of the SCF approximation for σ- and π-electrons[17]. It was found that the solutions (molecular orbitals) can be divided into symmetrical and antisymmetrical with respect to the reflection operation in the molecular plane. The SCF equations in terms of the LCAO-MO approximation (the Roothaan equations[9]) are divided into two systems of equations: for σ-electrons (symmetric solutions) and for π-electrons (antisymmetric solutions). These systems of equations are related (by the Coulombic interaction of σ- and π-electrons) and must be solved together. If only π-electrons are considered, the effect of σ-electrons may be taken into account by choosing effective parameters[17].

Calculations of this kind are made at present for specific molecules (the LCAO-MO SCF approximation for all valence σ-electrons and π-electrons). In calculations of this kind the effect of the σ-skeleton on the π-electron system and the nature of different degrees of the σ-electron approximation are elucidated[18,19]. So far such calculations are fairly crude because a parametrisation scheme has not been developed. This applies also to *ab initio* calculations. The latter are at present performed using equations of type (4) and specified functions $\varphi_p(\mathbf{r})$. In this sense such calculations resemble semiempirical calculations, since the functions $\varphi_p(\mathbf{r})$ are specified with the aid of certain constants. So far the *ab initio* calculations are crude and have a low predictive power. One may hope that, by varying the initial functions $\varphi_p(\mathbf{r})$, it will be possible to improve their accuracy. Moreover, we believe that in the distant future the *ab initio* calculations will reach the accuracy of the semiempirical theory.

The conclusions drawn from studies where σ- and π-electrons are considered jointly in terms of the SCF approximation are so far only qualitative. An improvement of the accuracy of such calculations will make it possible, in principle, to correct the π-electron approximation from the outside, from the standpoint of a more complete calculation.

In the present review we shall not consider the qualitative conclusions of modern *ab initio* calculations, since this would significantly increase its size. Moreover, we believe that the results of these calculations merit a separate and more detailed discussion. Much attention will be devoted to problems of the interaction of π-electrons with the σ-skeleton in the authors' next review "Adjustment of the Methods of Calculation and Semiempirical Parameters for Consistency in the Theory of Molecules with Conjugated Bonds", where an attempt will be made to keep the treatment within the framework of the π-electron approximation. Such tactics in relation to *ab initio* calculations are also dictated by the fact that so far we can only indicate the causes of a number of difficulties in the semiempirical theory, but complete recipes for overcoming the difficulties of the π-electron theory cannot as yet be proposed on the basis of modern *ab initio* calculations. The point is that such calculations for molecules are carried out in terms of a limited atomic orbital basis set (filled atomic orbitals are as a rule employed as the basis set). Correlation contributions, which, for example, have been found to be fairly significant in atoms (this was demonstrated in atomic calculations with a greatly extended basis set) are thereby neglected. On the other hand, in semiempirical calculations using a limited atomic orbital basis set these correlation contributions are largely included in the parameters. Therefore the role of modern *ab initio* calculations, carried out in terms of a restricted atomic orbital basis set, in proving the validity of the semiempirical molecular theory is so far limited.

III. THE PROPERTIES OF THE GROUND STATE OF CONJUGATED MOLECULES

1. The Geometrical Structure of Molecules (Bond Lengths and Angles)

An important characteristic of a conjugated molecule is its geometrical structure, bond lengths, and bond angles. The "bond length–bond order formula"[20]

$$R_{\mu\nu} = R_0 - bP_{\mu\nu} \qquad (7)$$

is usually employed to calculate bond lengths. Here $R_{\mu\nu}$ is the length of the $\mu\nu$ bond, $P_{\mu\nu}$ the π-electron order of the $\mu\nu$ bond, and R_0 and b are constants determined from a comparison with experiment. It has been found that Eqn. (7) is not an independent empirical relation, since its constants are expressed in terms of parameters describing the electronic structure of the molecule[21].

The presence of π-electrons leads to a slight change in bond lengths (by $\delta R_{\mu\nu}$) and angles (by $\delta\varphi_l$) compared with the lengths $R^0_{\mu\nu}$ and angles φ^0_l which would be observed in a hypothetical molecule without π-electrons. If the molecule does not contain heteroatoms, then usually all the $\varphi^0_l = 120°$ and all the $R^0_{\mu\nu} = R_0$ (for example, in benzene). We thus begin with the hypothesis of an ideal structure of the σ-skeleton and assume that all the distortions of this ideal structure are due to π-electrons. The σ-skeleton is regarded as elastic (characterised by force constants) and the total energy E is equal to the sum of the energies of the σ-skeleton (E_σ) and of the π-electrons (E_π): $E = E_\sigma + E_\pi$.

In terms of the Hückel approximation in the molecular orbital method, the molecular energy of alternant hydrocarbons is[21]

$$E = E^0_\sigma + \underset{(\text{w.r.t.atoms})}{\sum_n \alpha_n} + 2\underset{(\text{w.r.t.bonds})}{\sum_l \beta_l P_l} + \underset{(\text{w.r.t.bonds})}{\sum_l \frac{k_{1l}\delta R_l^2}{2}} + \underset{(\text{w.r.t.angles})}{\sum_l \frac{k_{2l}R_0^2\delta\varphi_l^2}{2}}, \qquad (8)$$

where P_l is the bond order between adjacent atoms and β_l is the corresponding resonance integral; the last two terms in Eqn. (8) are due to the distortion of the initial σ-skeleton having the energy E^0_σ, k_{1l} and k_{2l} being the force constants for the lengths R_l and angles φ_l respectively.

The resonance integral β_l can be conveniently represented by an expansion in terms of the deviation δR_l from the equilibrium length R_0 in the ideal σ-skeleton:

$$\beta_l = \beta^0_l + \beta'_l\delta R_l + \beta''_l\frac{\delta R_l^2}{2}, \qquad (9)$$

where β'_l and β''_l are the first and second derivatives of $\beta_l(R)$ with respect to the distance R calculated at the point $R = R_0$.

By varying the total energy E with respect to independent δR_l and $\delta\varphi_l$, we obtain the values of δR_l and $\delta\varphi_l$ for which this energy is a minimum. The number of independent δR_l and $\delta\varphi_l$ for a planar molecule with N conjugated atoms is $2N - 3$. The observed values of δR_l and $\delta\varphi_l$ depend in a complex manner on the bond orders. On substituting these expressions in the formula for E [(Eqn. 8)], we obtain the total energy E as a function of the coefficients of the molecular orbitals c^k_n. By varying E with respect to c^{k*}_n, we obtain non-linear equations for c^k_n (the bond orders P_l are quadratic functions of c^k_n and E is a non-linear function of P_l). These non-linear equations are solved for c^k_n with the aid of a procedure whereby adjustment for self-consistency is made.

If the molecule does not contain rings, all the $\delta\varphi_l$ are independent and variation with respect to them yields $\delta\varphi_l = 0$ (the angles are not distorted). By varying with respect to δR_l, we obtain:

$$\delta R_l = -\frac{2\beta'_l}{k_{1l} + 2\beta''_l P_l}P_l. \qquad (10)$$

The equation for c^k_n is

$$0 = 2(\alpha_n - E^k)c^k_n + 2\frac{\partial}{\partial c^{k*}_n}\left(\sum_l \beta_l P_l\right) + \frac{\partial}{\partial c^{k*}_n}\left(\sum_l \frac{k_{1l}\delta R_l^2}{2}\right).$$

If $\beta'^2_l/k_{1l}|\beta_l| \ll 1$, the terms non-linear in c^k_n in this equation may be neglected and the bond orders P_l can be determined from the equation with undistorted bond lengths. As a result, we arrive at a "bond length–bond order" formula[21]:

$$R_l = R_0 - \frac{2\beta'_l}{k_{1l} + 2\beta''_l P_l}P_l. \qquad (11)$$

If the distortions of the angles and terms of the order of P^2_l are neglected, the formula is found to apply also to molecules containing rings.

To determine the angles, terms corresponding to the interaction of π-electrons at non-adjacent atoms must be included in the formula for the energy. We may note that a successful albeit unique example of the calculation of angles by the above general method has been achieved for the naphthalene molecule[21]. It was found that approximately half the contribution to the angular distortion $\delta\varphi_l$ comes from the bond length distortion δR_l.

In the calculation of the π-electron energy of the molecule one can employ methods which include the interaction of the electrons. In terms of the PPP approximation, it is easy to show that the "bond length–bond order" formula is

$$R_{\mu\nu} = R_0 - \frac{2\beta'_{\mu\nu}P_{\mu\nu} + \gamma'_{\mu\nu}\left[(P_{\mu\mu} - N_\mu)(P_{\nu\nu} - N_\nu) - \frac{P^2_{\mu\nu}}{2}\right]}{\kappa_{1\mu\nu} + 2\beta''_{\mu\nu}P_{\mu\nu} + (\text{terms with } \gamma''_{\mu\nu})}, \qquad (12)$$

where N_μ and N_ν are the numbers of electrons introduced by the atoms μ and ν to the overall π-electron system and $\gamma'_{\mu\nu}$ and $\gamma''_{\mu\nu}$ are derivatives of $\gamma_{\mu\nu}(R)$ with respect to R at the point $R = R_0$. In alternant hydrocarbons $N_\mu = N_\nu = P_{\mu\mu} = P_{\nu\nu} = 1$. $P_{\mu\mu} - N_\mu$ is equal to the charge of the atom μ. Comparison of Eqn. (12) with Eqn. (11) of the Hückel method for alternant hydrocarbons shows that the entire difference has been reduced to the following change of parameters:

$$\beta_{\mu\nu}(\text{Hückel MO method}) \to \beta_{\mu\nu}(\text{PPP method}) - \tfrac{1}{4}\gamma_{\mu\nu}P_{\mu\nu}.$$

Thus the parameters in the formula for the bond length depend significantly on the parametrisation scheme for $\beta_{\mu\nu}$ and $\gamma_{\mu\nu}$.

The linear "bond length–bond order" relation [Eqn. (7)] usually describes satisfactorily the experimental bond lengths in conjugated molecules not only of hydrocarbons but also of compounds with the heteroatoms N, O, F, and S.[22,23] The average accuracy of the determination of bond lengths by Eqn. (7) is of the order of 0.01–0.02 Å (see, for example, Table 1). The causes of the individual discrepancies are the approximate nature of equations of type (7), the hypothesis that σ-bonds are additive, etc.

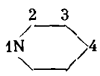
2. Heats of Formation of Conjugated Molecules

Another important characteristic of conjugated molecules is the heat of formation $-\Delta H$. The modern scheme for the calculation of this quantity was proposed by Dewar[22,23]. The formula

$$-\Delta H = n_H E_{CH} + \sum E^{\sigma}_{CC}(R) - E_{\pi} \qquad (13)$$

is used to calculate the heat of formation of a conjugated hydrocarbon. Its first term is the dissociation energy of all the C—H bonds (there are n_H such bonds in the molecule), the second term represents the dissociation energy of all the C—C σ-bonds, and the third term represents the π-electron energy with a minus sign. The usual hypothesis of the additivity of the energies of the σ-bonds and of σ- and π-energies was used here, as in Eqn. (8). The dissociation energy E_{CH} of C—H bonds is an empirical term. The C—C σ-bond energy $E^{\sigma}_{CC}(R)$ is described by a Morse function with empirical parameters. The π-electron energy E_{π} was calculated in terms of the LCAO-MO SCF approximation using the PPP Hamiltonian and $R_{\mu\nu}$, necessary for the calculation of $E^{\sigma}_{CC}(R_{\mu\nu})$, was evaluated with the aid of the empirical relation (7).

Table 1. The bond lengths in certain conjugated molecules[23].

Molecule	Bond	Bond length, Å	
		calc.	expt.
	12	1.333	1.334
	23	1.348	1.388
	12	1.338	1.340
	23	1.396	1.395
	34	1.397	1.395
	12	1.381	1.371
	23	1.347	1.354
	34	1.459	1.440

The parameters of the PPP Hamiltonian used by Dewar to calculate heats of formation[22,23] were approximately the same as in the calculation of absorption spectra. The resonance integral $\beta_{\mu\nu}$ was an exception. The values of $\beta_{\mu\nu}$ were determined by Dewar from the thermochemical conditions and exceeded by a factor of 1.3—1.4 the values used in the calculation of absorption spectra¶. This inconsistency of the parameters indicated a defect of the theory, although the agreement with experiments was very good[23] (Table 2).

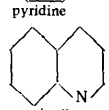
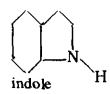
In Bazilevsky's studies[24,25] this theoretical difficulty was overcome. On the basis of the study by Fischer-Hjalmars[6], it was shown that it is possible to retain the spectroscopic values of $\beta_{\mu\nu}$, provided that in derivation of the model Hamiltonian all the terms which arise naturally on transformation from $2p_z$ functions to the orthogonal functions $\varphi_p(r)$ are retained. These additional terms, which are usually neglected†, make a new contribution to the total energy, which is[25]

$$\widetilde{\Delta E} = \sum K_{\mu\nu} S^2_{\mu\nu} + O(S^3),$$

where $K_{\mu\nu}$ are coefficients which depend on the molecule and $S_{\mu\nu}$ is the overlap integral of the $2p_z$ functions of the atoms μ and ν. The addition of $\widetilde{\Delta E}$ leads to the so called exchange repulsion of atoms and molecules. This exchange repulsion is well known, for example, in studies on the interaction of two helium atoms, non-bonded hydrogen atoms, etc., which was examined for the first time for non-polar conjugated systems by Bazilevsky, who proposed a simple formula for $\widetilde{\Delta E}$ containing a single empirical parameter[24], retaining $S_{\mu\nu}$ only for adjacent atoms μ and ν:

$$\widetilde{\Delta E} = \gamma \sum_{\substack{\mu\nu \\ \text{(adjacent)}}} S^2_{\mu\nu} \quad (\gamma > 0).$$

Table 2. The energies of formation of certain conjugated molecules[23].

Molecule	Energy of formation $-\Delta H$, eV	
	calc.	expt.
pyridine	51.87	51.79
 quinoline	85.322	85.18
pyrazine	46.272	46.44
pyridazine	45.741	45.59
 indole	78.438	78.06

The validity of this approximation for $\widetilde{\Delta E}$ was confirmed by the satisfactory agreement of the heats of formation with experiment (Table 3). This computational scheme can be improved by employing a more accurate formula for $\widetilde{\Delta E}$.[25]

As a result, the π-electron energy of the conjugated molecule becomes[24]

$$E_{\pi} = E_{\pi}\{\beta^{\text{spectr.}}\} + \gamma \sum_{\substack{\mu\nu \\ \text{(adjacent)}}} S^2_{\mu\nu}.$$

Here the first term is the π-electron energy calculated using spectroscopic values of the resonance integral $\beta^{\text{spectr.}}$. If $S_{\mu\nu}$ is calculated using Slater $2p_z$ functions,

$$\varphi_{2p_z}(r) = \frac{Z^{5/2}}{4\sqrt{2\pi}} r\cos\theta\, e^{-\frac{Zr}{2}} \quad (Z = 3.18), \qquad (14)$$

then γ = 8.7 eV.[24] This value of γ was determined by comparing $-\Delta H$ calculated by Eqn. (13) with the experimental value and depends both on the parameters of the σ-bond and on Z.

We may note that in calculations of absorption spectra there was no need for the additional exchange term $\widetilde{\Delta E}$, since it is the same for the ground and excited states (the changes in molecular geometry on excitation are usually small and are as a rule disregarded). However, this

¶ For the C—C bond length R = 1.4 Å, the spectroscopic value of the resonance integral is $\beta \simeq -2.4$ eV.

†These additional terms arise on passing to an orthogonal basis set using the formulae derived towards the end of Section II, 1.

additional term ΔE is significant in calculations on chemical reactions of conjugated systems, since terms proportional to $S^2_{\mu\nu}$ are significant in the energy of molecular interaction. Specifically exchange repulsion leads to a potential barrier and a positive activation energy for such reactions[25].

Table 3. The energies of formation of certain conjugated hydrocarbons calculated using a modified PPP method[24].

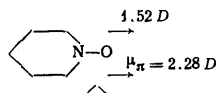
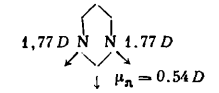
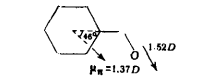
Molecule	Heat of formation $-\Delta H$, eV		Molecule	Heat of formation $-\Delta H$, eV	
	calc.	expt.		calc.	expt.
Ethylene	22.9	22.9	Phenanthrene	123.1	123.2
trans-Butadiene	41.6	41.6	Pyrene	137.4	137.5
Benzene	56.9	56.7	Naphthacene	155.7	156.0
Styrene	75.3	75.0	1,2-Benzanthracene	156.2	156.0
Naphthalene	90.0	89.9	Chrysene	156.5	156.5
Anthracene	122.6	122.5	Triphenylene	156.8	156.5

3. Dipole Moments

One of the difficult problems in quantum mechanics of molecules is the calculation of dipole moments, since such calculations require the knowledge of the wavefunction of all the electrons in the molecule. Brown and Coller[26] made a preliminary assessment of the many years of efforts to calculate the dipole moments of conjugated hydrocarbons containing N and O heteroatoms. It is suggested that σ- and π-electrons contribute to the overall dipole moment $\vec{\mu}$:

$$\vec{\mu} = \vec{\mu}_\sigma + \vec{\mu}_\pi.$$

Table 4. The dipole moments of certain conjugated hydrocarbon molecules with the N and O heteroatoms[26].

Molecule	Magnitude and directions of the σ- and π-contributions (μ_σ and μ_π) to the dipole moment	Overall dipole moment, D	
		calc.	expt.
Pyridine-*N*-oxide		3.8	4.24
Pyrimidine		2.32	2.0
Benzaldehyde		2.87	2.80

The component $\vec{\mu}_\pi$ is calculated from the distribution of π-electrons among the atoms in the molecule and the contribution to $\vec{\mu}_\sigma$ comes (by hypothesis) only from the lone electron pair localised in the sp^2 hybrid orbitals (belonging to the σ-skeleton) of the N and O atoms. These contributions of the lone electron pairs of the N and O atoms are respectively

$$\mu_N = 1.77\ D, \quad \mu_O = 1.52\ D.$$

The wavefunction χ_n of the sp^2 hybrid orbital of the lone pair is

$$\chi_n = \chi_{2s} + \theta\chi_{2p_\sigma}.$$

The contribution to $\vec{\mu}_\sigma$ is proportional to θ and in its calculation using Slater functions is given by[26]

$$\mu_n = 14.68\,\theta/Z\,(1+\theta^2)\,(D),$$

where Z is the effective Slater charge. Generally speaking, μ_n depends on the angles in the molecules (θ also depends strongly on these angles), but Brown and Coller[26] used for simplicity an estimate of μ_n from the sp^2 hybrid orbitals of neutral N and O atoms. This led to the values of μ_N and μ_O indicated above.

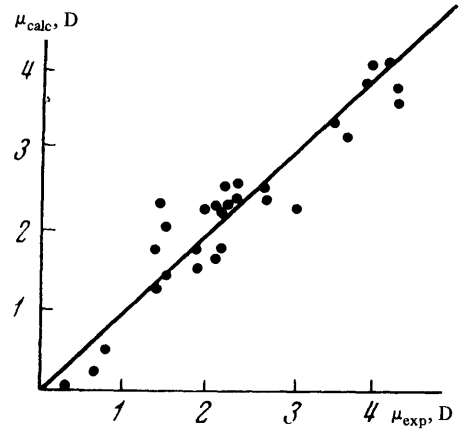


Figure 2. Correlation between the calculated (μ_{calc}) and experimental (μ_{exp}) dipole moments according to Brown and Coller[26].

To calculate $\vec{\mu}_\pi$, Brown and Coller[26] used a self-consistent method with a variable π-electronegativity. This method resembles that in Section IV, 2, but, in contrast to the latter, it does not take into account the redistribution of σ-charges in the molecule. This redistribution has an appreciable influence on the electronic excitation energies in molecules with heteroatoms (see Section IV, 2 below). However, Brown and Coller[26] neglected the contribution of σ-charges to the dipole moment.

The results of the calculation of $\vec{\mu}$ for certain molecules are presented in Table 4 together with experimental data. Fig. 2 illustrates the correlation between the experimental and calculated dipole moments. The overall accuracy of the prediction of the dipole moments of compounds with N and O heteroatoms proved to be to within about 0.4 D. This is probably all that can be expected of a theory with such rough allowance for the contribution by the σ-skeleton to $\vec{\mu}$. Table 4 shows that this contribution is very significant.

IV. CALCULATIONS ON EXCITED STATES OF CONJUGATED MOLECULES AND TWO MAIN SCHEMES FOR THE DETERMINATION OF THE EFFECTIVE PARAMETERS OF THE MODEL π-ELECTRON HAMILTONIAN

The theory of conjugated systems was developed initially and was improved by studying the properties of conjugated hydrocarbons. One of the greatest achievements in recent years has been the inclusion of calculations on systems with heteroatoms in the general scheme. This was done after a careful study of the entire parametrisation technique. As a result, several computational schemes were devised, differing in the methods used to introduce empirical information into the model Hamiltonian.

We shall consider in detail two modern parametrisation schemes for the model π-electron Hamiltonian. In one of these the parameters are introduced approximately as in the initial version of Pariser and Parr, i.e. they are calibrated against a series of simple molecules by comparing the calculated and experimental excitation and ionisation energies. This scheme is being developed by Scandinavian workers[6,27-36]. We shall call it "Scheme 1". In the second scheme ("Scheme 2") $2p_z$ functions [these are usually Slater functions defined in Eqn. (14) with different effective charges] and certain other quantities are parametrised. All the parameters are specified as before, which makes Scheme 2 less empirical than Scheme 1. Nevertheless all the parameters of Scheme 2 have been chosen empirically in the course of prolonged studies on molecular spectra using intermediate hypothesis and assumptions. Calculations on excited states by Scheme 2 have been carried out, for example, by Hammond[37], who also quotes all the references relevant to Scheme 2.

1. Scheme 1

Scheme 1 [27-36] is devised as follows. In the first place the ZDO approximation, which is natural for orthogonalised basis functions $\varphi_p(r)$ is used: the overlap integrals

$$S_{\mu\nu} = \delta_{\mu\nu},$$

the non-zero integrals of the skeleton

$$H_{\mu\mu} \equiv \alpha_\mu \text{ (definition) and } H_{\mu\nu} = \beta_{\mu\nu} \text{ for adjacent } \mu \text{ and } \nu;$$

and finally

$$\langle \mu\tau \mid \rho\nu \rangle = \gamma_{\mu\nu}\delta_{\mu\tau}\delta_{\nu\rho}, \quad \gamma_{\mu\nu} = \langle \mu\mu \mid \nu\nu \rangle.$$

Thus the PPP Hamiltonian [Eqn. (6)] is used.

The parameters of the skeleton are specified as follows.

$$\alpha_\mu = W_\mu - \sum_{\nu(\neq\mu)} \gamma_{\mu\nu}, \tag{15}$$

where the first term is the energy of the attraction of a π-electron of the atom μ to its positively charged ionic residue (W_μ is approximately equal to the ionisation potential of the atom μ with a minus sign) and the second term represents the energy of the attraction of a π-electron of the atom μ to the ionic residues of other atoms; the approximation for the integral $U(\nu:\mu\mu)$ for the attraction of a π-electron of the atom μ to the positively charged ionic residue of the atom ν, which is usual in the PPP method, was employed here:

$$U(\nu:\mu\mu) \simeq \gamma_{\mu\nu}.$$

Furthermore,

$$W_\mu = W_0 + \sum_{\substack{\nu \\ \text{(adjacent } \mu\text{)}}} \Delta W_\mu(R_{\mu\nu}). \tag{16}$$

Eqn. (16) takes into account the influence of neighbouring carbon atoms on the ionisation potential of the atom μ. The contributions to $H_{\mu\mu}$ by other atoms are a consequence of the orthogonalisation of the $2p_z$ functions, as shown by Fischer-Hjalmars[6]. Under these conditions, the main contribution comes from neighbouring atoms, which is reflected in Eqn. (16). If there are no neighbouring atoms, the sum in Eqn. (16) is missing and $W_\mu = W_0$. Therefore the ionisation potential of the CH_3 radical with a minus sign is chosen as the value of W_0 ($W_0 = -9.84$ eV).

The contributions to W_μ by adjacent atoms depend on distance according to the formula

$$\Delta W_\mu(R_{\mu\nu}) = \Delta W_0 + \delta(R_{\mu\nu} - R_0). \tag{17}$$

Here (and subsequently) it is assumed that the functions of $R_{\mu\nu}$ can be represented by expansions in terms of the deviations $(R_{\mu\nu} - R_0)$ from the standard line $R_0 = 1.397$ Å (the C–C bond length in benzene‡). In view of the smallness of these deviations (usually $|R_{\mu\nu} - R_0| \leqslant 0.2$ Å), one need retain only two terms of the expansion. It was found that $\Delta W_0 = 0.09$ eV and $\delta = 8.63$ eV Å^{-1}. The values of these and the remaining parameters were determined by a least squares fit of the ionisation potentials and electronic transition energies in the CH_3 radical and in the C_2H_4 (ethylene), C_6H_6 (benzene), and C_4H_8 (butadiene) molecules.

A formula of type (17) was proposed also for the resonance integral:

$$\beta_{\mu\nu} = \beta_0 + \delta_\beta \cdot (R_{\mu\nu} - R_0) \text{ (adjacent } \mu \text{ and } \nu\text{)} \tag{18}$$

$\beta_0 = -2.43$ eV and $\delta\beta = 3.1$ eV Å^{-1}.

The following formulae have been proposed for the parameters of the Coulombic repulsion of π-electrons:

$$\begin{aligned} \gamma_{\mu\mu} &= 11.97 \text{ eV} \\ \gamma_{\mu\nu} &= \gamma_0 + \delta_\gamma(R_{\mu\nu} - R_0) \text{ (adjacent } \mu \text{ and } \nu\text{)} \end{aligned} \tag{19}$$

$\gamma_0 = 6.95$ eV and $\delta_\gamma = -4.65$ eV Å^{-1}; for non-adjacent μ and ν, we have

$$\gamma_{\mu\nu} = \gamma_{\mu\mu}[\gamma_{\mu\mu} R_{\mu\nu} + \exp(-\gamma_{\mu\mu} \cdot R_{\mu\nu})]^{-1}. \tag{20}$$

In terms of the ZDO approximation, the electronic transition energies depend only on differences between type I Coulombic integrals [see Eqn. (6) and Refs. 8 and 14–16]:

$$\gamma_{11} - \gamma_{1p}, \quad \gamma_{12} - \gamma_{1p}, \quad \gamma_{13} - \gamma_{1p}, \quad \ldots$$

or between type II integrals

$$\gamma_{11} - \gamma_{12}, \quad \gamma_{12} - \gamma_{13}, \quad \gamma_{13} - \gamma_{14}, \quad \ldots$$

(Here γ_{1p} denotes the Coulombic integral for the most remote atoms in the molecule). As a result, for small molecules it is important to know how $\gamma_{\mu\nu}$ depends on the distance between adjacent atoms, while the variation for larger distances $R_{\mu\nu}$ is less important. This is reflected in Eqns. (19) and (20) and explains certain arbitrary features in the selection of the formula for $\gamma_{\mu\nu}$ with non-adjacent μ and ν.

If the variation of the theoretical parameters with interatomic distances is known, it is possible to obtain formulae for bond lengths and angles, as noted above, and also to

‡ A similar method for the introduction of parameters of functions, which depend on the bond length, was used in our earlier studies[21,38].

calculate the vibration frequencies of conjugated molecules. Thus semiempirical parameters must be calibrated so as to reproduce satisfactorily both the electronic spectra and the geometrical characteristics of the conjugated molecules. We approached the choice of the parameters in the Hückel method from these general standpoints: the force constants of the σ-skeleton and the variation of the resonance integral with bond length were determined, which led to six very satisfactory frequencies of the in-plane vibrations of benzene[38] and to the correct coefficient in the "bond length–bond order" formula[21].

The problem of a similar adjustment for consistency between empirical parameters and experimental data, based on optical and infrared spectra and geometrical structures of conjugated molecules, has not so far been solved for the PPP Hamiltonian. Although the problem of the in-plane vibrations of benzene has been solved in terms of the PPP approximation[39-42], only three frequencies were considered, which hinders the calibration of the parameters. A similar situation arises in the adjustment of the parameters for consistency with the geometrical structure. When the parameters of Scheme 1 for $\beta(R)$ and $\gamma(R)$ [Eqns. (18) and (19)] and the elastic constant of the σ-skeleton k_1 = 47.6 eV Å^{-2} are used[39], we find that in the formula for conjugated hydrocarbons

$$R_{\mu\nu} = R_0 - bP_{\mu\nu} \qquad (7)$$

the parameter b = 0.162 (for $P_{\mu\nu}$ = 2/3 in the case of benzene) according to Eqn. (12), instead of the value b = 0.18 used in Scheme 1.[20]

As in Dewar's studies[22,23], empirical formulae of type (7) with the parameters R_0 and b, which depended on the type of adjacent atoms, were used to calculate the bond lengths in conjugated molecules with heteroatoms[29-36]. The results obtained for these bond lengths agreed with experiment to within the same limit (about 0.01–0.02 Å) as in Dewar's work[23].

In the calculation of electronic excitation energies for molecules with heteroatoms (N, O, S, etc.) the same parametrisation method was used as for hydrocarbons: equations of type (16)–(20), in which the corresponding constants were fitted by least squares to experimental ionisation potentials and electronic transition energies in a number of simple molecules containing one of the heteroatoms, were employed for the parameters of the Hamiltonian. Thus the computational scheme was extended to the large classes of molecules with heteroatoms[29-36].

Recently the authors of Scheme 1 have tended to reduce the total number of empirical parameters, because each heteroatom introduces several parameters into the calculation. It was noted[43] that the dependence of the resonance integral on the distance between the atoms C and X (X = C, N, O, or F) may be described satisfactorily by two types of relations, which are usually employed in different parametrisation schemes:

$$\beta = \beta_0 + \delta\,(R - R_0) \qquad (21)$$

and

$$\beta = k\,S, \qquad (22)$$

where S is the overlap integral calculated using the Slater functions (14) for the $2p_z$ functions of the atoms C and X with the corresponding values of $Z_{\text{eff}} = 2\zeta$. For all the CX bonds, δ = 3.05 eV Å^{-1}, R_0 = 1.397 Å, β_0 = −2.42 eV, and k = −8.98 eV were adopted. The values of ζ for different atoms together with the values of β for R = 1.34 Å, calculated by Eqns. (21) and (22), are presented in Table 5, which shows a close similarity between the parameters of Scheme 1 and Scheme 2, where, as will be shown below, the resonance integral is calculated by a formula of type (22) and the ζ values are close to those in Table 5.

Table 5. Resonance integrals calculated in different ways[43].

X	βCX, eV		$\zeta = Z_{\text{eff}}/2$	X	βCX, eV, ∞		$\zeta = Z_{\text{eff}}/2$
	Eqn.(21)	Eqn.(22)			Eqn.(21)	Eqn.(22)	
C	−2.59	−2.65	1.56	O	−1.80	−1.61	2.22
N	−2.25	−2.06	1.92	F	−1.30	−1.29	2.55

The general scheme for calculations on molecules is of the usual type for the PPP method. Initially calculations are made on the ground state by the LCAO-MO SCF method, the molecular orbital coefficients and bond orders are found, and the bond lengths are calculated. Next linear combinations of singly excited molecular configurations are set up on the basis of molecular orbitals of the ground state. The coefficients of the configurations, which define the wavefunction of the excited state, are found together with the excitation energies from the minimum in the average molecular energy calculated using the PPP Hamiltonian for the nuclear configuration of the ground state. According to Koopmans' theorem, the ionisation potential is assumed equal to the energy of the highest occupied molecular orbital with the sign reversed[9].

The results of calculations in accordance with Scheme 1[29-36] will be discussed below after examining a further parametrisation scheme.

2. Scheme 2

Hammond[37] carried out calculations on a large number of conjugated molecules within the framework of a single approach (Fig. 3). We shall now consider the parametrisation scheme adopted (Scheme 2).

The Fock equation is

$$F\chi = \varepsilon\chi, \qquad (23)$$

where ϵ are the orbital energies of the molecular orbitals, χ is the column–vector of atomic function coefficients, and F is the Fock matrix with the following elements:

$$F_{pp} = H_{pp} + N_p\gamma_{pp} - \frac{1}{2}P_{pp}\gamma_{pp} + \sum_q (P_{qq} - N_q)\,\gamma_{pq},$$
$$F_{pq} = H_{pq} - \frac{1}{2}P_{pq}\gamma_{pq}\ . \qquad (24)$$

Here $H_{pp} = -I_p$ when the atom p contributes one electron to the π-electron system and N_p = 1 and $H_{pp} = -I_p - \gamma_{pp}$ when N_p = 2; the non-diagonal elements H_{pq} are non-zero for all p and q:

$$H_{pq} = \text{const} \cdot \frac{H_{pp} + H_{qq}}{1 + S_{pq}} \cdot S_{pq}\ , \qquad (25)$$

where const. = 0.56 [from the condition H_{pp+1}(benzene) = −2.45 eV]. The overlap integrals S_{pq} are calculated from the Slater functions (14). The values of ζ_p, I_p, and γ_{pp} are listed in Table 6.

As already mentioned, formula (25) is similar in form to formula (22) and the Slater exponents $\zeta_p = Z_p/2$ listed in Tables 5 and 6 are also similar. This similarity is not fortuitous, since both parametrisation schemes (Schemes 1 and 2) are based on the same experimental data.

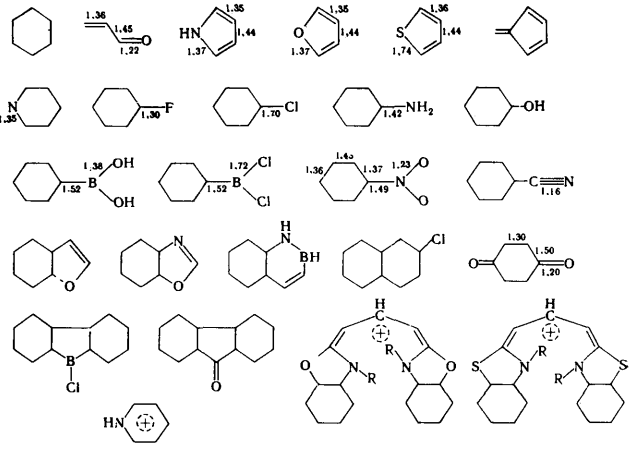


Figure 3. The molecules and ions for which calculations were made by Hammond[37] with parametrisation according to Scheme 2. The bond lengths (in Å) used in the calculation are indicated.

The following formulae were adopted for the parameters of the Coulombic repulsion of electrons in Scheme 2:

$$\gamma_{pq} = \frac{14.397}{a_{pq} + R_{pq}}, \quad a_{pq} = \frac{28.794}{\gamma_{pp} + \gamma_{qq}} \quad . \tag{26}$$

It is found that γ_{pq} for adjacent hydrogen atoms is smaller by 1.6 eV according to this scheme than according to Scheme 1. These differences are probably compensated when a special procedure is used to take into account the polarisation of the σ-skeleton and the mutual influence of σ- and π-electrons as well as the changes in other parameters.

In calculations on systems with heteroatoms an important factor is the correct allowance for effects associated with the mutual influence of atoms. This influence via the σ-skeleton has been taken into account in Scheme 2 with the aid of the concept of the atomic electronegativities ω_p of the σ-bond orbitals. The fraction of σ-electron n_p in the atom p due to the presence of the σ-bond with the atom q can be expressed in terms of ω_p and ω_q:

$$n_p = \frac{2\omega_p}{\omega_p + \omega_q}. \tag{27}$$

In each σ-bond pq there are two σ-electrons:

$$n_p + n_q = 2.$$

As a result of the influence of neighbouring atoms, the effective Slater charge Z^0_p of an isolated atom p is replaced by Z'_p according to the formula

$$Z'_p = Z^0_p + 0.35 \sum_{\substack{q \\ \text{(adjacent } p\text{)}}} \left(\frac{2\omega_q}{\omega_p + \omega_q} - 1\right)\left(\frac{1.41}{R_{pq}}\right)^2. \tag{28}$$

where 0.35 is the Slater screening constant and the multiplier $(1.41/R_{pq})^2$ characterises the rate of decrease of the inductive effect with distance, becoming unity when R_{pq} = 1.41 Å. If all the atoms are the same (all $\omega_p = \omega_q$), then the Slater functions (14) have the same $Z'_p = Z^0_p$ and the mutual influence of atoms is taken account only via the π-electron system in the usual way.

Table 6. The atomic parameters used in calculations on conjugated molecules by Scheme 2.[37]

Atom p	N_p	$Z^0_p = 2\zeta_p$	I^0_p, eV	γ^0_{pp}, eV	ω_p
B	0; 1	2.25; 2.60	8.33	6.91	1.96
C	1	3.25	11.16	11.13	2.75
N	1; 2	3.90; 4.25	14.12	12.34	4.13
O	1; 2	4.55 4.90	17.7	15.23	5.54
F	2	5.55	20.86	17.36	3.90
S	2	5.80	12.7	9.94	3.46
Cl	2	6.45	15.03	11.30	2.95

As a result of the σ-inductive effect, I^0_p and γ^0_{pp} of isolated atoms are replaced by I'_p and γ'_{pp} according to the following formulae:

$$I'_p = I^0_p - 0.324\,[(Z^0_p)^2 - (Z'_p)^2] - 6.03\,(Z^0_p - Z'_p),$$
$$\gamma'_{pp} = \gamma^0_{pp}\,(Z'_p/Z^0_p). \tag{29}$$

Z'_p, I'_p, and γ'_{pp} are the initial values for the first π-electron calculation: Eqn. (23) is solved with the above parameters. After determining the bond order matrix P_{pq}, allowance is made for the π-inductive effect, according to which the effective charge becomes

$$Z'_p = Z_p - 0.35\,(P_{pp} - 1). \tag{30}$$

The quantities I''_p and γ''_{pp} for the next π-electron calculation (using Z''_p) are evaluated by Eqn. (29), etc. Several iterations are performed until the successive P_{pq} agree to within the required accuracy.

This scheme for taking into account inductive effects involves a logical inconsistency, which, however, may be concealed by the special selection of parameters. This inconsistency was noted earlier[44,45] in relation to the Hückel method with parameters which depend on P_{pq}. As noted by Bagatur'yants[46], the point is that, by minimising the total average energy and by deriving the Fock equation, we should take into account the dependence of the parameters γ_{pp} and I_p on bond orders already at this stage. Otherwise the iterative procedure does not lead to a minimum in the total energy. The complete scheme for taking into account the changes in parameters when P_{pq} is altered, developed by Karlsson[47] for the PPP approximation, is free from this disadvantage but is very cumbersome and has not so far been used.

The excitation energies for each molecule were calculated taking into account 10 singly excited configurations for the given configuration of the nuclei: the experimental bond lengths and angles or their values for fragments of known molecules were used. The variation of several bond lengths in a series of molecules had little effect on the calculated excitation or ionisation energies, which were also determined using Koopmans' theorem. The results of the calculations of the excitation energies and

ionisation potentials are compared with experiment in Fig. 4. The average deviation of the calculated excitation energies and ionisation potentials from the experimental values proved to be 0.1—0.2 eV and about 0.4 eV respectively. The satisfactory overall agreement between the theory and experiment can be accounted for by the logic of the fundamental postulates of the theory and the exact choice of parameters. Since the same conclusions and estimates are valid for the results of calculations with the parameters of Scheme 1, these results will not be quoted. We shall only note that in calculations with the parameters of Scheme 1 the excitation energies agree better with experiment than the ionisation potentials.

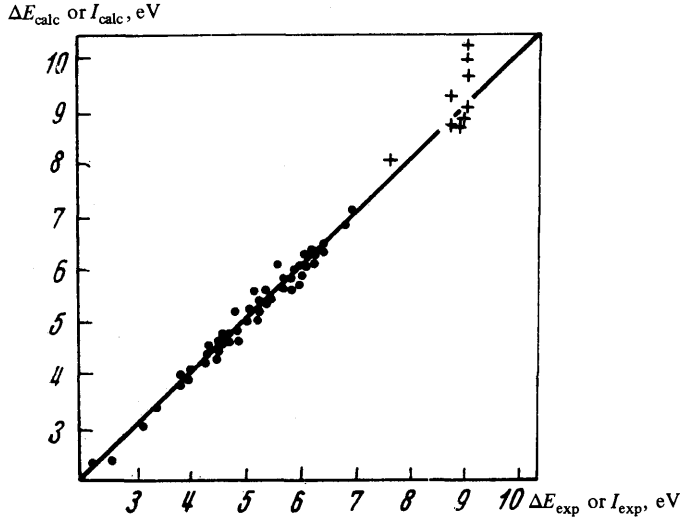


Figure 4. Correlation between the calculated and experimental excitation energies (ΔE) and ionisation potentials (I) for the molecules shown in Fig. 3. The calculated values are plotted against the experimental values[37]: ●—ΔE; +—I.

V. THE DIFFICULTIES OF THE THEORY IN THE CALCULATION OF THE INDIVIDUAL PROPERTIES OF EXCITED STATES

1. Ionisation Potentials

Large discrepancies between theory and experiment for ionisation potentials, reaching 1 eV, are characteristic of the π-electron approximation and are related to the approximate nature of Koopmans' relation:

$$I = -\varepsilon^{\pi}_{h.occ} \qquad (31)$$

where I is the ionisation potential and $\epsilon^{\pi}_{h.occ}$ the energy of the highest occupied molecular orbital. Roothaan[9] showed that Koopmans' theorem [Eqn. (31)] is valid in the LCAO-MO SCF approximation. The reasons for the large discrepancies with experiment are as follows: (1) the change in the molecular orbital energies ϵ_i on passing from the molecule to the ion is neglected; (2) the correlation contributions to the energies of the ground states of the molecule and the ion are neglected. Thus in the derivation of Eqn. (31) it was assumed that all the molecular orbital energies $\epsilon_i^{(o)} = \epsilon_i^{(+)}$, where the superscripts o and + refer to the neutral molecule and the cation respectively. Moreover, the approximate nature of the method of calculation itself (LCAO-MO SCF) has an effect. In it the ground state energy is calculated in terms of the single-configuration approximation, which implies neglect of the π-electron correlation energies, the latter being taken into account to some extent by the choice of the parameters of the effective Hamiltonian.

The calculation of the ionisation potentials of a number of conjugated molecules showed[48] that, as a rule, the calculated I_{calc} exceed the experimental values I_{exp} and the differences between them depend on the choice of parameters. Furthermore, it has been shown[48] that the agreement with experiment can actually be impaired if doubly excited configurations are included in the calculation for the same values of the parameters. This is because the parameters of the effective Hamiltonian must depend on the method of calculation: in the parameters of the SCF method correlation effects are to some extent taken into account and when these effects are taken into account explicitly other parameters must be used.

Table 7. The calculated (I_{calc}) and experimental [I^{el}_{expt} (electron impact) and I^{ph}_{expt} (photoionisation)] ionisation potentials[50].

Molecule	I_{calc}	I^{el}_{exp}	I^{ph*}_{exp}	Molecule	I_{calc}	I^{el}_{exp}	I^{ph*}_{exp}
Benzene	(9.56)	9.56	9.25	Benzaldehyde	9.87	9.82	9.50
Ethylene	10.39	10.62	—	Pyridine	9.65	9.70	9.30
trans-Butadiene	9.3	9.3	—	Quinoline	8.69	—	8.62
Aniline	8.78	8.32	7.7	*p*-Benzoquinone	9.76	—	9.96
Phenol	9.21	9.16	8.7				

*According to Potapov[51].

It has been shown[49,50] that the agreement between I_{calc} and I_{exp} is improved (Table 7) when Koopmans' relation with the correction

$$I_{calc} = -\varepsilon^{\pi}_{h.occ} - \Delta \qquad (\Delta \simeq 1\,eV) \qquad (32)$$

is employed.

In order to understand the reasons for this correction, we shall consider the results of the calculations on urazole and pyrrole and their anions and cations in terms of the SCF approximation with all the σ- and π-electrons[18]. It was found that a change in the number of π-electrons in the system alters the effective potential of the σ-skeleton for the π-electrons. This leads to a decrease of all the molecular orbital energies when the number of π-electrons is reduced:

$$\varepsilon_i^{(-)} > \varepsilon_i^{(*)} > \varepsilon_i^{(+)}. \qquad (33)$$

In order to make some allowance for this change in molecular orbital energies, it is necessary to introduce a positive correction Δ. We may note that a similar formula has been proposed[52] for the electron affinity E_A:

$$E_A = -\varepsilon^{\pi}_{1.free} - \Sigma \qquad (\Sigma \simeq 2-3\ эв) \qquad (34)$$

where $\epsilon^{\pi}_{l.free}$ is the energy of the lowest unoccupied molecular orbital of the conjugated molecule and a positive sign of Σ follows from Eqn. (33). The corrections Δ and Σ can eliminate only the average systematic error, leaving an inaccuracy of about 0.5 eV. This inaccuracy is characteristic of calculations of ionisation potentials using Koopmans' relations (31) and (32).

2. Energies of Triplet States

As stated above, the energies of electronic singlet excited states can be calculated with a high accuracy (to within 0.1—0.2 eV). The same satisfactory accuracy is characteristic of calculations using other parametrisation schemes[15,49,53-61]. The situation is less satisfactory for calculations of the energies of triplet levels. This is probably why the authors of Schemes 1 and 2 did not calculate the energies of triplet states and it has actually been suggested[62] that the parameters be altered in calculations on such states.

Table 8. The energies of the triplet states of benzene (eV) (relative to the ground state)[63].

Symmetry of level	Calc.	Expt.
$^3B_{1u}$	3.37	3.66
$^3E_{1u}$	4.85	4.65
$^3B_{2u}$	5.33	5.76
$^3E_{2g}$	6.31	6.56
$^3E_{2g}$	8.70	8.55

In fact the best agreement between theory and experiment for the energies of the triplet states of benzene has been achieved[63] with parameters which are not optimal for the calculation of the singlet energy levels (Table 8). Furthermore, the discrepancies between the calculated and experimental energies of triplet states can reach 1 eV.[56-58] Finally in the calculation of the energies of the $T-T$ transitions for a large number of aromatic molecules[64,65] it was found that a satisfactory agreement between theory and experiment (to within about 0.1—0.2 eV on average) is achieved only when all the calculated transition energies are reduced by 0.4 eV. This adjusting constant was determined from the $T-T$ transition in naphthalene.

The decrease of accuracy in the calculation of the energies of triplet states is associated with the different effects of the σ-skeleton on the singlet and triplet energy levels. In order to understand the reason for this, we shall consider the wavefunctions $\Psi_{S=0}$ and $\Psi_{S=1}$ for the singlet and triplet molecular states. These functions will be expressed as sums of products of the wavefunctions of π-electrons ($\Psi^{\pi}_{S_\pi}$) and σ-electrons ($\Psi^{\sigma}_{S_\sigma}$) with different spin multiplicities:

$$\Psi_{S=0} = N_0(\Psi^{\sigma}_{S_\sigma=0}\Psi^{\pi}_{S_\pi=0} + C_0\,\Psi^{\sigma}_{S_\sigma=1}\Psi^{\pi}_{S_\pi=1} + \ldots),$$

$$\Psi_{S=1} = N_1(\Psi^{\sigma}_{S_\sigma=0}\Psi^{\pi}_{S_\pi=1} + C_1\Psi^{\sigma}_{S_\pi=1}\Psi^{\pi}_{S_\pi=0} + \ldots),$$

where the coefficients C_0 and C_1 characterise the contributions of the excited states of the σ-skeleton to the singlet and triplet states of all the electrons in the molecule and N_0 and N_1 are normalising factors. In terms of the π-electron approximation, $C_0 = C_1 = \ldots = 0$ and $\Psi_{S=0} \rightarrow \Psi^{\pi}_{S_\pi=0}$ and $\Psi_{S=1} \rightarrow \Psi^{\pi}_{S_\pi=1}$. The coefficients C_0 and C_1 are inversely proportional to the differences between the energies corresponding to the first two terms in the singlet and triplet functions $\Psi_{S=0}$ and $\Psi_{S=1}$. This difference is greater for the singlet function than for the triplet function, namely

$$(E^{\sigma}_{S=1} + E^{\pi}_{S=1}) - (E^{\sigma}_{S=0} + E^{\pi}_{S=1}) > (E^{\sigma}_{S=1} + E^{\pi}_{S=0}) - (E^{\sigma}_{S=0} + E^{\pi}_{S=1})$$

owing to the self-evident inequality $E^{\pi}_{S=1} > E^{\pi}_{S=0}$. Therefore the admixture of the second term is smaller for the singlet than for the triplet,

$$|C_0|^2 < |C_1|^2,$$

which indicates a greater influence of the σ-skeleton on triplet states.

As already mentioned, the effect of the σ-skeleton is taken into account in principle by an empirical choice of the parameters of the effective Hamiltonian. Owing to the different contributions of the σ-skeleton to the singlet and triplet states, the optimal values of the parameters for the calculation of the energies of the singlet and triplet levels should differ, as has actually been observed in a number of calculations[62,63].

We may also note that, in the calculation of excitation energies (singlet and triplet), it is generally speaking necessary to take into account fully the electron interactions. If the treatment is limited to singly excited configurations, it is found that different energy levels are calculated with different accuracies, because the contributions of the neglected configurations (doubly excited, etc.) will be different for different excited states. In this connection there has been a notable failure in the calculation of transition energies between excited singlet and triplet levels of a number of molecules[66]. Another reason for this failure is associated with the increase of error in the calculation of the transition energies between excited states: when the average accuracy in the determination of the energies of excited singlet states is 0.1—0.2 eV, larger deviations are possible, being on average doubled for energy differences, i.e. for transition energies.

3. Transition Probabilities (Oscillator Strengths)

Yet another weak point in the theory is the calculation of transition probabilities (oscillator strengths) for electronic excitations of conjugated molecules. We have analysed the results of studies by a Scandinavian group of investigators[27-36], who employed the parameters of Scheme 1 and failed to find any correlation between the calculated (f_{calc}) and experimental (f_{exp}) oscillator strengths for a large number of electronic transitions. In the plot of f_{calc} against f_{exp} (Fig. 5) most of the points are distributed between two straight lines: $f_{calc} = 3f_{exp}$ and $f_{calc} = \frac{1}{3}f_{exp}$. Thus values of f_{exp} differing by a factor of 10 can correspond to the same f_{calc}. For this reason, in the majority of later studies the f_{calc} are not compared with f_{exp} but with $\lg\epsilon$, ϵ being the extinction coefficient at the corresponding maximum in the experimental absorption spectrum. The parallel variation of f_{calc} and $\lg\epsilon$ for the spectral maxima is regarded as constituting satisfactory agreement.

In the calculation of oscillator strengths one usually employs an approximation without a specific atomic orbital basis set. Suppose that ψ_0 and ψ_a are the wavefunctions

of the ground and excited states respectively and suppose that ψ_a represents a superposition of the singly excited configurations $\Phi_{i\to k}$:

$$\psi_a = \sum_{i,k} A^a_{i\to k}\Phi_{i\to k},$$

where $\Phi_{i\to k}$ is the wave function of the configuration formed from the configuration of the ground state by the transfer of an electron from the ith to the kth molecular orbital and $A^a_{i\to k}$ is a coefficient defining the contribution of this configuration to the excited state. Then the oscillator strength for the transition to the singlet state can be calculated from the formula:

$$f_{0a} = \frac{2m}{3\hbar^2 e^2}\Delta E_{0a}\vec{\mu}^2_{0a},$$

(e is the charge of the electron, m its mass, h the Planck constant, and ΔE_{0a} the excitation energy), where

$$\vec{\mu}_{0a} = \langle\psi_0|\vec{\mu}|\psi_a\rangle = e\sqrt{2}\sum_{i,k} A^a_{i\to k}\sum_\nu c^*_{\nu i}c_{\nu k}\mathbf{R}_\nu.$$

In this equation $\mathbf{R}_\nu$ is the coordinate of the atom ν, and $c_{\nu i}$ and $c_{\nu k}$ are the coefficients of the basis function $\varphi_\nu(\mathbf{r})$ in the LCAO—the expansions of the ith and kth molecular orbitals respectively.

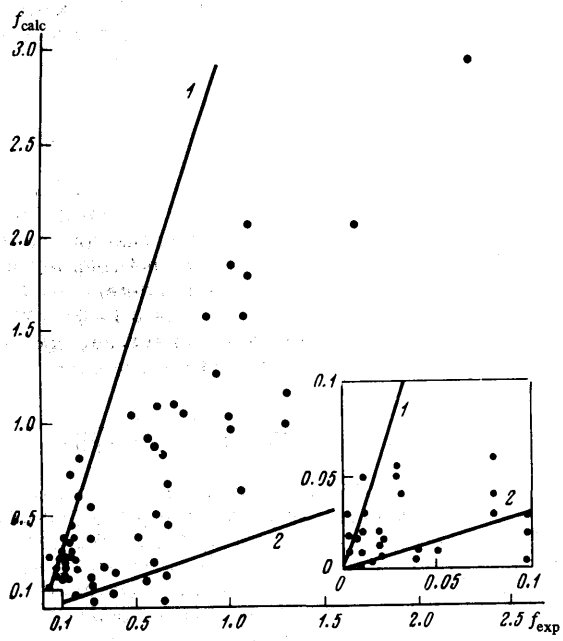


Figure 5. Correlation between the calculated (f_{calc}) and experimental (f_{exp}) oscillator strengths for 86 allowed electronic transitions in conjugated molecules according to the literature[27-36]. The section with $f < 0.1$ is shown separately on an enlarged scale: 1) $f_{calc} = 3f_{exp}$ line; 2) $f_{calc} = \frac{1}{3}f_{exp}$ line.

In the calculation of $\vec{\mu}_{0a}$ the dipole length operator

$$\vec{\mu} = e\sum_i \mathbf{r}_i$$

(summation with respect to all the electrons) was used, and in the matrix element μ_{0a} only the terms diagonal with respect to the atomic orbital indices were retained:

$$\int \varphi_p(\mathbf{r})\,\mathbf{r}\,\varphi_\nu(\mathbf{r})\,d\mathbf{r} \simeq \delta_{p\nu}\,\mathbf{R}_\nu.$$

In this formula the approximate equality $\varphi_p(\mathbf{r}) \simeq \chi_p(\mathbf{r})$, where $\chi_p(\mathbf{r})$ is the atomic orbital of the pth atom, was used. In fact (see Section II above) the orthogonal basis functions $\varphi_p(\mathbf{r})$ represent superpositions of the atomic functions $\chi_i(\mathbf{r})$, so that this approximation neglects all terms with the overlap integrals of the atomic function $\chi_i(\mathbf{r})$. As a result, the dependence of the oscillator strengths on the type of atomic functions is lost.

The development of experimental methods for the investigation of excited singlet and triplet molecular states and the important role of these states in the elementary steps of chemical and photochemical reactions should stimulate the development and improvement of theories of electronic transitions. In the calculation of transition probabilities (oscillator strengths) it is apparently necessary to describe very accurately the real (ground and excited) states of the system: account must be taken of changes in the geometry (bond length) of the molecules in the excited state and of the vibrations of the nuclei.

We shall now consider a series of studies[67-69] in which the effect of temperature on the probability of the electronic excitation and ionisation of complex molecules was investigated. As a result, a criterion was obtained for the determination of the true ionisation potential from the ionisation curve (the variation of the ion current with the energies of the photons which dislodge an electron from the molecule). This criterion is suitable for the determination of the position of the line of 0—0 transitions in the absorption spectra of complex conjugated molecules with unresolved vibrational structure and has in fact been used for this purpose[70].

The extent to which the interelectron interaction is taken into account is also of definite importance in the calculation of oscillator strengths. Thus the inclusion of doubly excited configurations in the calculation altered f_{calc} severalfold[56-58]. However, whereas in some studies[56,57] these changes improved the agreement with experiment, in one investigation[58], for other types of molecules, the agreement with experiment was impaired to such an extent that the results of the calculation were not even quoted.

Certain possible ways of improving the theory of oscillator strength have been analysed in a series of studies[71-73]. In the first of these[71] it was suggested that the gradient operator instead of the dipole length operator should be used in the calculation of f. The oscillator stengths calculated by the two procedures are

$$f_1 = \frac{2}{3}|M|^2\Delta,\quad f_2 = \frac{2}{3\Delta}|G|^2,$$

where

$$M = \left\langle\psi_0\left|\sum_i \mathbf{r}_i\right|\psi_A\right\rangle a_0^{-1},\quad \Delta = (E_A - E_0)\cdot\frac{a_0}{e^2},$$

(a_0 is the Bohr radius and e the electronic charge) and

$$G = \left\langle\psi_0\left|\sum_i \nabla_i\right|\psi_A\right\rangle a_0.$$

For the exact wavefunctions of the initial (ψ_0) and final (ψ_A) states with the energies E_0 and E_A, the equality $f_1 = f_2$ should hold. This equality does not hold for approximate variational functions involved in the theory of conjugated systems. It has been found[71-73] that, for benzene, ethylene, polyenes, and polyacenes, we always have

$f_1 > f_2$ and $f_1 > f_{exp}$. As a result, the use of f_2 instead of f_1 improved the agreement with experiment (Table 9). This agreement is fortuitous, since as a rule $f_2 < f_{exp}$ and the differences between f_2 and f_{exp} are also not small.

The reasons for the unsatisfactory situation in the theory as regards the calculation of oscillator strengths have been discussed[74,75]. It was suggested that the failures are caused by the employment of a finite basis set of atomic functions and the neglect of correlation effects in the wavefunctions (this disagrees with the results of studies[56-58] where an effect of doubly excited configurations on f_{calc} was noted). In this connection it is suggested that the approximation of random phases, which combines the simplicity of molecular orbital methods with allowance for correlation effects, be used. The random phase approximation has already been employed in the calculation of oscillator strengths[76-79]. However, in one study[76] a satisfactory parallel variation of f_{calc} with $\lg \epsilon$ was merely noted and in others[77-79] no comparison with experiment was made.

Table 9. The calculated (f_1 and f_2) and experimental (f_{exp}) oscillator strengths for certain allowed transitions in a number of molecules[71-73].

Molecule	f_1	f_2	f_{exp}	Molecule	f_1	f_2	f_{exp}
ylene	0.597	0.272	0.29	Hexatriene	2.312	0.446	~0.7
Benzene	2.369	0.945	0.88	Naphthalene	0.53	0.18	0.11
Butadiene	1.423	0.35	0.55		2.10	0.87	1.2
				Anthracene	2.77	1.21	1.6

Analysis of the solutions of certain model problems[74,75] has shown that in most cases $f_1 > f_{exact}$ and $f_2 < f_{exact}$. However, for different types of transitions, a wide variety (as regards sign and magnitude) of deviations of f_1 and f_2 from f_{exact} may be encountered. As mentioned by Dancz and Harris[75], there exists an infinite set of operators, apart from the dipole length and velocity operators, which yield the same oscillator strength f_{exact} in calculations using exact functions. In calculation with variational functions, which are not solutions of the Schrödinger equation, all these operators yield different f_{calc}: $f_1 \neq f_2 \neq \ldots \neq f_{exact}$. We believe that, in order to overcome this difficulty in a theory in which the matrix elements of operators and not wavefunctions are used, it is necessary to make sure that the matrix elements are chosen in accordance with commutative relations for the operators. For example, operators for the momentum $\hat{p} = i\hbar(\partial/\partial \bar{r})$ and the coordinate $\bar{r}$ satisfy definite commutative relations and therefore the choice of the parameters p_{mn} and r_{mn} must not conflict with these relations. With this choice of parameters, it is possible to minimise the inaccuracies associated with the employment of variational functions on a limited atomic orbital basis set. Interesting possibilities for a correct choice of parameters p_{mn} and r_{mn}, which are used in calculation of f_2 and f_1, were demonstrated by Linderberg[80]. We believe that the approach to the problem of oscillator strengths from such general standpoints will make it possible to develop a scheme (which is not at present available) for the determination of parameters, including consistently calculated oscillator strengths and other characteristics of molecular systems.

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New Reactions of *N*-Methylated Oxopurines

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The reactions of *N*-methylated oxopurines with phosphorus chlorides, resulting in the formation of highly reactive amidochloride compounds (amidochlorides or adducts), are described. Two isomeric series of $C_{(2)}$- or $C_{(6)}$-substituted oxopurine derivatives as well as $C_{(6)}$- or $C_{(2)}$-iminopurines can be obtained from such compounds.
The properties and characteristics of the compounds, their structures, and the demethylation reactions of the amidochlorides and the adducts, accompanied by the elimination of methyl chloride, are discussed.
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I. INTRODUCTION

The synthesis of various derivatives of *N*-methylated xanthines (2,6-dioxopurines) from natural purine alkaloids (theobromine, theophylline, and caffeine) has been for a long time one of the popular ways of seeking new medicinal preparations, mainly with cardiovascular activity, in the purine series.

Hitherto, the protons at the $N_{(1)}$ or $N_{(7)}$ atoms in 3,7-dimethyl-or 1,3-dimethyl-xanthines (theobromine or theophylline)[1] as well as the hydrogen linked to the $C_{(8)}$ carbon atom of the imidazole ring in all three purine alkaloids[2] were usually substituted by various groups for this purpose.

The substitution at ring nitrogen and carbon atoms does not entail a change in the xanthine structure. Therefore new sometimes extremely valuable properties, appearing as a result of the introduction of additional substituents, are always manifested against the background of the manifold pharmacological activity characteristic of the initial purine alkaloids, although individual aspects of this activity may vary within fairly wide limits.

Such studies were begun as early as 60—70 years ago. Nevertheless, they cannot be regarded as exhausted: the literature of the last decade contains numerous examples of the synthesis of previously unknown theobromine, theophylline, and caffeine derivatives as well as certain monomethylxanthines, which, although not fundamentally different from those described earlier, contain substituents with a more complex structure, frequently simultaneously in the 1-, 7-, and 8-positions.

Reactions of *N*-methylated xanthines which lead to the loss of the xanthine structure and hence of the set of pharmacological properties characteristic of this structure have also been known for a long time. One of the clearest examples of this is provided by the interaction of theobromine with phosphoryl chloride in a closed system at a high temperature, described for the first time by Fischer as early as the end of the last century, which leads to the elimination of the methyl in the 3-position and to the formation of 2,6-dichloro-7-methylpurine, from which it is subsequently easy to obtain various derivatives of 7-methylpoxanthine and oxygen-free purine, as well as paraxanthine, its derivatives, and many other compounds[1,3,4].

Although the mechanism of this reaction has been little investigated and has remained obscure until recently, the principles underlying it subsequently acquired considerable preparative value, since the synthetic possibilities in the purine series were greatly extended with the aid of similar reactions[5].

Studies dealing with the reactions of theobromine with phosphorus chlorides under milder conditions than those described by Fischer have been published since 1962. Such reactions lead to the formation of various derivatives of 6- or 2-oxodihydropurines retaining both methyl groups in the 3- and 7-positions—compounds which differ significantly in their structure and in their chemical and physical properties not only from methylated xanthines but also from all other purine derivatives described previously. These extremely reactive compounds can be of considerable interest as a new potential source of biologically active compounds.

The present review deals with problems of their synthesis and structure and also with certain aspects of the mechanism of their formation.

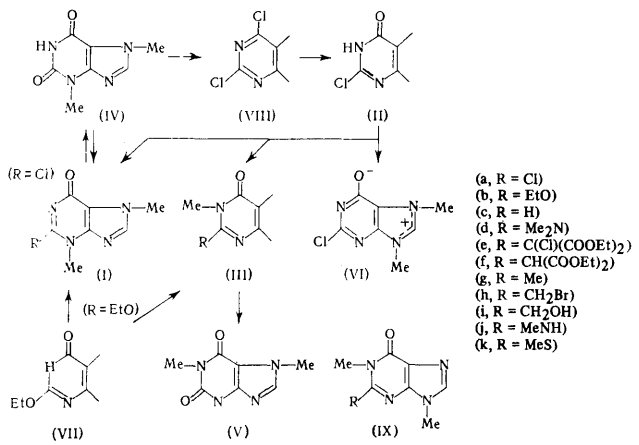
II. DERIVATIVES OF DIHYDRO-3,7-DIMETHYLMONOXOPURINES

1. Synthesis of $C_{(2)}$-Substituted Derivatives of 3,7-Dimethylhypoxanthine (3,6-Dihydro-3,7-dimethyl-6-oxopurine)

The first representative of the 3,7-dimethylhypoxanthine (I) series, namely 2-chloro-3,7-dimethylhypoxanthine (Ia), was recently isolated[6] as one of the side products in the methylation of 2-chloro-7-methylhypoxanthine (II) to form 2-chloro-1,7-dimethylhypoxanthine (IIIa), which, like (II), is an intermediate in the conversion of theobromine (IV) into paraxanthine (1,7-dimethylxanthine) (V).[3,4] This reaction has been known for a long time. 2-Chloro-6-oxo-7,9-dimethylpurinium betaine (VI), which is stable on heating with inorganic acids, is yet another side product in the methylation of (II) by dimethyl sulphate (DMS) in an aqueous alkaline medium[7]. It is formed as the main product when the reaction is carried out in dimethylformamide (DMF).[8]

2-Chloro-3,7-dimethylhypoxanthine (Ia), which is readily hydrolysed to theobromine, is converted on treatment with sodium ethoxide into the 2-ethoxy-derivative (Ib), identical with the side product isolated in a small amount in the analogous methylation of 2-ethoxy-7-methylhypoxanthine (VII).[9]

A single-stage preparative method for the synthesis of the key chloride (Ia) directly from theobromine was discovered somewhat later. A 1:10 mixture of theobromine and $POCl_3$ is heated until the former dissolves, the excess $POCl_3$ is distilled off, and the residue is treated with ice in the presence of $NaHCO_3$. Apart from the chloro-derivative (Ia), about 10% of 2,6-dichloro-7-methylpurine (VIII) can be isolated in this reaction[5]. If the treatment with ice is carried out in the absence of $NaHCO_3$, i.e. at a low pH, the entire chloro-derivative formed hydrolyses and the initial theobromine (IV) is regenerated (see below).

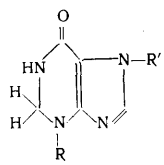


The above easy method of synthesising the chloro-derivative (Ia) and the high mobility of its chlorine atoms made it possible to synthesise many derivatives of 3,7-dimethylhypoxanthine substituted in the 2-positions by various groups [for example compounds (Ib)—(Ik) and many others][10,11], in which the presence of the methyl group in the 3-position fixes one of the double bonds of the pyrimidine ring in the 1,2-positions. Owing to the *p*-quinonoid structure of the ring due to the distribution of the substituents, the entire series of compounds (I), probably differs fairly significantly in its properties from compounds of the 2-R-1,9-dimethylhypoxanthine series (IX) and (III) with the same substituents R,[12-14] i.e. from the isomeric 2-substituted derivatives of *NN*-dimethylhypoxanthines with a "normal" bond distribution.

The characteristics of compounds (I), due to the high electrophilicity of the second ring carbon atom, have been noted in many reactions. They are shown by the enhanced reactivity of the substituents at this carbon atom, which is particularly evident in certain reactions of the chloro-derivative (Ia): it is not only exceptionally readily hydrolysed with elimination of chlorine at low pH, but it also undergoes nucleophilic substitution reactions when treated with alkoxides, ammonia, primary and secondary amines, and other nucleophilic agents, much more vigorously than the isomeric 2-chloro-1,9- and 2-chloro-1,7-dimethylhypoxanthines (IXa) and (IIIa). Such reactions of compound (Ia) usually do not require heating and actually occur with evolution of heat.

The system of compounds (I) as a whole exhibits an enhanced reactivity. This is shown, in particular, by the fact that the catalytic dehalogenation of (Ia) in the presence of Pd/C or Raney nickel results in the formation of a mixture of the expected compound (Ic) and its dihydro-derivative—1,2,3,6-tetrahydro-3,7-dimethyl-6-oxopurine (X).[10]

The catalytic debenzylation of 3-benzyl-7-β-D-ribofuranosylhypoxanthine, i.e. a compound which does not differ from (Ic) in the distribution of the double bonds in the pyrimidine ring, resulted in a mixture of 7-β-D-ribofuranosylhypoxanthine and a dihydro-derivative of the initial compound, which should be regarded as 3-benzyl-1,2,3,6-tetrahydro-6-oxo-β-D-ribofuranosylpurine (XI) on the basis of the results of a study of the ^1H NMR spectra[15].



(X, R+R′=Me)

(XI, R = $PhCH_2$, R′ = β-D-ribofuranosyl

Comparison of the abilities of 2-ethoxy-derivatives of three *NN*-dimethylhypoxanthines (the 3,7-, 1,7-, and 1,9-dimethyl derivatives) to function as ethylating agents with respect to malonic ester by splitting off their ethoxy-group (which is described in greater detail in another review[2]) demonstrates yet again that the isomer (Ib), containing *N*-methyl groups in the 3- and 7-positions, is the most reactive and forms ethylmalonic ester in a high yield. Data obtained by quantum-chemical calculations for the electronic structures of (Ib), the isomeric compounds (IIIb) and (IXb), their 8-chloro-derivatives, and three dimethylmonoxopurines unsubstituted at $C_{(2)}$ and $C_{(8)}$ [compounds (Ic), (IIIc), and (IXc)] confirmed that the electron density and the free valence index at $C_{(2)}$ in 3,7-dimethyl-6-oxopurines are appreciably reduced and therefore compound (Ib) and its 8-chloro-derivative should indeed exhibit the maximum alkylating capacity[16]. It has also been noted that the dialkylamino-group in the 2-position in compounds of type (Id) is readily hydrolysed in the presence of inorganic acids with regeneration of theobromine[2,17].

The replacement of chlorine in compound (Ia) by a dialkylamino-group and its subsequent hydrolytic elimination in the last stage can be used in the synthesis of $C_{(8)}$—C derivatives of theobromine as a method of protecting the proton at the first nitrogen atom[18].

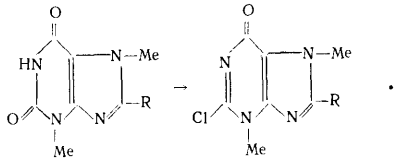
Not only the Cl—$C_{(2)}$ and N—$C_{(2)}$ bonds but also the C—$C_{(2)}$ bond can readily undergo hydrolytic cleavage in compounds (I). An example of this reaction is provided by the formation of theobromine as a result of heating 2-chloromalonate (Ia) with inorganic acids[19].

It is interesting that the $C_{(2)}$—C bond in 1,7- and 1,9-dimethylhypoxanthines with chloromalonic acid groups [compounds (IIIe) and (IXe)] does not undergo cleavage and the main reaction products are the corresponding 2-hydroxymethyldimethylhypoxanthine (IIIi) or 2-chloromethyldimethylhypoxanthine (IXi).[13,14]

In derivatives of compounds (I) the $C_{(2)}$—C bond is not cleaved when the malonic acid residue does not contain chlorine: in compound (If) only the ester groups are hydrolysed with decarboxylation. 2,3,7-Trimethylhypoxanthine (Ig) was obtained in this way and was subsequently converted by treatment with dibromodioxan into the monobromo-derivative (Ih). A wide variety of compounds can be obtained from the latter on replacing the bromine by various substituents (including groups with a complex structure). When the purinylmalonate (If) is treated with ethanol in the presence of catalytic amounts of hydrogen

chloride, only one ethoxycarbonyl group is split off. The resulting ethyl ester of 3,7-dimethylhypoxanthine-2-acetic acid was converted into its amides by treatment with ammonia and amines[19].

The series of compounds with structure (I), whose synthesis is based on the reaction of theobromine with $POCl_3$, can be greatly extended by introducing a second substituent at the $C_{(8)}$ atom of the imidazole ring. For this purpose, instead of theobromine one may treat with $POCl_3$ its 8-substituted derivatives—8-chlorotheobromine (XII) or 8-methyltheobromine (XIII)—which are thereby converted into the dichloro-derivative (XIV) or into 2-chloro-3,7,8-trimethylhypoxanthine (XV).[20-22] The use of the former leads to the greatest possibilities: by successive substitution of the chlorine atoms, initially at $C_{(2)}$ and then at $C_{(8)}$, it is possible to vary the nature of the substituents at the ring carbon atoms in both rings of the purine molecule.



(XII, R=Cl) (XIV, R=Cl)
(XIII, R=Me) (XV, R=Me)

The above reactions of 8-chlorotheobromine and the synthesis from it of 2,8-disubstituted derivatives of 3,7-dimethylhypoxanthine result in relative freedom from restrictions on the structure of the substituents at $C_{(8)}$, while that of the substituents at $C_{(2)}$ may sometimes be subject to limitations due to the characteristics of the system, mentioned above, probably due to its *p*-quinonoid structure.

On the other hand, syntheses from 8-methyltheobromine provide a considerable scope for the preparation of 3,7,8-trimethylhypoxanthines with a wide variety of substituents in the 2-position. However, the attempts to modify subsequently the substituent at $C_{(8)}$ by replacing one of the hydrogen atoms of the methyl group by a halogen[2] were unsuccessful. Nor is it always possible to employ as starting materials 8-substituted theobromine derivatives with a specified structure of the substituent at $C_{(8)}$ joined to the ring via a C—C bond; such compounds char appreciably on heating with $POCl_3$.[17,22]

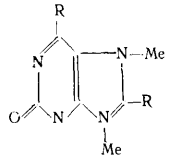
Derivatives of 3,7-dimethylhypoxanthine differ from the isomeric 1,7- and 1,9-dimethylhypoxanthines not only in their chemical properties but also in their physical properties[10]. For example, the ultraviolet spectrum of (Ia) exhibits an 8 nm bathochromic shift of the long-wavelength maximum accompanied by an increase of ϵ relative to the ultraviolet spectrum of the chloro-derivative (IIIa); a similar shift is characteristic of the majority of compounds (I) obtained from the chloro-derivative (Ia) as a result of the replacement of its chlorine atom by other substituents. Comparison of the infrared spectra of the isomeric 3,7- and 1,7-dimethylhypoxanthines shows clearly in the latter a shift of the characteristic bands of the amide carbonyl towards longer wavelengths, in full agreement with data[23] indicating a decrease of the C—O vibration frequency in purines having the *p*-quinonoid structure relative to other purine derivatives.

Certain characteristics of compounds of type (I) arising from their structure are not typical for this series alone (cf. Refs. 24—26). They are typical to some extent for many purines, including those substituted at the nitrogen atoms of the pyrimidine ring, but not for 6- or 2-aminopurines unsubstituted in the imidazole ring. Such aminopurines have been obtained in different ways, for example by direct alkylation or glucosidation of adenine[27-31], *N*-benzoyladenine, or 6-dimethylaminopurine[32], by synthesis from the corresponding 4,5-diaminopyrimidines[33-35], or from 3-methylguanine by the reaction of the latter with P_2S_5 and subsequent alkylation of the resulting 2-amino-6-mercapto-3-methyl-3,6-dihydropurine and substitution of the alkylthio-group in the 6-position by various groups[26,32].

It has been shown convincingly by ultraviolet spectroscopy and ^1H NMR that these compounds exist in the amino- and not in the imino-form and that consequently substitution at $N_{(1)}$ or $N_{(3)}$ should be accompanied by the transfer of a proton from the imidazole ring of the aminopurines to the pyrimidine ring and migration of double bonds, which results in an *o*- or *p*-quinonoid structure of the purine stabilised by the substituent at the ring nitrogen atom. These and many other purine compounds with an unusual fixed distribution of double bonds differ from purine derivatives having the "classical" structure by their chemical behaviour and spectroscopic characteristics. These differences are shown particularly clearly when there is a substituent at the $N_{(3)}$ atom and in most cases they are very similar to the differences characteristic of compounds of series (I), which were mentioned above. It is self-evident that substitution at the nitrogen atom of the imidazole ring of aminopurines is not reflected in the state of the system, since it involves merely a simple replacement of the proton and does not entail changes in the distribution of double bonds[36].

2. Synthesis of $C_{(6)}$-Substituted Derivatives of 2,3-Dihydro-3,7-dimethyl-2-oxopurine

The applications of the reaction of theobromine with phosphoryl chloride are not limited to the synthesis of compounds of series (I). This reaction is also used to synthesise certain isomeric derivatives of the 6-R-2,3-dihydro-3,7-dimethyl-2-oxopurine series (XVI). 8-Chloro- and 8-methyl-derivatives of (XVI) [compounds (XVII) and (XVIII)] can be obtained similarly from the 8-chloro- and 8-methyl derivatives of theobromine [(XII) and (XIII)].



(a, R = MeO)
(b, R = EtO)
(c, R = PrO)
(d, R = BuO)
(e, R = MeS)
(f, R = NH_2)
(g, R = MeNH)
(h, R = Me_2N)
(i, R = Cl)

(XVI; R=H); (XVII; R=Cl);
(XVIII; R=Me)

6-Alkoxypurines (XVI, a—d) have been obtained by treating with the corresponding alcohols the product of the reaction of theobromine with $POCl_3$ and subsequent hydrolysis with $NaHCO_3$ solution[37].

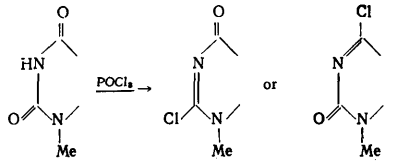
The structures of these compounds have been confirmed by many reactions and that of compound (XVIb) has been demonstrated unambiguously by its identification with the compound obtained by allowing sodium ethoxide to react with 1,2-dihydro-3,7-dimethyl-6-methylthio-2-oxopurine (XVIe) known previously under the trivial name "6-methylthiotheobromine"[38,39]. When compound (XVIb) was heated with ammonia, methylamine, and dimethylamine, the corresponding 6-amino-derivatives (XVIf), (XVIg), and

(XVIh) were obtained, the last two being identical with the compounds synthesised by allowing the same amine to react with compound (XVIe).[40]

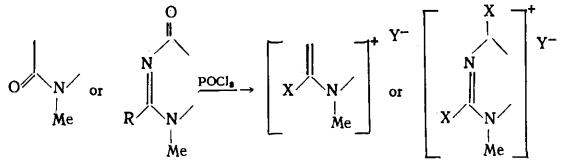
It is noteworthy that the properties of compound (XVIa) agree fully with those described for dihydromethoxy-3,7-dimethyloxopurine obtained by the methanolysis of the tetra-acetate of theobromine β-D-glucoside[41].

The above syntheses are not merely of preparative value. They throw light on the essential features of the reactions, occurring when *N*-methyloxopurines are heated with $POCl_3$ and also on certain problems concerning the structures of the primary products of these reactions (this is discussed in greater detail in Section III).

Depending on the method of treatment of the residue obtained after distilling off the excess $POCl_3$ from the reaction mass (treatment with $NaHCO_3$ solution or with alcohol first and only then with aqueous $NaHCO_3$), it is possible to obtain from compound (IV) either the chloro-derivative (Ia) [10] or one of the compounds of type (XVI, a–d),[40] each in a yield exceeding 50%. This undoubtedly shows that the members of both isomeric series, (I) and (XVI), have a common precursor, which is formed by the reaction of both carbonyl groups with $POCl_3$. One of them (probably either one) should react with $POCl_3$, by virtue of the presence of a proton at the neighbouring ring nitrogen atom, via the general mechanism of the conversion into the corresponding chloro-derivative of 2- and 4-oxo-(hydroxy)pyrimidines[42], α-oxo(hydroxy)purines[1], and also oxo(hydroxy)-derivatives of other nitrogen heterocycles:

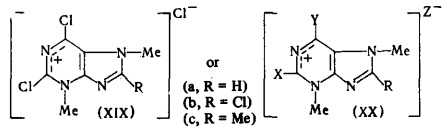


The second carbonyl probably reacts with $POCl_3$ as an *N*-substituted cyclic amide, which may result in the formation of a fairly stable compound containing the amidochloride group[43]:



(where X and Y are both Cl or Cl and $OPOCl_2$)

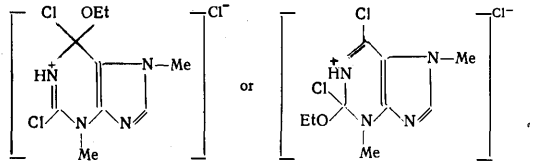
Since each carbonyl group of theobromine or its derivatives (XII) and (XIII) is probably capable of reacting in either way, the primary products of their interaction with $POCl_3$ are compounds (XIX) or (XX):



(X, Y and Z = Cl or Cl and $OPOCl_2$)

The presence of amidochloride groups in these compounds has been confirmed by numerous reactions[43], primarily by their ability to combine with an alcohol molecule to form the hydrochlorides of amidoester chlorides.

In the present instance the crystalline substances formed when alcohols are allowed to react with the products of the reaction of (IV), (XII), or (XIII) with $POCl_3$ are of this kind. The overall formula $C_9H_{13}N_4Cl_3O$ of the crystalline compound obtained from (IV) after treatment with ethanol makes it possible to attribute to it the structure of the hydrochloride of 2,6-dichloro-6(or 2)ethoxy-3,6(or 2,3)-dihydropurine [(XXI) or (XXII)]:



Many reactions of this compound—hydrolytic cleavage at low pH, aminolysis, interaction with thiourea, etc.—are consistent with both structure (XXI) and (XXII) and there are no grounds for making a choice between them, since in either case the same products should be obtained: theobromine, the hydrochloride of 6(2)-amino-3,6(3,2)-dihydro-2(6)-imino-3,7-dimethylpurine and 2,6-dithiotheobromine[44]. On the other hand, the formation from it of 6-ethoxy-2,3-dihydro-3,7-dimethyl-2-oxopurine (XVIb) on hydrolysis in a neutral medium undoubtedly indicates that the ethoxy-group is at $C_{(6)}$, i.e. there is evidence that the compound has the structure (XXI). This is also shown by another reaction characteristic of amidoester chlorides, namely the thermal cleavage of the ester chloride group accompanied by the evolution of an alkyl chloride and the regeneration of the initial amide[43].

When the above amidoester chloride is heated, ethyl chloride is liberated and the chloro-derivative (Ia) is formed in a high yield. Since the fragment C(Cl)(OEt) must be the precursor of the carbonyl group, the formation of the chloro-derivative (Ia) as a result of the thermal cleavage constitutes yet another confirmation of the presence of the ethoxy-group in the amidoester chloride at $C_{(6)}$ and not at $C_{(2)}$, i.e. of structure (XXI) rather than (XXII).

On the other hand, the formation of the amidoester chloride (XXI) from the amidochloride compound (XIXa) or (XXa) suggests that the ring carbon atom $C_{(6)}$ in the latter is more electrophilic than $C_{(2)}$ and that consequently the substituents in the 6-position in (XIX) and (XX) should undergo hydrolytic cleavage first, with regeneration of the carbonyl group. Therefore it is quite reasonable that hydrolysis at pH 7 of the intermediates obtained from theobromine on heating the latter with $POCl_3$ results in the formation of the monochloromonoxopurine (Ia) as the main product, both substituents (at $C_{(6)}$ and $C_{(2)}$ atoms) undergoing hydrolytic cleavage only under more severe conditions (pH 2–3).

This sequence in the hydrolytic cleavage of the intermediate does not, however, rule out the probability of the simultaneous formation in the hydrolysis also of a certain amount of another monoxopurine, namely the isomeric 6-chloro-2,3-dihydro-3,7-dimethyl-2-oxopurine (XVIi). In practice it proved impossible to isolate this compound from the reaction mass (see below), but the study of similar reactions with 8-substituted theobromine derivatives, (XII) and (XIII), showed that 2-chloro-6-oxopurines (XIV) and (XV) are not the only products of hydrolytic cleavage at pH ~7 of the intermediates (XIX, b and c) or (XX, b and c) and that the formation of small amounts of the isomeric 6-chloro-2-oxo-derivatives (XVIIi) and (XVIIIi) does indeed occur[20,22].

It was also impossible to isolate 6,8-dichloro-2-oxopurine (XVIIi) in a pure state after hydrolysis, but its presence in the unpurified dichloro-derivatives (XIV) was demonstrated chromatographically and confirmed by the

formation of the 6-ethoxy-derivatives (XVIIb) in the reaction with sodium ethoxide. It was identified with specimens of the compound (XVIIb) obtained in two ways: by treating (XVIb) with sulphuryl chloride[45] and by the hydrolysis of the 8-chloro-derivative of the amidoester chloride (XXI).[20] Both isomeric monochloro-oxo-3,7-dimethylpurines ($C_8H_8ClN_4O$) were comparatively readily isolated in 43 and 9% yields only in the reaction of 8-methyltheobromine (XIII) with $POCl_3$. The former was characterised as the 2-chloro-6-oxo-derivative (XV) and the latter proved to be 6-chloro-2-oxopurine (XVIIIk). As a result of the substitution of chlorine by other groups, they gave rise to two series of compounds—8-methyl derivatives of (I) and (XVIII).

The ultraviolet spectra of compounds (I) and their 8-methyl derivatives with the same substituent R proved to be very similar, just as the ultraviolet spectra of (XVI) and (XVIII) are similar, differing from the former pair by the bathochromic shift of the long-wavelength maximum. Possibly this can be accounted for by the presence in these compounds of the straight conjugation chain $O{=}C_{(2)}{-}N{=}C_{(6)}R{-}C_{(5)}{=}C_{(4)}{-}N{=}C_{(8)}$.[20] The study of the ultraviolet spectrum of unpurified (Ia), isolated directly in the hydrolytic reaction at pH 7 of the product of the interaction of theobromine with $POCl_3$, suggests that in this case a small amount of a second isomer, i.e. (XVIi), can nevertheless be formed in the course of the hydrolysis. The isomer (XVIi) probably cannot be isolated from the reaction mixture because it is formed in comparatively small amounts and, by virtue of its high reactivity, is completely hydrolysed to theobromine[46].

III. AMIDOCHLORIDE DERIVATIVES OF THE PURINE SERIES

1. Phosphorodichloridates and Their Structure

The ability of theobromine and its 8-substituted derivatives to be converted on heating with $POCl_3$ into compounds of the amidochloride type† is not a distinctive feature of 3,7-dimethyldioxopurines. It is characteristic also of other oxopurines methylated at $N_{(1)}$ or $N_{(3)}$, which react with phosphorus chlorides in the form of cyclic *N*-methylamides[47-49].

The properties of amidochlorides and adducts of the amidochloride type have been investigated in comparative detail only recently. The initial objects of these investigations were DMF and other aliphatic acid amides[50,51] and then cyclic *N*-substituted lactams—1-methylpyridone, 1-methylquinolone, etc.[52] In 1966 an adduct obtained from 4-dimethylamino-1,3-dimethyluracil was described[53]. The hypothesis of the formation of cyclic amidochlorides or adducts as a result of the reaction of $POCl_3$ with *N*-methyloxopurines was put forward somewhat earlier[47] and the first experimental data confirming it were published.

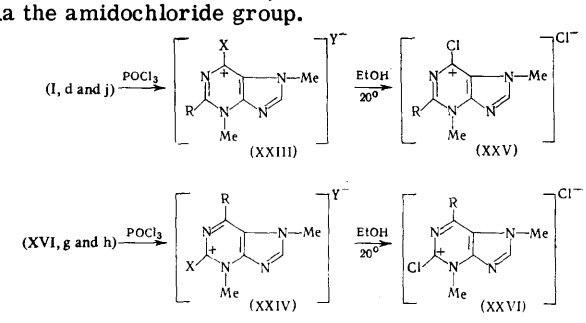
† In this review the name amidochlorides is given only to the true amidochlorides having the general structure [N—C(Cl)—]$^+$Cl$^-$, for example compound (XIX), while all the amidochloride products obtained by the addition of acid chlorides to *N*-methyloxopurines will be referred to by the general term adducts. These therefore include the phosphorodichloridates [N—C(X)—]$^+$Y$^-$ (X and L = Cl and $OPOCl_2$) formed as a result of the addition of $POCl_3$ to *N*-methyloxopurines for example (XX).[43]

Depending on the nature of the initial *N*-methylated oxopurine, the products of the reactions with $POCl_3$, isolated from the reaction mass on cooling the latter or after partial distillation of $POCl_3$, may be amidochlorides or, as happens in most cases, the phosphorodichloridates [—N(Me)—C(X)—]$^+$Y$^-$ or [—N(Me)—CR=N—C(X)—]$^+$Y$^-$ (X and Y = Cl and $OPOCl_2$). The reaction product is sometimes a mixture of the amidochloride and the phosphorodichloridate[48,49,54].

The conversion of 1,9- and 3,7-dimethylxanthines (2,6-dioxopurines), their 8-substituted derivatives, and 2-chloro-derivatives of 1,9- and 3,7-dimethylhypoxanthines (IX, R = Cl) and (Ia) into phosphorodichloridates requires fairly prolonged refluxing with $POCl_3$. For other monooxopurines, for example, 6-R-2,3-dihydro-3,7-dimethyl-2-oxopurines (XVI), heating at 50—60°C for 5—30 min is sufficient, while the majority of the isomeric 2-R-3,7-dimethylhypoxanthines (I), with the exception of the chloro-derivative (Ia), react vigorously with $POCl_3$ at 20°C, the reactions in many instances occurring with spontaneous evolution of heat[54].

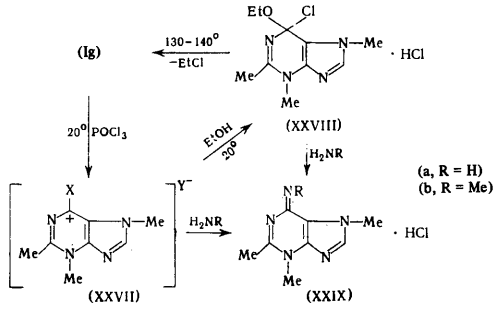
Purine phosphorodichloridates and amidochlorides are crystalline substances, almost insoluble in non-polar solvents and usually fairly and sometimes very soluble in $POCl_3$. Therefore the isolation of the phosphorodichloridates from the reaction solutions obtained as a result of the reflexing of *N*-methyloxopurines with $POCl_3$ sometimes involves appreciable difficulties. In particular, the phosphorodichloridate (XXa), formed when theobromine is refluxed with $POCl_3$, cannot be isolated from the reaction solution. It has to be converted, by being passed through a solution of hydrogen chloride, into the less soluble amidochloride (XIXc), which crystallises from the solution. To obtain the phosphorodichloridate (XXa) in a pure state and to characterise it, the purified chloro-derivative (Ia) was made to react briefly with a small amount of $POCl_3$ at a moderate temperature (60—80°C).[46] The crystalline adduct (XXa) formed is hydrolysed at pH ~7 to the initial chloro-derivative (Ia), exactly like the overall product of the reaction of compound (IV) with $POCl_3$, obtained after the distillation of the latter from the reaction solution.

Like other adducts of the purine series, the phosphorodichloridates have the properties of the amidochlorides. One of these, the ability to combine with an alcohol molecule and be converted thereby into the hydrochlorides of amidoester chlorides, does not, however, extend to all purine phosphorodichloridates. For example, those which have been obtained from the isomeric 2- and 6-methylamino-derivatives of 3,7-dimethyloxopurines [I, d and j) or (XVI, g and h)], i.e. the phosphorodichloridates (XXIII) and (XXIV), react slowly with alcohols at room temperature and are converted into the corresponding amidochloride (XXV) or (XXVI), but do not combine with alcohol via the amidochloride group.

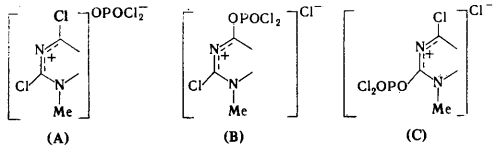


(R = MeNH or Me_2N; X and Y = Cl or $OPOCl_2$

In contrast to these, the phosphorodichloridate (XXVII), obtained from the 2-methyl derivative (Ig) is readily converted on treatment with alcohol into the hydrochloride of the amidoester chloride (XXVIII), which was found to undergo all the reactions characteristic of compounds belonging to this class. Thus, on treatment with ammonia or monoalkylamines, it is converted into the hydrochlorides of 6-amino(or alkylimino)-2,6-dihydro-2,3,7-trimethylpurine (XXIX, a and b) and its ester chloride group is cleaved on heating with evolution of ethyl chloride and the formation of the hydrochloride of the initial oxopurine (Ig).[54]



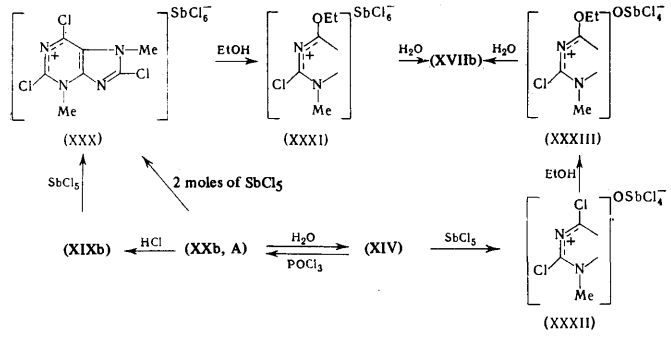
In order to make a choice between the three possible structures of the phosphorodichloridates (XX)—(A), (B), and (C)—a study was made of the interaction of (XXb) with antimony pentachloride[55].



The reaction with two moles of antimony pentachloride led to an almost quantitative yield of the hexachloroantimonate (XXX), i.e. to the replacement of the $\overset{\oplus}{O}POCl_2$ residue by the $SbCl_6$ residue. When the adduct (XXX) was treated with alcohol, one of the chlorine atoms was exchanged for the ethoxy-group and the resulting hexachloroantimonate of the ethoxy-derivative, i.e. the adduct (XXXI), was converted as a result of hydrolysis in a neutral medium into the known compound (XVIIb). These last two reactions also take place with high yields.

Analysis of the quantitative aspects of the above reactions—the theoretical yield of the hexachloroantimonate (XXX) and the high yields of compounds (XXXI) and (XVIIb) obtained from it—permitted the conclusion that the initial phosphorodichloridate (XXb) is a pure compound and not a mixture of the isomers (A), (B), and (C) and that the $SbCl_6$ residue in compound (XXX) and hence the $OPOCl_2$ residue in the initial phosphorodichloridate (XXb) constitute the anionic part of the molecules of these adducts and not a fragment of their cationic component. On the basis of these findings, it is suggested that the phosphorodichloridate (XXb) most probably has the structure (A), which is in full agreement with current ideas about the structure of the adduct obtained when $POCl_3$ is allowed to react with DMF: $[-HC(Cl)NMe_2]_2OPOCl_2^-$.[56]

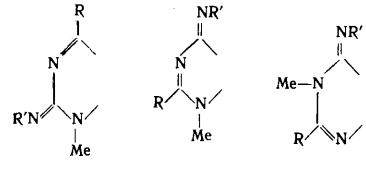
The adduct (XXX) is also formed as a result of the addition of one mole of antimony pentachloride to the amidochloride (XIXb), which in turn is obtained by the reaction of hydrogen chloride with a solution of the phosphorodichloridate (XXb) in $POCl_3$.[55] Yet another antimony-containing purine adduct (XXXII) with the $OSbCl_4$ residue is formed when 2,8-dichloromonoxopurine (XIV) reacts with antimony pentachloride, by analogy with the method of the synthesis from it of the phosphorodichloridate (XXb) by reaction with $POCl_3$.[46] Like the adduct (XXX), it reacts with alcohol, whereby it is converted into the ethoxy-derivative (XXXIII), in which the position of the ethoxy-group at $C_{(6)}$ was confirmed by the formation of (XVIIb) from it. The entire series of the above reactions fits the scheme illustrated below[55,57]:



Phosphorodichloridates, other purine adducts, amidochlorides, and also amidoester chlorides are comparatively stable in the absence of moisture, but are rapidly hydrolysed by water with regeneration of the initial oxopurines. They are particularly reactive in reactions with nucleophilic agents—ammonia, amines, alkoxides, etc.[2]

2. *C*-Iminopurines

Amidochloride compounds of different classes—aliphatic, aromatic, and heteroaromatic—are known to react with ammonia and primary amines to form amidines[50,52,58,59]. In the amidines obtained from purine amidochlorides, adducts, and amidoester chlorides[54] one of the nitrogen atoms forms part of the pyrimidine ring in the purine system.

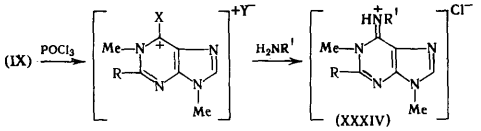


Consequently these amidines are $C_{(2)}$ or $C_{(6)}$-iminopurines, which differ from *C*-aminopurines by their high basicity (pK_a = 10—12, instead of 3—4).

The first iminopurines alkylated at the nitrogen atoms of both rings of the purine system, namely $N_{(1)}$-alkyl-6-iminopurines, were described about 30 years ago. They were obtained from 4-amino-5-cyano-1-methylimidazole[60] or by the alkylation of adenosine, adenylic acid, and other adenine derivatives substituted at the nitrogen atom of the imidazole ring[61–66].

The method of preparation of *C*-iminopurines from *NN*-dimethyloxopurines, based on the intermediate formation of amidochloride compounds and treatment of the latter with ammonia or monoalkylamines[67], has led to new possibilities in the synthesis of this unusual group of purine derivatives. It permits the variation of the structure of the substituents at the exocyclic nitrogen atom by employing a wide variety of primary amines and also the introduction of additional groups at the second ring carbon atom of the pyrimidine part of the molecule.

The first series of iminopurines obtained in this way—the hydrochlorides of 2-R-1,6-dihydro-6-imino-1,9-dimethylpurines (XXXIV)—were synthesised from compounds (IX) in accordance with the following scheme[48,49]:



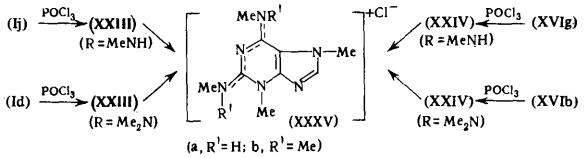
(X and Y = Cl or $OPOCl_2$; R' = H or Me)

The hydrochlorides of $C_{(6)}$- and $C_{(2)}$-imino(or alkylimino)-3,6(or 2,3)-dihydro-3,7-dimethylpurines, including 6-imino-2,3,7-trimethylpurines (XXIX, a and b) mentioned above, were synthesised similarly from 2-R(or 6-R)-3,7-dimethyloxopurines (I) and (XVI).[54]

If the substituent R in (XXIII) and (XXIV) is an amino- or monoalkylamino-group, it is possible to obtain the same aminoiminopurine from the corresponding representatives of two different series—(I) and (XVI). For example, the hydrochloride of 2,6-di(methylamino)-3,7-dimethylpurine (XXXVa) was obtained from (Ij) and (XVIg) by treatment with methylamine[67].

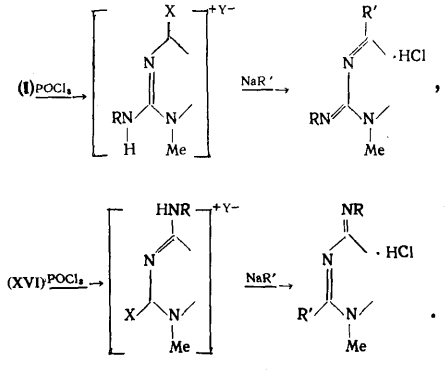
The problem of which exocylic nitrogen atom (at $C_{(2)}$ or at $C_{(6)}$) undergoes protonation in this case remains open.

Under similar conditions, the two isomeric phosphorodichloridates obtained from (Id) and (XVIh) react with dimethylamine to form 2,6-bis(dimethylamino)-3,7-dimethylpurinium chloride (XXXVb).



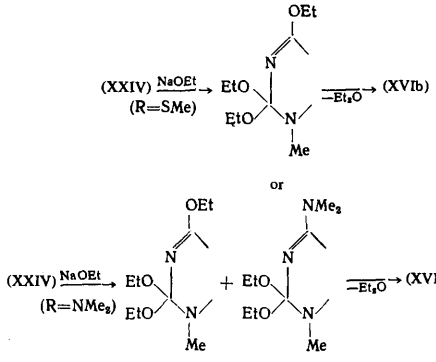
(a, R'=H; b, R'=Me)

This method of synthesis of *C*-iminopurines can be usefully employed to obtain compounds substituted at the second ring carbon atom ($C_{(2)}$ or $C_{(6)}$) by alkoxy-groups or other substituents capable of reacting with $POCl_3$ or of being substituted by amines. The *C*-methyl group also interferes with the reaction, since its presence entails charring of the reaction mass on heating with $POCl_3$. In such cases the synthesis can be carried out in accordance with another, more universal scheme based on the use of *C*-amino- or monoalkylamino-oxopurines as starting materials. The amino-group in the phosphorodichloridates or amidochlorides formed from them plays the role of a potential imino-group, while the labile substituent is introduced into the latter by treatment with nucleophilic agents such as alkoxides, sodiomalonic ester, sulphides, etc.

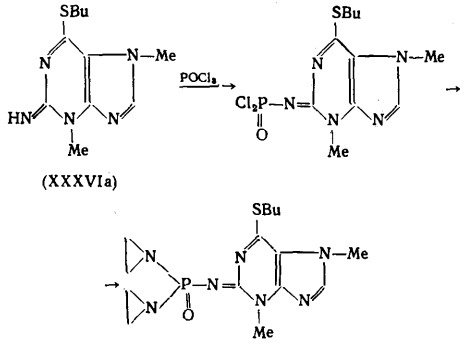


(X, Y=Cl, $OPOCl_2$)

When purine amidochloride or phosphorodichloridate, in which the substituent R is an alkylthio-, dialkylamino-, or other group without a hydrogen atom capable of migrating to form a tautomer, is acted upon by an alkoxide, the final reaction product is the initial oxopurine. Its formation from the amidochloride compound is accompanied by the formation of a dialkyl ether, probably as the result of the cleavage of an unstable intermediate acetal[68]. In such reactions there is a possibility also of a simultaneous replacement of the residue R, linked to $C_{(6)}$, by an alkoxy-group, for example:

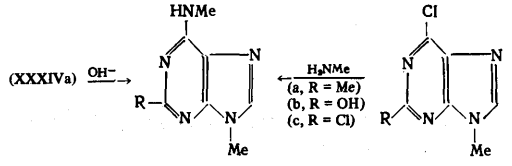


As was to be expected, the *C*-iminopurines, whose basicity is close to that of aliphatic amines, are much more vigorously acylated and, in particular, react much more vigorously with $POCl_3$ than *C*-aminopurine, which are much less basic. Whereas the formation of acid dichlorides of 7(or 9)-methyl-6-phosphoramidopurines requires prolonged heating of the initial $C_{(6)}$-aminopurines with an excess of $POCl_3$,[69] the iminopurine bases, for example (XXIX), (XXXIVa, R = Me), the two isomeric $C_{(6)}$- and $C_{(2)}$-butylthio-2-imino-3,7-dimethylpurines (XXXVIa), and the corresponding 6-imino-derivatives (XXXVIb) react with a calculated amount of $POCl_3$ in methylene chloride at a temperature as low as 15—20°C. A number of diaziridides of *NN*-dimethylpurinylphosphoramidic acids were synthesised in this way for biological tests from the acid dichlorides of *NN*-dimethylpurinylphosphoramidic acids by reaction of the latter with aziridine in the presence of hydrogen chloride acceptors[70]. These reactions are illustrated schematically below using compound (XXXVIa) as an example:



When 6-imino-1,9-dimethylpurines (XXXIV) are heated with a solution of alkali, various reactions take place, which are greatly influenced by the substituent R in the 2-position. Compound (XXXIVa) undergoes the Dimroth rearrangement in an alkaline medium, i.e. is converted into 2,9-dimethyl-6-methylaminopurine (XXXVIIa), which

is identical with the compound obtained from 6-chloro-2,9-dimethylpurine (XXXVIII) and monomethylamine:



(R'=Me) (XXXVII) (XXXVIII)

When monoalkylamino-derivatives (XXXIV, R = NHMe) are acted upon by alkali, there is partial hydrolytic cleavage of the 6-imino-group and the final reaction product consists of a mixture of the initial iminopurines and 2-monoalkylamino-1,9-dimethylhypoxanthines.

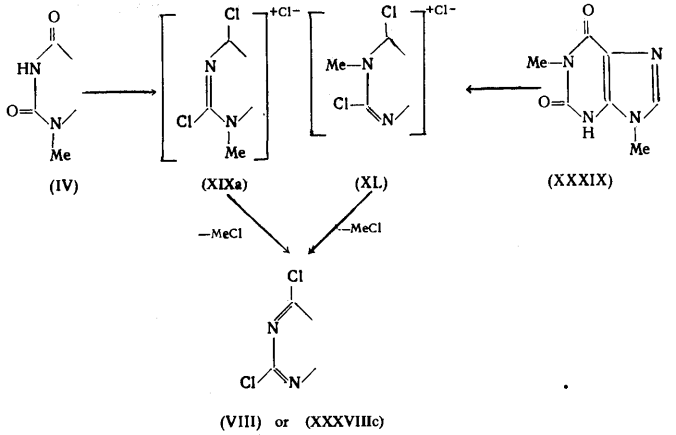
On the other hand, when the dimethylamino-group is present in the 2-position, the reaction product is 2-hydroxy-6-monomethylamino-9-methylpurine (XXXVIIb), since in this case two processes probably take place: the Dimroth rearrangement and hydrolytic elimination of the dimethylamino-group[49].

3. The Cleavage of Purine Adducts and Amidochlorides

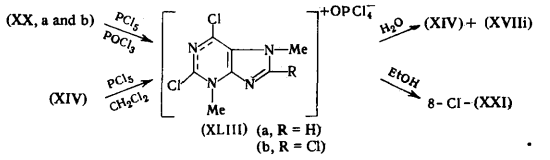
Another feature of *NN*-dialkylamidochlorides, which is of considerable preparative importance together with nucleophilic substitution reactions, is their capacity to undergo cleavage with liberation of an alkyl chloride and to be converted thereby into imidochlorides:

$$Alk_2N{-}CO{-}\rightarrow [Alk_2N{-}C(Cl){-}]^+Cl^- \xrightarrow{-AlkCl} AlkN{=}C(Cl){-},$$

i.e. to undergo the reaction on which a method of dealkylation of dialkylamines, known for a long time, is based[71]. Accordingly, the conversion of theobromine into 2,6-dichloro-7-methylpurine (VIII) and also the analogous conversion of the isomeric 1,9-dimethylxanthine (XXXIX) into 2,6-dichloro-9-methylpurine (XXXVIIIc) [11] can be represented as the demethylation of cyclic *N*-methylamides, which leads to the formation of cyclic iminodchlorides and proceeds with formation of the intermediate amidochlorides (XIXa) and (XL).



The amidochlorides (XIX, a and b) are readily cleaved on heating with $POCl_3$, liberating methyl chloride[57], and are converted at the same time into 2,6-dichloro-7-methylpurines (VIII) and its 8-chloro-derivative (XLI) in high yields. In contrast to these, the phosphorodichloridates (XX, a and b) undergo such cleavage only to a slight extent even on prolonged refluxing with $POCl_3$.

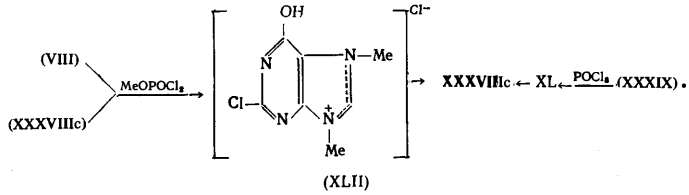


The reason for this difference may be that, on being cleaved, the phosphorodichloridates split off not only the volatile methyl chloride but also the high-boiling methyl phosphorodichloridate ($MeOPOCl_2$), which remains in the reaction sphere and alkylates the imidochlorides formed as a result of the cleavage.

The hypothesis that this ester can alkylate (cf. Lugovkin and Arbuzov[72]) 2,6-dichloropurines was confirmed by the preparation of 8-chlorotheobromine (XII) by heating the trichloride (XLI) with $MeOPOCl_2$ in $POCl_3$ and by the hydrolysis of the product:

$$(XLI) + MeOPOCl_2 \rightarrow (XXb) \xrightarrow{H_2O} (XII).$$

The ring nitrogen of not only the pyrimidine component but also of the imidazole component of the molecule can be methylated under these conditions: when $MeOPOCl_2$ was allowed to react with the two isomeric $N_{(7)}$- and $N_{(9)}$-methyl derivatives of 2,6-dichloropurine [(VIII) and (XXXVIIIc)], the same compound was isolated after treating the products with water—2-chloro-7,9-dimethylhypoxanthinium chloride (XLII):



The same chloro-derivative (XLII) was detected in the reaction product after heating 1,9-dimethylxanthine (XXXIX) with $POCl_3$ (cf. Pfleiderer[73] and Gutorov[74]).

The formation of 2,6-dichloro-7-methylpurines from the phosphorodichloridates (XX) can also be facilitated by agents other than hydrogen chloride, the purines being converted into the readily cleaved amidochlorides (XIX). Tertiary amines have also come to be used in reactions of this kind. For example, on heating with $POCl_3$ in the presence of *NN*-dimethylaniline[75], theobromine is known to be converted into the dichloro-derivative (VIII) in 25% yield instead of 10—15%.[3] It has been suggested that in this reaction tertiary amines can partly promote the processes occurring because they prevent the elimination from the reaction sphere of the hydrogen chloride which promotes the conversion of the phosphorodichloridate (XXa) into the readily cleaved amidochloride (XIXa). Indeed, the use of dimethylanilinium hydrochloride instead of the base increased the yield of (VIII) to 35—40%. Nevertheless the yields in this reaction or in the analogous syntheses of (XLI) or (XXXVIIIc) continued to be fairly low, evidently due to side processes involving the *para*-condensation of the intermediate amidochloride and the adduct with dimethylaniline[2,76].

In order to rule out the possibility of the *para*-condensation side reaction, dimethylanilinium hydrochloride was replaced by triethylammonium hydrochloride (the hydrochloride of a tertiary amine), which cannot block the

intermediate phosphorodichloridates. This replacement immediately led to an appreciable enhancement of the yields: 2,6-dichloro-7-methylpurine (VIII) and its 8-chloro-derivative (XLIII) were obtained in 90—95% yield and the yield of 2,6-dichloro-9-methylpurine from 1,9-dimethylxanthine (XXXIX) was 75%.[76]

The most effective method for synthesising 2,6-dichloro-7-methyl- or 2,6-dichloro-9-methyl-purines [(VIII), (XLI) and (XXXVIIIc)] from the corresponding $N_{(3)}$- or $N_{(1)}$-methyloxopurines involves the conversion of the intermediate phosphorodichloridates into more readily cleaved phosphorus-containing adducts, which differ from the phosphorodichloridates by the fact that their anion is $OPCl_4^-$ instead of $OPOCl_2^-$.[57]

The formation of these new adducts, which for brevity may be called phosphorotetrachloridates, is achieved by treating solutions of phosphorodichloridates in $POCl_3$ with phosphorus pentachloride. Being much less soluble in this solvent than the initial phosphorodichloridates, the phosphorotetrachloridates can be crystallised comparatively rapidly. The phosphorotetrachloridates (XLIII, a and b)‡ were obtained in this way from the phosphorodichloridates (XX, a and b) and the phosphorotetrachloridate (XLIIIb) was obtained in addition by treating 2,8-dichloro-6-oxopurine (XIV) in methylene chloride with phosphorus pentachloride.

The ability to be readily cleaved with formation of 2,6-dichloropurines constitutes the most significant difference between phosphorotetrachloridates and phosphorodichloridichloridates. Their cleavage is accompanied by the liberation of $POCl_3$ and methyl chloride. It takes place comparatively rapidly on heating not only in $POCl_3$ but also in chlorobenzene, as well as in the absence of a solvent at the melting point and leads to the formation of 2,6-dichloropurines in high yields[57]. An example of the employment of the principle of the conversion of phosphorodichloridates into phosphorotetrachloridates is provided by the preparative syntheses of 2,6-dichloro-7-methylpurines (VIII) and (XLI) from theobromine[5,20,21].

The remaining properties of the phosphorotetrachloridates are very similar to those of the phosphorodichloridates and they exhibit all the features typical for purine adducts and amidochlorides. For example, the hydrolysis of the phosphorotetrachloridate (XLIIIb) in a neutral medium leads to the formation of a mixture of 2,8- and 6,8-dichloro-3,7-dimethylmonoxopurines (XIV) and (XVIIj), while in the reaction with ethyl alcohol it is converted into the amidoester chloride [the 8-chloro-derivative of (XXI)][57].

Presumably the phosphorotetrachloridates are not the last link in the long chain of reactions undergone by dimethylxanthines on treatment with $POCl_3$ compounds which are completed by the elimination of $N_{(3)}$- or $N_{(1)}$-methyl groups and the formation of 2,6-dichloropurines (VIII), (XLI), or (XXXVIIIc). It appears most likely that the cleavage of the phosphorotetrachloridates is a two-stage consecutive process and that the true precursors of 2,6-dichloro-7-methyl- or 2,6-dichloro-9-methyl-purines are the thermally unstable amidochlorides formed as a result of the elimination of $POCl_3$ from the phosphorotetrachloridates.

The principal stages of the process, illustrated by the schemes quoted in this review, can be followed experimentally for 3,7-dimethylxanthines. Nevertheless one cannot claim that this represents all the features of the complex conversion of *NN*-dimethylxanthines into the corresponding 2,6-dichloromonomethylpurines. It is quite probable that this process includes also additional hitherto undetected stages, which should be investigated further.

‡ The conversion of phosphorodichloridates into phosphorotetrachloridates is probably a result of the chlorination of the $OPOCl_2^-$ anion by phosphorus pentachloride and not of the exchange of its phosphorus-containing component $POCl_2$ for the PCl_4 residue. This hypothesis followed from the experimental preparation of the phosphorotetrachloridate (XLIIIb) by treating the phosphorodichloridate (XXb) with $^{32}PCl_5$ at 20°C in $POCl_3$: the yield of the resulting phosphorotetrachloridate was 92—94% and its molar radioactivity hardly reached 5% of the value for the initial $^{32}PCl_5$.

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Stereochemical Results of Electron Transfer

Z.V.Todres

Data characterising the contribution of electron transfer processes to the stereochemistry of reactions of organic compounds are discussed and the stereochemical changes accompanying electron transfer are analysed. It is shown that the decrease of the barrier to rotation in electron transfer facilitates the *cis–trans* isomerisation of ethylenes and an increase of the difference between the energies of the rotational isomers of certain radical-ions relative to neutral molecules decreases the rate of mutual rotation. The influence of the formation of ion pairs by the anionic and cationic components of the radical-ion salts on the stabilisation of unusual geometrical forms of the molecule is discussed. The conversion of cyclopolyenes into ionic forms with a ring current of delocalised electrons, which fixes the ring atom in a single plane, is considered as a special case of electron transfer. The chemical and physical properties of cyclo-octatetraene, azocine, and their ionic forms are compared. The bibliography includes 143 references.

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I. INTRODUCTION

Electron transfer processes occupy an increasingly important position in modern ideas about reaction mechanisms[1,2]. It is assumed that the migration of atoms or atomic groups in a chemical reaction is preceded by electron transfer from one of the reacting molecules to the other[3]. Thus, by taking into account the role of electron transfer processes, it is possible to extend significantly the available information about the mechanism of the given reaction and facilitate thereby the selection of the optimal conditions for its occurrence. Naturally, the study of electron transfer processes has become possible only when new instrumental research techniques, particularly ESR, NMR, and microwave spectroscopy of chemically polarised nuclei, have been introduced into chemical practice.

Electron transfer results in products with new interesting properties. We may note that one-electron transfer gives rise to products corresponding to the transfer of a unit charge from the donor (D) to the acceptor (A). Products of incomplete transfer (donor–acceptor complexes) have been adequately investigated. Since the studies of Izmail'skii[4,5] and then Brackman[6] and Mulliken[7], considerable advances have been made in the elucidation of the structure of charge-transfer complexes and their thermodynamic and spectroscopic characteristics[8,9]. Much attention is devoted at present to the determination of the role of these complexes in reaction mechanisms[10,11]. Molecular complexes are formed when the interaction between D and A is insufficient for complete charge transfer; in complete charge transfer the products are radical-ion salts or even free radical-ions:

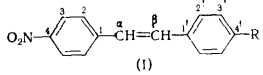
$$D + A \rightarrow [D^{\delta+}, A^{\delta-}] \rightarrow [D^{\cdot}, A^{\cdot-}] \rightarrow D^{+} + A^{-}.$$

Naturally, molecules involved in charge transfer undergo changes in their electronic structure to a greater extent the stronger the donor–acceptor interaction. There is also then a possibility of a qualitatively new result when the change in electronic structure leads to a change in molecular geometry. However, due attention has not so far been paid to the geometrical consequences of electron transfer. In considering the properties of charge-transfer complexes it has usually been assumed that on formation of the complex neither the donor nor the acceptor undergoes a change in its geometry (see, for example, Hanstein et al.[12]). This was based on the conclusion reached by Orgel and Mulliken[13] that the geometry of charge-transfer complexes (or the steric effect) does not in general influence the position of the spectral charge-transfer bands.

On the other hand, X-ray diffraction studies have shown that the formation of the radical-ion salt $[D^{+}, A^{-}]$ entails a serious distortion of the geometry of the initial molecule. For example, the conversion of the neutral molecule of 7,7,8,8-tetracyanoquinodimethane into the radical-anion is accompanied by an increase in the length of the multiple bonds and a shortening of the single bonds. This effect has been observed for the rubidium[14], morpholinium[15], and *N*-ethyl-1-methylbenzimidazolium[16] salts.

II. GEOMETRICAL ISOMERISATION AS A RESULT OF ELECTRON TRANSFER

The addition of a further electron to the 7,7,8,8-tetracyanoquinodimethane molecule leads to a change in its electronic structure: the multiple bond orders are reduced and those of single bonds are increased[14]. A similar change in bond orders is revealed also by quantum-mechanical calculations by the Hückel molecular orbital method for electron transfer to *p*-nitrostilbene and its substituted derivatives with the general formula (I).[17] In the radical-ion the order of the $\alpha-\beta$ bond is reduced and those of the $1-\alpha$ and $\beta-1'$ bonds are increased. The orders of the $2-3$ and $2'-3'$ bonds in the ring are also increased, while those of the $1-2$ ($1'-2'$) and $3-4$ ($3'-4'$) are diminished.



(I)

Similar results were obtained in calculations on the radical-ions of *p*-nitrobiphenyls [18]. Thus calculations have shown that electron transfer to nitrostilbenes (I) can lead to changes in the electronic structure which verge on the formation of a quinonoid structure or the ethylenic $\alpha-\beta$ bond approaches a single bond. In the ground state of the stilbene molecule the rotation of the benzene rings around the ethylenic bond is forbidden. However, the partial decrease of the double-bond character of the link between the atoms α and β as a result of electron transfer should probably lead to some decrease of the energy barrier to rotation. The presence of the nitro-group in stilbenes naturally promotes this conversion into the quinonoid form. Therefore, recent calculations on the ionic forms of unsubstituted stilbene, carried out by a combination of the Coulson–Hay and LCAO-MO methods [19] are extremely interesting. These calculations have shown that the conversion of stilbene into a radical-cation or a radical-anion lowers the barrier to *cis–trans* isomerisation almost by a factor of 2. The results of the calculations are presented in Fig. 1. In order to assess their validity, it is important to note that the calculated energy of the *cis–trans* isomerisation of the neutral stilbene molecule agrees well with thermochemical measurements [19]. The calculated geometrical parameters of stilbene and the results of X-ray diffraction analysis are also satisfactorily consistent [19]. The calculated barrier to the *cis–trans* isomerisation of stilbene (35.4 kcal mole^{-1}) agrees well with the experimental value (36.7 kcal mole^{-1}) and the predicted value for the first excited state is extremely low, as has in fact been assumed in the familiar models for the photoisomerisation of stilbene [19].

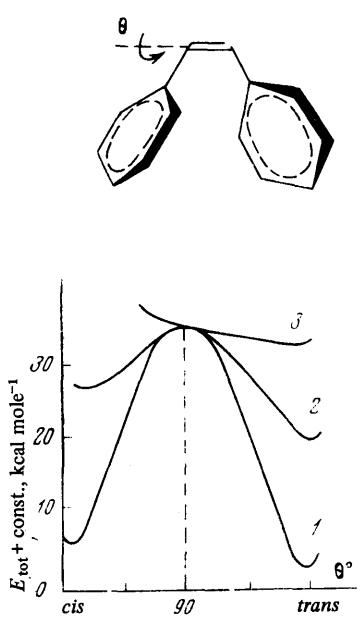
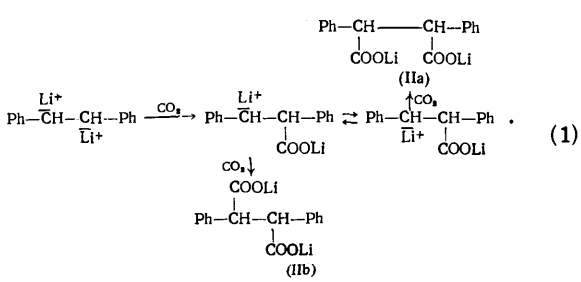


Figure 1. Changes in the energy E_{tot} of the stilbene molecule and radical-ion as a function of the angle of rotation of the ring θ about the central ethylenic bond ($\theta = 0°$ for the *cis*-configuration): 1) neutral molecule; 2) radical-anion or radical-cation; 3) molecule in the first excited state.

From the standpoint of the results of these calculations, it is interesting to consider the experimental data concerning the behaviour of olefins in reactions where electron transfer may be an intermediate stage. Schlenk and Bergmann [20,21] established that, when ethylenic compounds are treated with alkali metals in ethers, the products are adducts which react with carbon dioxide to from dicarboxylic acids. The steric structures of these acids were found to be determined by the nature of the metal employed and not by the configuration of the initial ethylene. It was discovered that the reaction of vicinal and organodimetallic derivatives with methyl iodide gives rise to the initial ethylenes and not to methylation products. Under these conditions, only the *trans*-isomer is obtained from both *trans*- and *cis*-stilbenes after treatment with metals and then with methyl iodide. An admixture of *trans*-stilbene appeared in certain experiments on the carboxylation of the products obtained by the treatment of *cis*-stilbene with alkali metals.

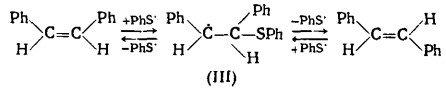
The results of Schlenk and Bergmann were tested by Wright and coworkers [22,23] and by Doran and Waack [24]. It was found that olefins give rise very readily to products resulting from the addition of two alkali metal atoms (dianions) with a change in colour. The electronic spectra of the stilbene dianion and radical-anion differ little [24] and the ESR spectra have not been recorded. On treatment with dimethyl sulphate, the stilbene metallation product gives rise to 2,3-diphenylbutane, while the reaction with methyl iodide, methyl alcohol and benzoyl chloride regenerates the stilbene, which always has the *trans*-structure. Since alkali metals, which can cause exhaustive reduction of the ethylenic double bond, were used in the reaction, it may be that these observations are due to the characteristics of the structure of the stilbene dianion. Szwarc and coworkers [25] believe that the *cis*-stilbene radical-anion is stable and that the product of the two-electron transfer (the dianion) actually undergoes isomerisation. According to Suzuki et al. [26], the stilbene dianion is almost planar and its alkali metal salts in ethereal solvents are ionic aggregates in which cations are located close to the carbon atoms of the central ethylenic bond above and below the plane of the molecule. The substitution of one of the ethylenic carbon atoms results in mutual rotation [27]. This is why the same mixture of the dilithium salts of *meso*- and (±)-diphenylsuccinic acids, (IIa) and (IIb), in proportions of 2 : 1 [reaction (1)] was obtained by Wright [22] in the carboxylation of the dilithium adducts of both *cis*- and *trans*-stilbenes.



(1)

cis-Stilbene is converted similarly into the *trans*-form on heating in the presence of traces of thiophenol. It was established that [28] the isomerisation is due to the addition

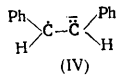
(and subsequent elimination) of the phenylthiyl radical to stilbene [reaction (2)]:



(2)

(III)

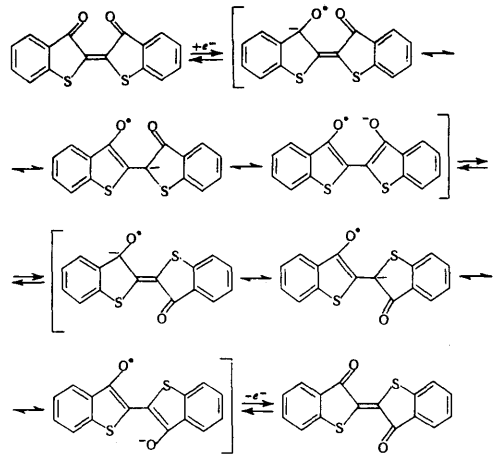
In contrast to the transfer of two electrons, the capture of one electron does not by itself convert stilbene into the almost "hydrogenated" product. However, the state of the central ethylenic bond in this radical-anion (IV) approaches that of the radical (III).



(IV)

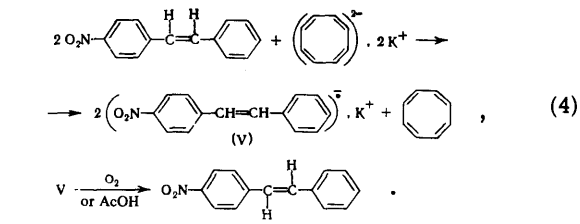
Johnson and Chang [29,30] attempted to compare the ESR spectra of the radical-anions of *cis*- and *trans*-stilbenes and to compare the rates of electron transfer from these radical-anions to the corresponding neutral molecules. They assumed that the ESR spectra should differ at least slightly and that the rate of electron transfer to *cis*-stilbene should differ from the rate of simple electron exchange between *trans*-stilbene and its radical-anion if the process is associated with a change in configuration. Electron exchange between species with similar configurations should be faster [31]. It was found that the ESR spectra of the potassium or tetra-alkylammonium salts of the radical-anions of *cis*- or *trans*-stilbene do not differ significantly. However, Johnson and Chang emphasise that the absence of differences between the ESR spectra does not alone indicate that *cis*- and *trans*-stilbenes give rise to radical-anions with the same structure. It was not possible to discover differences between the rates of electron transfer from the radical-anion to the neutral molecule either. In the formation of the stilbene radical-anion in the presence of a large amount of the *cis*-isomer, it was impossible to measure the broadening of the ESR line during the exchange and hence calculate the electron transfer rate constant. Having modified the method for the formation of the radical-anions, Chang and Markgraf [32] were able to detect by ESR a difference between the kinetics of electron transfer reactions involving *cis*- and *trans*-stilbenes. For this purpose, it was necessary to employ ultraviolet irradiation. However, irradiation sharply reduces the activation barrier to isomerisation (cf. Fig. 1). Clearly, under such conditions one observes only the rates of complex processes and the values obtained cannot be attributed to electron transfer alone. The reaction rate constants for *trans*- and *cis*-stilbenes are 10^9 and 10^3 litre mole^{-1} s^{-1} respectively. If the electron transfer rate constants differed by this amount, the implication would be that the stilbene radical-anions have the *trans*-configuration. However, it has been noted in a number of studies that irradiation of the radical-anions with ultraviolet light entails their *cis*–*trans* isomerisation and not *trans*–*cis* isomerisation, as for the corresponding neutral compounds [33,34].

Chang et al. [35] used a combination of the ESR and ultraviolet irradiation methods also in the investigation of the radical-anions formed in the reduction of thioindigo with metallic potassium. No difference was observed in the rates of electron exchange between the thioindigo radical-anion and the *cis*- and *trans*-isomers of thioindigo. However, the authors nevertheless suggest that the paramagnetic species formed from thioindigo has the *trans*-structure. They believe that the mutual repulsion of the carbonyl groups, which is sharply enhanced after electron transfer [reaction (3)], is the driving force of the isomerisation.



(3)

Direct evidence for *cis*–*trans* isomerisation as a result of electron transfer was obtained [36] in a study of the reaction of the dipotassium derivative of cyclo-octatetraene with nitro-derivatives of stilbene of type (I, R = H or NO_2) in tetrahydrofuran (THF). The reaction is homogeneous in THF. Dipotassiocyclo-octatetraene is a fairly weak reducing agent. After giving up its electrons, it is converted into neutral cyclo-octatetraene, whose yield can be readily determined. All these factors make it possible to specify exactly the amount of donor, to estimate the extent of electron transfer, to determine the nature of the products, and to elucidate their reactivities. It was established that under these conditions 4-nitro-*cis*-stilbene (I, R = H) gives rise to the potassium salt of a radical-anion, whose ESR spectrum was obtained and analysed. After treatment of the products of reaction (4) with oxygen, 4-nitrostilbene was isolated as a mixture of the *cis*- and *trans*-isomers in proportions of 1.5 : 1 in an overall yield of 80%. The electron transfer reaction went to completion under these conditions (there was a quantitative formation of cyclo-octatetraene). When equimolar amounts of the donor and acceptor were used, i.e. under the conditions of two-electron reduction of 4-nitro-*cis*-stilbene, only partial *cis*–*trans* isomerisation was again observed. Oxygen abstracts an electron from the radical-anion, for example the reaction of the potassium salt of nitrobenzene with oxygen in THF results in the formation of nitrobenzene in 80% yield. The neutral compound is formed also on treatment of the potassium salt of nitrobenzene in THF with water [37]. When the products of the electron transfer to 4-nitro-*cis*-stilbene are treated with water or acetic acid, the same mixture of the *cis*- and *trans*-isomers of 4-nitrostilbene is formed in an overall yield of 90%. [36] Since neither oxygen nor the resulting potassium acetate gives rise to any chemical changes in the 4-nitro-*cis*-stilbene solution in THF, it was concluded that the reaction proceeds in accordance with reaction (4).



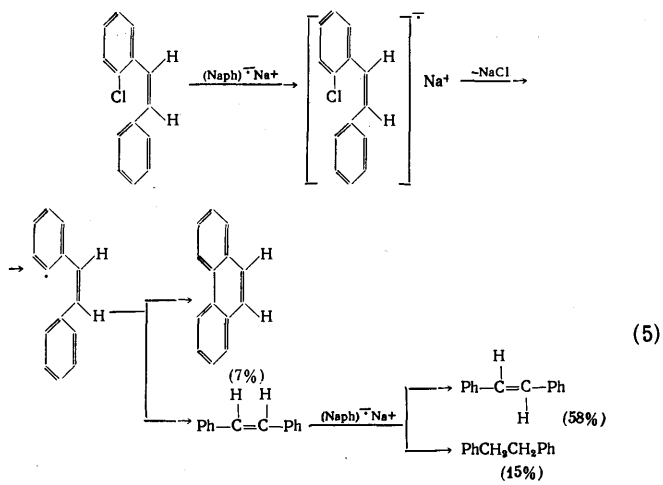
(4)

(V)

The one-electron transfer to 4-nitro-*trans*-stilbene under these conditions leads to the recovery of the initial

trans-isomer and the quantitative formation of cyclo-octatetraene. The absence of the isomerisation of 4-nitro-*trans*-stilbene is probably due to the fact that, under the reaction conditions, the energy barrier to the rearrangements of the radical-anion of this compound to the *cis*-isomer is much higher than for the *trans*-trans-formation of the radical-anion of 4-nitro-*cis*-stilbene. Thus, according to Golebiewski and Parczewski [19], the conversion of the *cis*-stilbene radical-anion into the *trans*-isomer requires approximately 10 kcal mole^{-1}, while the conversion of the *trans*-form into the *cis*-form of the radical-anion requires about 18 kcal mole^{-1} (Fig. 1). The symmetrical 4,4'-dinitro-*cis*-stilbene is completely converted into the *trans*-isomer on treatment with dipotassio-cyclo-octatetraene and then with oxygen or acetic acid [38]. It is interesting that protonation of the radical-anions or dianions of *p*-nitrostilbenes does not lead to the formation of *p*-nitrobibenzyls, i.e. the ethylenic bond is not hydrogenated. This finding is unexpected, since electron-transfer from sodionaphthalene to stilbene in THF leads to bibenzyl after protonation [see reaction (5)]. [39] The introduction of the nitro-group into stilbene should, of course, promote reduction. In nitrostilbene the additional electron is probably effectively held by the nitro-group, which prevents the addition of protons to the carbon atoms of the ethylenic bond. In other words, the degree of electron saturation of the central ethylenic bond in the products under consideration is sufficient for isomerisation but not for the addition of protons.

The conclusions reached in the study of the stereochemical results of electron transfer are consistent with the literature data concerning the behaviour of the corresponding neutral compounds under conditions where electron exchange is possible. Thus selective reduction of 4,4'-dinitrostilbene with tin in hydrochloric acid leads to 4,4'-diamino-*trans*-stilbene regardless of whether the initial dinitro-compound has the *cis*- or *trans*-configuration [40]. On treatment with potassium methoxide, 4-nitro-*cis*-stilbene is converted into a mixture of the *cis*- and *trans*-isomers [41]. On treatment with lithium in ether and then with carbon dioxide, 4-chloro-*cis*-stilbene gives rise to a mixture of products consisting of 4-chloro-*trans*-stilbene, 4-chloro-*cis*-stilbene, and *trans*-stilbene-4-carboxylic acid [42]. The reaction of 2-chloro-*cis*-stilbene with an excess of sodionaphthalene [(Naph)$^-$Na$^+$] in THF leads to phenanthrene, bibenzyl, and *trans*-stilbene. Singh and Kumar [39] explain the observed reactions in terms of reaction (5).



(5)

The addition of an electron to the double bond evidently lowers the barrier to rotation about the bond. The one-electron reduction of ethylenic compounds can be regarded in a certain sense as a stage in the conversion into ethane derivatives. From this point of view, it is important, in principle, to know the stereochemical results of the abstraction of an electron from the double bond. Calculations have shown [19] that the enhanced stability of the *trans*-form is also characteristic of the stilbene radical-cation, i.e. the one-electron oxidation product. The experimental confirmation of this finding is still inadequate. It is known [43] that fuming nitric acid induces the *trans*-isomerisation of *cis*-stilbene. The conversion of *cis*-stilbene into *trans*-stilbene under the influence of iodine [43] may proceed via the formation of the stilbene radical-cation and the iodide anion, which then give rise to neutral stilbene (*trans*-form) and iodine. In this case complete charge transfer may not, of course, necessarily occur. The isomerisation takes place in a complex where the donor and acceptor orbitals strongly overlap. Indeed, *cis*- and *trans*-stilbenes form in hexane solution different complexes with iodine, which give rise to charge-transfer bands at 354 and 365 nm respectively [44]. It is not clear from the literature whether the bands merge after a time and microwave spectroscopic studies have not been made on the system. Furthermore, it would be interesting to show whether the interaction leads to the appearance of paramagnetic species, i.e. whether the ^{1}H NMR signal of the olefinic protons of *cis*-stilbene shifts as a result of the mixing of the reactants. For example, in the presence of the stable 2,2,6,6-tetramethylpiperidin-1-oxy-radical the signal of the $\overset{|}{=}C-H$ protons in dimethyl maleate shifts towards a high field [45]. The signals of the methyl protons of dimethyl maleate remain in the same position. Hence it follows that a complex is formed in which the orbitals of the unpaired electron of the radical overlap with the π orbitals of the dimethyl maleate double bond. In the presence of nitroxy-radicals there is a sharp increase in the rate of isomerisation of dimethyl maleate to dimethyl fumarate and the radicals are not consumed. The probability of the isomerisation of maleate in a complex with the radical exceeds by seven orders of magnitude the probability of the isomerisation of its free molecule [45].

According to Il'ina [46], the oxidation of *cis*-stilbene by the salts $Mn(OAc)_3$ and $Co(OAc)_3$ in acetic acid or by the salt $Tl(OCOCF_3)_3$ in trifluoroacetic acid leads to a mixture of acetates (or trifluoroacetates) of hydrobenzoin (*meso*-type) and isohydrobenzoin [(±)-type]. As in the synthesis of diphenylsuccinic acids according to Scheme 1, the amount of *meso*-derivatives obtained is approximately twice as large as that of the (±)-derivatives. This ratio of stereoisomers holds for *trans*-stilbene, but the oxidation is faster. When $Mn(OAc)_3$ in acetic acid is used, *trans*-stilbene is oxidised seven times faster than *cis*-stilbene. Part of the olefin remains unchanged at the end of the process and an appreciable amount of the *trans*-isomer is produced from *cis*-stilbene. Bivalent metal salts, for example $Mn(OAc)_2$, formed as a result of the reaction cannot induce the *trans*-isomerisation of *cis*-stilbene. Such isomerisation is not caused by trifluoroacetic acid either. When $Tl(OCOCF_3)_3$ in CF_3COOH was used as the oxidant, stilbene radical-cations were detected, their amount decreasing in the course of the reaction. Il'ina [46] proposed reactions (6) and (7), according to which one-electron oxidation of stilbene involves the intermediate formation of the radical-cation, possibly in the form of the complex (VI). This stage is reversible. If the

starting compound in reaction (6) is *cis*-stilbene, then the organic part of the complex (VI) is capable of at least partial *cis–trans* isomerisation. The conversion of (VI) into an acetoxy-derivative and oxidation of the resulting radical (VII) lead to the complex (VIII), which decomposes with formation of the final products (IXa) (*meso*-type) and (IXb) [(±)-type], as in reaction (7).

$$\underset{(cis\text{- or }trans\text{-})}{PhCH{=}CHPh} + Tl(OCOCF_3)_3 \overset{CF_3COOH}{\rightleftharpoons} \underset{(VI)}{[PhCH\dot{C}HPh][Tl(OCOCF_3)_3]^-} \xrightarrow{CF_3COOH}$$

$$\rightarrow \underset{(VII)}{[PhCH(OCOCF_3)CHPh]} + Tl(OCOCF_3)_2;$$

$$2Tl(OCOCF_3)_2 \xrightarrow{fast} Tl(OCOCF_3)_3 + TlOCOCF_3\ , \qquad (6)$$

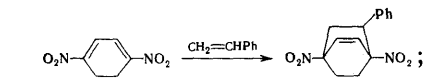
$$VII + Tl(OCOCF_3)_3 \xrightarrow{CF_3COOH} \underset{(VIII)}{[PhCH(OCOCF_3)\dot{C}HPh][Tl(OCOCF_3)_3]^-} \xrightarrow{CF_3COOH}$$

$$\rightarrow \underset{(IX)\ [a)meso\text{-};\ b)\ (\pm)\text{-}]}{PhCH(OCOCF_3)CH(OCOCF_3)Ph} + Tl(OCOCF_3)_2;$$

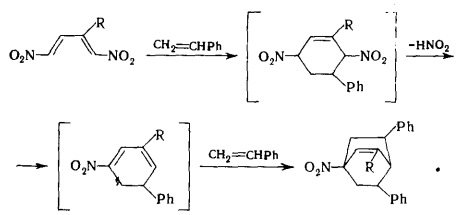
$$2Tl(OCOCF_3)_2 \xrightarrow{fast} Tl(OCOCF_3)_3 + TlOCOCF_3\ . \qquad (7)$$

The salt $Tl(OCOCF_3)_2$, which should be paramagnetic disproportionates very rapidly[47] [see reactions (6) and (7)]. This leads to the formation of the diamagnetic thallium(III) and thallium(I) trifluoroacetates and the ESR spectrum reveals the presence of the stilbene radical-cations only. Owing to its high acidity, in trifluoroacetic acid the addition of the acetoxy-group to the double bond proceeds via the one-electron oxidation to the radical-cation and not via the addition of Tl^{3+} to one of the olefinic atoms (as in acetic acid[48]).

From the standpoint of the changes in geometry induced by electron transfer, it is interesting to consider again the mechanism of the 1,4-addition of dienes to the ethylenic bond (the Diels–Alder reaction). An early charge transfer stage[49], associated with a change in the geometry of the initial reactants, is also possible in this process. Naturally, this effect can appear most clearly when there is a difference between the polarities of the diene and dienophile. The reaction of styrene with 1,4-dinitrobuta-1,3-diene constitutes an example with a very large difference of this kind. Clearly the dinitro-derivative must be regarded as an electron acceptor in relation to styrene. Dienes of this type are inactive in the classical diene synthesis reaction[50], but they do react with nucleophilic dienophiles of the styrene type[51]. The reaction is therefore of "inverse" electronic type. 1,4-Dinitrocyclohexa-1,3-diene reacts with styrene under comparatively mild conditions (100°C, 10 h, in xylene) with formation of a 1 : 1 adduct [reaction (8)].[51] The fixed *S-cis*-configuration of this diene remains unchanged also in the intermediate stages, which ensures that the familiar rules of Alder and Stein[49] hold. Since the configuration of the open-chain 1,4-dinitro-1,3-dienes may change in the initial stage of the reaction, more severe conditions are required for the formation of adducts. The reaction proceeds only on heating at 140°C for 40 h in the absence of solvent and is accompanied by the elimination of the nitro-group and a second interaction with the dienophile [reaction (9)].[51] Presumably, more severe conditions are needed to impart to the diene component of the transition complex the configuration required for the formation of the ring†.



(8)



(9)

The occurrence of *cis–trans* isomerisation in the chemical reaction involving an electron transfer stage was confirmed by Fraser and Taube[53], who investigated the reaction of Cr^{2+} or V^{2+} ions with complex salts containing the (methyl maleato)pentamminecobalt(III) cation. In an acid medium an oxidation–reduction reaction takes place, as a result of which there is not only a decrease of the charge of the complex cation by unity but the cation also exchanges the methyl maleate ligand for water [reaction (10)]:

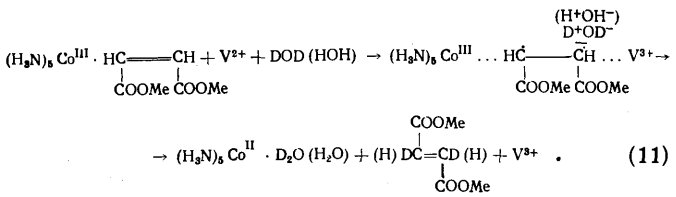
$$[Co(NH_3)_5 \cdot (CHCOOMe)_2]^{3+} + Cr^{2+}\ (or\ V^{2+}) + H_2O \xrightarrow{HClO_4}$$

$$\rightarrow [Co(NH_3)_5 \cdot H_2O]^{2+} + Cr^{3+}\ (or\ V^{3+}) + (CHCOOMe)_2\ . \qquad (10)$$

The liberated ligand is hydrolysed in an acid medium to ethylene-1,2-dicarboxylic acid. Under these conditions, not all the acid formed has the *cis*-configuration corresponding to the ligand in the initial complex. Fumaric acid (*trans*) is formed together with maleic acid (*cis*); the amount of the latter is greater the higher the concentration of perchloric acid in the reaction mixture. A mixture of isomeric acids is formed in the presence of D_2O and the C–D bond is present only in fumaric acid but not in maleic acid. When the (methylfumarato) pentamminecobalt(III) cation is reduced in D_2O [reaction (10)], only fumaric acid without an admixture of maleic acid is formed and which does not contain C–D bonds. Probably electron transfer from Cr^{2+} or V^{2+} to the complex ion proceeds via the mechanism of the socalled "double exchange"[54]. The reducing agent (Cr^{2+} or V^{2+}) transfers an electron to the bridging group (maleate) and the latter transfers it further to the oxidising agent [cobalt(III)]. Thus the bridging $(CHCOOMe)_2$ group is alternately reduced and oxidised with isomerisation of maleic acid to fumaric acid. When the electron is localised at the ethylenic bond, the addition of a proton (deuteron) takes place. After the abstraction of an electron from the ethylenic bond, the H^+ ion (in H_2O) or H^+ and D^+ ions in (D_2O) are split off. Hydrogen isotope exchange involving the –C=C– bond is observed. The conversion of cobalt(III) into the bivalent form proceeds simultaneously with the substitution of the ethylenedicarboxylic acid diester in

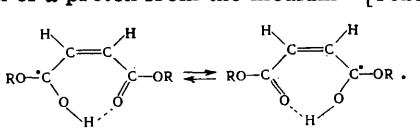
† A somewhat similar situation arises in the dehydration of fumaric acid to maleic anhydride on heating. Eliel believes[52] that at a high temperature the dehydration is preceded by the migration of the double bond. Thermal isomerisation has been observed for many olefins; in all such compounds there is a barrier to rotation about the double bond of about 40 kcal $mole^{-1}$.[52]

the inner sphere of the complex by a water molecule [reaction (11)].



(11)

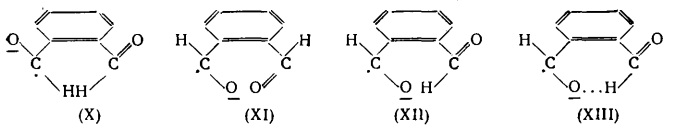
The absence of hydrogen isotope exchange involving the ethylenic bond in the dimethyl fumarate ligand can be explained by the fact that in this case the bridge is not directly involved in the electron transfer. The role of this ligand is more likely to be to bring closer together the two positively charged ions for "direct electron exchange" [54] between their overlapping orbitals. Fraser and Taube's study [53] contributed much to the elucidation of the mechanism of the inner-sphere electron transfer. At the same time an explicit relation between electron transfer and geometrical transformations was first noted. A few more studies were then made in which the properties of the products resulting from electron transfer to dialkyl fumarates or dialkyl maleates were compared [55-59]. It was shown that in pyridine, dimethyl sulphoxide (DMSO), and dimethylformamide (DMF) these compounds are reduced in stages [55-57]. Radical-anions capable of undergoing one-electron oxidation are formed in the first stage. The half-wave potentials for the reduction of maleate and fumarate differ but the one-electron oxidation of the resulting radical-anions is characterised by the same half-wave potentials. The above relations between the $E_{1/2}$ for the cathodic and anodic waves hold also at a very high alternating frequency, up to 500 Hz. [57] This implies that the radical-anions formed from maleate and fumarate have similar energies. The ESR spectra of the products of the electrochemical reduction of dimethyl fumarate and maleate are identical at the potential of the limiting currents of the first waves regardless of the temperature at which they are recorded [58]. According to the authors, it is unlikely that the ESR spectra of the *cis*- and *trans*-radical-anions are completely identical. Thus, if it is assumed that the ESR spectra of the *cis*- and *trans*-radical-anions should differ, the above observation indicates a rapid and almost complete *trans*-isomerisation of the *cis*-radical-anions. At the same time, if the radical-anions are obtained in a proton-donating medium, the *cis*- and *trans*-isomers give rise to different ESR [60] and electronic [59] spectra. Under these conditions, maleates evidently give rise to unusually stable radical-anions, whose structure is fixed by the formation of a ring with participation of a proton from the medium [59] [reaction (12)].



(12)

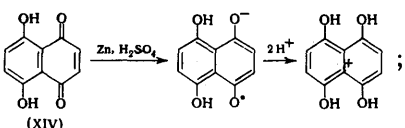
III. INFLUENCE OF COORDINATION INTERACTIONS ON THE STEREOCHEMISTRY OF ELECTRON TRANSFER PRODUCTS

Carbonyl compounds capture an electron and are converted into ketyls, which contain a negatively charged oxygen atom. This atom is a particularly powerful proton acceptor. Reaction (12) shows how the formation of a hydrogen bond prevents the *cis*–*trans* isomerisation of the maleate ester, which can occur on electron transfer. The enhancement of the affinity of the negatively charged carbonyl oxygen for a proton ensures the formation of stable hydrogen bonds with molecular fragments which are otherwise incapable of it. An example is provided by the C–H fragment of the aldehyde group. The radical-anion of phthalaldehyde is planar [61] and therefore might exist in three forms: *exo*- (X), *enao*- (XI), and *meso*- (XII):

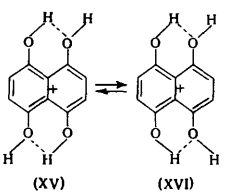


(X) (XI) (XII) (XIII)

Only the *meso*-conformer, in which the mutual orientation of the functional groups ensures the formation of a hydrogen bond involving the proton of one aldehyde group and the negatively charged oxygen atom of the other [structure (XIII)], can be detected by ESR. The influence of hydrogen bonds of this type on the conformation of electron transfer products is shown also when the negative charge of the oxygen atom is neutralised by protons from the medium. Thus the reduction of naphthazarin (XIV) with zinc dust in sulphuric acid leads to the radical-cation of naphthazarin semiquinone [reaction (13)], whose ESR spectrum changes with temperature [62]. This variation has been attributed to mutual interconversions of the *cis*- and *trans*-forms (XV) and (XVI) respectively. The equilibrium position (and hence the form of the ESR spectrum) can be represented at a specified temperature with satisfactory accuracy if it is assumed that the isomerisation mechanism includes the dissociation of the intramolecular hydrogen bond via mechanism (14). The exchange of the hydroxyl protons of the radical-cation with the medium is then much slower than isomerisation. The height of the potential barrier to isomerisation is 3–5 kcal and is comparable to the energy of the hydrogen bond in systems of type (XV) (3–7 kcal). [62]

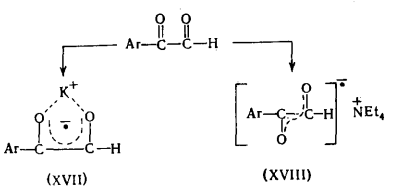


(XIV) (13)



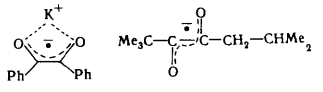
(XV) (XVI) (14)

The conformation of the semidione is fixed even more rigidly when an alkali metal cation is coordinated to the two carbonyl groups. Thus the one-electron reduction of 3,4,5-trimethoxyphenylglyoxal with potassium t-butoxide in DMSO gives rise mainly to the *cis*-semidiones (XVII), while in the electrolysis in DMF, in the presence of tetraethylammonium perchlorate as the carrier electrolyte, the main product is the *trans*-isomer (XVIII) [63] [reaction (15)].



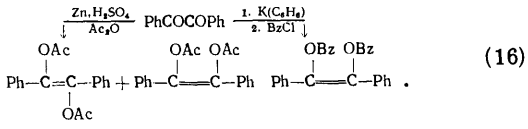
(XVII) (XVIII) (15)

The ESR spectrum of the sodium salt of the benzil ketyl in THF shows splitting due to Na^+ (0.6 G), while in the ESR spectrum of the sodium salt of the ketyl of 2,2,6,6-tetramethylhexane-3,4-dione in THF there is no splitting whatever due to Na^+.[64] While the benzil ketyl can give rise to the contact ion pair (XIX), the formation of a species of type (XX) from the 3,4-dione is difficult owing to steric hindrance. This semidione exists in the form of a free ion or an ion pair separated by solvent molecules.



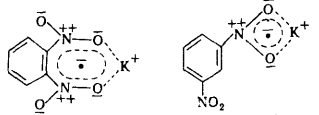
(XIX) (XX)

If the benzil ketyl ion does not form part of an ion pair, it exists in the *trans*-form, but in the case of the potassium salts the *cis*-form, in which both charged oxygen atoms are in the vicinity of the metal cation, [as in compound (XIX)] is more stable[65]. On benzoylation, such a radical-ion pair gives rise mainly to *cis*-dibenzoylethylene[65], while the reduction of benzil under conditions which do not stabilise the contact ion pair is not stereospecific[65,66] [reaction (16)].



(16)

The coordination of the potassium cation to two oxygen atoms in the radical-anion of *o*-dinitrobenzene leads to the stabilisation of the unusual configuration in which the nitro-groups are spread out in a single plane. In neutral *o*-dinitrobenzene the coplanarity of the two nitro-groups is ruled out both by calculation[67] and experiment[68,69]. In the potassio-derivative of *o*-dinitrobenzene (XXI) the coordination of the metal cation to both nitro-groups leads to the formation of a condensed "ring" in which there is a possibility of additional delocalisation of the unpaired electron. Indeed, the ESR spectra in dimethoxyethane (DME) or in THF show that the unpaired electron in (XXI) is equally delocalised over the two nitro-groups (the constants for the splitting by the nitrogen atoms $a_N^1 = a_N^2 = 3.2$ G),[70] while in the potassium salt of the radical-anion of *m*-dinitrobenzene (XXII) the delocalisation is essentially over only one of the two groups ($a_N^1 = 9.3$ G, $a_N^2 \leq 0.2$ G).[71,72] This contrasts sharply with ESR spectroscopic data for the radical-anions obtained by electrolysis in acetonitrile in the presence of tetra-n-propylammonium perchlorate as the supporting electrolyte: $a_N^1 = a_N^2 = 3.16$ G for *o*-dinitrobenzene and $a_N^1 = a_N^2 = 4.68$ G for *m*-dinitrobenzene[73]. The difference can be understood if account is taken of the nature of the counterion. When the counterion is a small cation (potassium), the formation of a closely knit ion pair is possible. The K^+ ion can than make its vacant *d* and *p* orbitals available for the π electrons of the radical-anion system[54]. When a tetraalkylammonium cation is used as the counterion, the mutual approach of species with different charges is hindered by the alkyl groups. Ion pairs with the potassium cation are stable, i.e. exist longer than is required for the detection of the ESR signal. This follows from a comparison of the polarographic behaviour of the three isomeric dinitrobenzenes in the same solvent (DMF) using tetraethylammonium or potassium perchlorate as the carrier electrolyte[74]. The half-wave potentials corresponding to the conversion of *p*- and *m*-dinitrobenzenes into radical-anions are independent of whether tetraethylammonium or potassium counterions are employed. The radical-anion is formed from *o*-dinitrobenzene at a potential more positive almost by 100 mV when tetraethylammonium perchlorate is replaced by potassium or sodium perchlorate. Changes in the composition and structure of the electrical double layer do not influence under these conditions the reduction mechanism, which has been shown by a special study[75] to consist of the reversible transfer of one electron. Since the transfer of one electron to *o*-dinitrobenzene in the presence of potassium perchlorate as the carrier electrolyte proceeds at a less negative potential than in the presence of tetraethylammonium perchlorate, it is clear that the potassium salt does indeed have the minimum energy, i.e. is characterised by the highest degree of delocalisation of spin density.

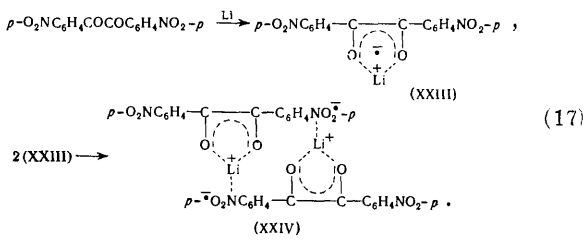


(XXI) (XXII)

The structure (XXI) favours greater delocalisation of the unpaired electron, but the anionic component of the salt is then forced to assume an unusual conformation. These properties of *o*-dinitrobenzene should be manifested also in chemical reactions, where, as can be seen from reaction (12), the role of the ring-closing species may be played by the proton. Indeed, the reduction of both nitro-groups at once is observed in the electrolysis of *o*-dinitrobenzene in the presence of water[76], while in the *para*-[76] or *meta*-isomer[77] only one nitro-group is reduced.

The relation between the distribution of spin density in the products of electron transfer to organic molecules and the behaviour of these products in reactions is important but has so far been little investigated. It would be especially useful to know the reason for the particular sequence of chemical changes in the groups present simultaneously in the molecule.

From this standpoint, it is interesting to examine electron transfer to 4,4'-dinitrobenzil [reaction (17)]. Paramagnetic species whose ESR spectra depend on temperature and concentration, are then formed. It has been shown[78] that such electron transfer products can exist in the monomeric or dimeric forms [(XXIII) or (XXIV) respectively]. The former is present at high dilution and the latter at an increased concentration or at a low temperature.



(XXIII) (XXIV) (17)

In form (XXIII) the unpaired electron is delocalised mainly over the dicarbonyl group and in form (XXIV) over the nitro-groups. Under these conditions, 4,4'-dinitrobenzophenone gives rise to radical-anions in which the nitro-group and not the carbonyl group carries the maximum electron density[78]. These results of the analysis of the ESR spectra are consistent with chemical data; on

reduction with tin in hydrochloric acid, 4,4′-dinitrobenzophenone is converted into 4,4′-diaminobenzophenone[79] and 4,4′-dinitrobenzil is converted into 4,4′-diaminodeoxybenzoin (p-$H_2NC_6H_4CH_2COC_6H_4NH_2$-$p$).[80]

IV. CONFORMATIONAL INHOMOGENEITY OF THE ELECTRON TRANSFER PRODUCTS

The radical-anions obtained from aromatic nitro-compounds retain a twofold symmetry axis. It follows from the analysis of the hyperfine structure of the ESR spectrum of the nitrobenzene radical-anion that this species contains protons of three kinds only; *ortho*-, *meta*-, and *para*-[81,82] [structure (XXV)].

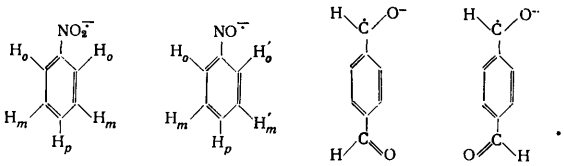
The situation is quite different in the conversion of nitrosobenzene into the corresponding radical-anion. According to ESR data[82,83], the nitroso-group is to some extent fixed in the plane of the ring after electron transfer. This leads to the appearance of five kinds of protons, since the two *meta*-positions (as well as the *ortho*-positions) become non-equivalent [structure (XXVI)].

The one-electron reduction of acetophenone leads to an ESR spectrum comprising 128 lines, corresponding to the three equivalent protons of the methyl group and the five non-equivalent ring protons[84].

The ESR spectrum of the products of the reversible one-electron reduction of benzaldehyde in DMF in the presence of tetra-alkylammonium supporting electrolytes contains 64 lines[84]. This form of the spectrum shows that the absence of a symmetry plane is characteristic of the benzaldehyde radical-anion. It was noted[85] that this unexpected result cannot be attributed solely to the interaction of the negatively charged carbonyl group with the nearest ring atoms. A more interesting phenomenon is probably involved—an unusual polarisation of the π-electron system of the radical-anion by the electric dipole of the charged carbonyl group.

The ESR spectra of the radical-anions of nitrobenzonitriles, obtained electrochemically in DMF,[86] show that the equivalence of the positions with respect to the nitrile group is maintained. This can be due either to the free rotation of the nitrile groups or to their linear disposition with respect to the symmetry axis of the molecule. The ESR spectra of the potassium salts of the radical-anions of terephthalonitrile in DME[87] demonstrate the equivalence of both the cyano-groups in the *para*-positions with respect to one another and of the benzene ring protons. It follows from the analysis of the hyperfine structure of the spectra that the constants for the splitting by the two nitrogen atoms are equal; also equal are the constants for the splitting by all the hydrogen atoms.

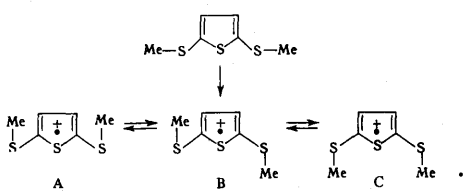
At the limiting current potential of the first reduction wave in DMSO in the presence of tetra-n-propylammonium perchlorate as the carrier electrolyte terephthalaldehyde gives rise to radical-anions, which exhibit two ESR spectra superimposed on one another. These spectra are characterised by the same g-factor, but have significantly different splitting constants[61,85]. If the rate (frequency) of rotation of the aldehyde groups were much higher than the frequency differences between the splitting constants of the rotational *cis*- and *trans*-isomers, the ESR spectrum of the radical-anions of terephthaldehyde would be averaged out. On the other hand, if the rate of mutual rotation of the groups were comparable to the frequency difference corresponding to the splitting in the spectra of the rotational *cis*- and *trans*-isomers, the ESR spectral lines would be broadened. Since a superposition of the spectra is observed, the implication is that the frequency of rotation is much smaller than the frequency difference corresponding to the splitting. It is unlikely that the observed superposition of the spectra could arise due to the presence of ion pairs with the same radical-anion but with different separations of the latter from the cation: a tetra-alkylammonium cation, which hardly forms ions pairs, was used in the above experiment[61,85]. Thus electron transfer to terephthalaldehyde leads to the formation of the two conformers (XXVIIa) and (XXVIIb).



(XXV) (XXVI) (XXVIIa) (XXVIIb)

The conformers (XXVIIa) and (XXVIIb) are physically distinguishable and the duration of their existence at any rate exceeds the ESR time constant, i.e. is greater than 1 ms. It follows from the analysis of the intensities of the corresponding signals that the rotational *cis*- and *trans*-isomers are formed in proportions of 1 : 1.4.[61,85] Conformationally inhomogeneous products were obtained also in electron transfer to 1,4-diacetylbenzene[88] and thianthrene-5,10-dioxide[89]. Durosemiquinone[90] and naphthazarin[62] are known to give rise to rotational *cis*- and *trans*-isomers of the radical-cations.

The oxidation of oximes leads to iminoxy-radicals having the general formula $R_2C{=}N{-}O^{\cdot}$. Under these conditions, *syn*-benzaldoxime yields both *syn*- and *anti*-isomers[91] and a similar result was obtained in the oxidation of benzophenone and fluorenone oximes[92]. Thiophen substituted in the 2- and 5-positions by methylthio-groups exists as one conformer only. One-electron oxidation with aluminium chloride in nitromethane results in the formation of conformationally inhomogeneous products, which may have structures A, B, or C. ESR showed the presence of the asymmetric conformer B and of one symmetrical conformer (A or B).[93]



A B C

The hindered rotation of the dimethylamino-groups about the bonds between the nitrogen atoms and the ethylenic carbon atoms is responsible for the presence of two types of methyl protons in the radical-cation of tetrakis(dimethylamino)ethylene[94]. Another instance of the restriction of the freedom of the mutual rotation of the groups was observed in Coppinger's cation, which is formed on oxidation of 3,3′,5,5′-tetra-t-butylbis-(4-hydroxyphenyl)methane[95].

The examples enumerated above are sufficient to illustrate the fact that the conjugation conditions in neutral molecules and in the corresponding one-electron transfer products are different. This entails a significant change in the mobility of the groups and ultimately a change in the energy relations of the rotational isomers. Thus calculations have shown[96] that the energies of the rotational *cis*- and *trans*-isomers of terephthalaldehyde differ by not more than 0.012 eV. On the other hand, in the series of

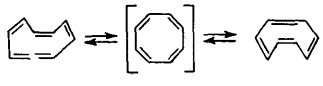
the corresponding radical-anions the *trans*-isomer (XXVIIb) is more stable than the *cis*-isomer (XXVIIa) by 0.083 eV, i.e. almost by 2 kcal. These calculations describe fairly completely the electronic structures of the molecules considered (the extended Hückel method with allowance for valence electrons by the Wolfsberg–Helmholtz method was used[97]). At the same time solvation and intermolecular electrostatic interaction effects would not of course be reflected when this approach is used. Therefore the observed quantitative difference between (XXVIIa) and (XXVIIb) can be far from the true values. Nevertheless, all the results show that electron transfer can significantly enhance the difference between the energy relations of the conformers.

Detailed study of the causes responsible for the conformational inhomogeneity of electron transfer products is one of the most attractive aspects of the present state of the investigations. There is a possibility of discovering general relations which are important and not self-evident.

V. ELECTRON TRANSFER AND CONFORMATIONS OF CYCLOPOLYENES

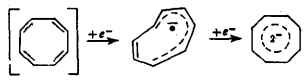
While in the instances discussed above electron transfer alters the conjugation conditions and hence the conformational mobility of the molecule, in cyclopolyenes electron transfer can lead to the formation of π-electron ring systems embracing all the ring atoms as a result of which the ring is maintained in one plane. We shall consider this phenomenon using cyclo-octatetraene and azocine as examples.

It is generally accepted that the structure of cyclo-octatetraene is best represented by the bent boat form (XXVIII) with L_{2d} molecular symmetry[98,99]. Single (1.462 Å) and double (1.334 Å) bonds, whose lengths do not differ significantly from the normal values for bonds of the C–C (sp^2–sp^2) (1.479 Å) and C=C (sp^2–sp^2) (1.338 Å) types respectively, alternate in the molecule[100]. The p_z orbitals located at the end of each single bond cannot overlap. This implies that there is no cyclic conjugation in cyclo-octatetraene and the bonds are localised. Cyclo-octatetraene, which is a vinylogue of benzene, behaves as a typical olefin. Some authors state[101,102] that it exhibits "blatant and unquestionable non-aromaticity". According to NMR data[102,103], there is a rapid and reversible migration of the double and single bonds in the cyclo-octatetraene molecule, leading to the conversion of the form (XXVIIIa) into (XXVIIIb) [reaction (18)].



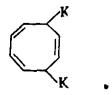
(XXVIIIa) (XXIX) (XXVIIIb) (18)

It follows from the spectra that the activation energy for this transition is 14 kcal mole^{-1}, which is close to the 17 kcal mole^{-1} calculated by the LCAO-MO SCF method[104]. The planar conformation of cyclo-octatetraene (XXIX) is an intermediate form in equilibrium (18). It is believed[104] that the above inequality of bond lengths should persist in form (XXIX). The planar or almost planar form (XXIX) is involved in electron transfer. The unpaired electron in the resulting radical-anion (XXX) can probably be delocalised to some extent over the perimeter of the molecule[105]. In other words, one can imagine this radical-anion as a fairly planar cyclic system with nine π-electrons. This system should tend to capture yet another electron and become converted into the completely planar dianion (XXXI) with ten delocalised electrons, satisfying the familiar Hückel aromaticity rule ($4n + 2$; $n = 2$). Electron transfer thus prevents the bending of the planar form [see reactions (18) and (19)].



(XXIX) (XXX) (XXXI) (19)

The transfer of a second electron is of course associated with the expenditure of appreciable additional energy, since it requires the final flattening of the molecule and the overcoming of the mutual repulsion of the free electrons[106]. However, this results in the formation of the stable aromatic cyclo-octatetraene dianion. In THF solutions cyclo-octatetraene reacts fairly rapidly with two equivalents of metallic potassium and on extensive cooling well formed crystals of the dipotassium salt of the dianion (XXXI) may be precipitated. These crystals have not so far been investigated by X-ray diffraction. On drying or on contact with air, they explode. However, the solutions are stable. The vibrational spectrum of the dipotassium salt of the cyclo-octatetraene dianion resembles those of other planar aromatic systems[107]. The transition energy in the short-wavelength region of the electronic spectra of this dianion and benzene, calculated by the free electron method, are close[108]. The method of calculation used is said[109] to represent fairly well the qualitative features of the electronic spectra, including the transition energies. The protons of the dianion (XXXI) are represented in the NMR spectrum by a sharp singlet. The ^{1}H NMR spectrum of cyclo-octatetraene also consists of a singlet with a very similar chemical shift[110]. These characteristics of the spectrum can be in no way related to the previously proposed[111] structure of the dipotassio-compound (XXXII).



(XXXII)

The fact that the compound with a double negative charge does not exhibit a shift of the ^{1}H NMR signal to a high field is evidence for a ring current. The hypothesis of a π-electron ring current is described, for example, by London[112] and the problem is discussed by Peacock[109] and Musher[113]. The ^{7}Li NMR spectrum was used to demonstrate the presence of a π-electron ring current in the dilithium salt of the cyclo-octatetraene dianion (see Table and Fig. 2).

^{1}H NMR data[110,116] show that the dipotassium salt of the cyclo-octatetraene dianion exists preferentially in the form of a close ion pair. If a π-electron ring current is possible in the organic component of the dilithium salt (XXXI), the chemical shift of the ^{7}Li signal should differ from the usual value, for example, from the ^{7}Li shift in lithium alkyls. The ^{7}Li signal for the salt (XXXI) should be displaced towards both lower and higher fields, depending on whether the metal atom is in the deshielding or shielding zone (Fig. 2, zones A or B). The data in the Table show that, compared with n-butyl-lithium, dilithiocyclo-octatetraene resonates in a much higher field. The ^{7}Li shift for the salt (XXXI) is close in magnitude to the shift for cyclopentadienyl-lithium and the aromaticity of the cyclopentadienyl anion has already been reliably demonstrated (see, for example Rafiel'[101]). Since the ^{7}Li signal in the (XXXI) spectrum is significantly displaced towards a high

field, the following conclusions may be reached: (1) Li^+ is associated with the π-electron system of the dianion; (2) the π-electron system of the dianion can indeed induce a local magnetic field, i.e. ring currents; (3) the Li^+ cations are in the regions of increased shielding, i.e. below and above the plane of the dianion (Fig. 2).

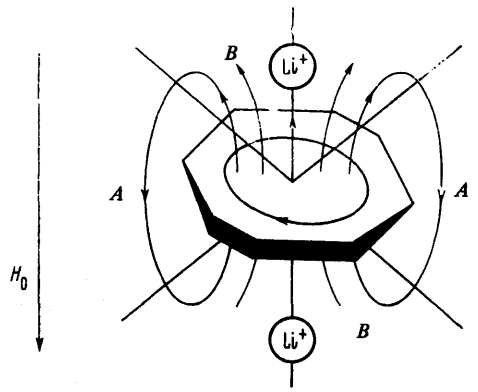


Figure 2. Graphical representation of the effect of the π-electron ring current in the dilithium salt of the cyclo-octatetraene dianion; A—deshielding zones; B—shielding zones.

It would be interesting to test these conclusions experimentally, particularly since, according to the results of recent studies [117,118], the possibility of the electrochemical synthesis of the ten-π-electron cyclo-octatetraene dianion is in fact ruled out. It was found that, after the formation of the radical-anions in THF, DMF, acetonitrile or pyridine ($E_{1/2} = -1.746$ V relative to the saturated calomel electrode), the addition of a second electron does not occur. The radical-anion is protonated by the hydrogen atom of the tetra-alkylammonium salt present in solution as the carrier electrolyte and this is followed by the one-electron reduction of the resulting radical $C_8H_9^{\cdot}$ [reaction (20)]. The anion $C_8H_9^-$ formed shows a smaller tendency than the radical-anion $[C_8H_8]^{\cdot-}$ to react with the supporting electrolyte cation and to be converted into cyclo-octatriene in the interaction with submillimolar (10^{-5} M) admixtures of water, which remain even in absolute solvents. Thus the electrochemical reduction of C_8H_8 consists of stages involving electron transfer and chemical reduction of the products; the process as a whole is irreversible:

$$C_8H_8 \xrightarrow{+\bar{e}} [C_8H_8]^{\cdot-} \xrightarrow{Bu_4N^+} C_8H_9^{\cdot} + Bu_3N + CH_3CH_2CH{=}CH_2;$$
$$C_8H_9^{\cdot} \xrightarrow{+\bar{e}} C_8H_9^- \xrightarrow{H_2O} C_8H_{10} \xrightarrow{+ne^-} \text{products.} \qquad (20)$$

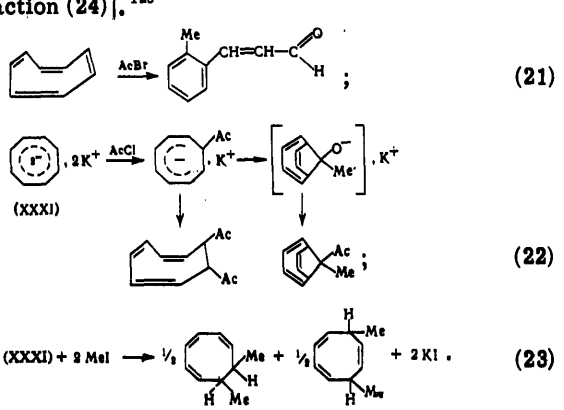
It has been noted [117] that, when no account is taken of the interactions between the dianion $C_8H_8^{2-}$ and the medium, leading to a specific organisation of the solvation shell, it is possible to estimate the difference between the potentials of the reduction of C_8H_8 to $[C_8H_8]^{\cdot-}$ and of the latter to $C_8H_8^{2-}$ as 3 V. Therefore, under the conditions of the electrochemical process, it is difficult to create potential differences such that the dianion $C_8H_8^{2-}$ can be formed.

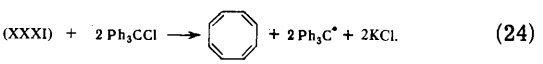
On the other hand, earlier investigators, for example Allendoerfer and Rieger [106], concluded on the basis of both classical and a.c. polarographic data that electrochemical electron transfer to the radical-anion $[C_8H_8]^{\cdot-}$ in DMF, DMSO, and acetonitrile is rapid, reversible, and takes place at a moderately negative potential. It is now necessary to either regard this conclusion as erroneous or to undertake a detailed test of the behaviour of cyclo-octatetraene in these systems. At the same time it would be necessary to compare the structures and properties of the two-electron reduction products obtained at the electrode and with the aid of alkali metals. A fairly high stability of alkali metal salts of the cyclo-octatetraene radical-anion and dianion in THF, DME, and even in liquid ammonia has been noted [119]; the dipotassium salt (XXXI) is capable of undergoing one-electron oxidation in THF solution with formation of $C_8H_8^{\cdot-}$, K^+. [120] The conversion of cyclo-octatetraene into an aromatic dianion is probably significantly facilitated by the formation of contact aggregates with the alkali metal cation. The latter increases the stability of the electron transfer products and at the same time itself interacts with the delocalised electron cloud.

The ^7Li chemical shifts for certain organolithium derivatives (relative to LiCl).

0.3 M soln. of compound in THF	σ (^7Li), p.p.m.	References
$Me(CH_2)_3CH_2Li$	1.5	114
	−8.55	114
	−8.37	115

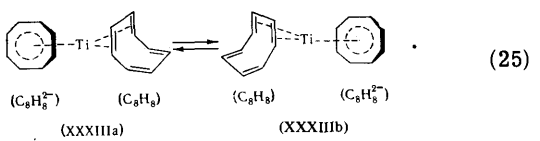
It is noteworthy that the chemical properties of the salts (XXXI) are determined primarily by the presence of the double negative charge. The chemical reactions cannot by themselves demonstrate whether this dianion has a planar or a non-planar structure. The results of the acylation of cyclo-octatetraene [121] and its dipotassio-derivatives [122] are presented in formulae (21) and (22). The alkylation of the salt (XXXI) by methyl iodide [reaction (23)] proceeds in the same way as reaction (22). [123] However, when triphenylmethyl chloride is used as the halide, disubstituted derivatives are not formed (cf. Azatyan [124]) and the reaction stops at the electron transfer stage [reaction (24)]. [125]





(24)

Electron transfer from (XXXI) to titanium tetrachloride leads to the reduction of the cation Ti^{4+} with simultaneous binding of two C_8H_8 rings into the complex $(C_8H_8)_2Ti$.[126] It follows from X-ray diffraction studies[127] that one eight-membered ring in this complex is bent, while the other is planar and that the rings are linked in different ways to the central metal atom. According to NMR data[128], at about 60°C there is intramolecular electron transfer via the metal, from one ligand to the other, so that form (XXXIIIa) is converted into (XXXIIIb) [reaction (25)].



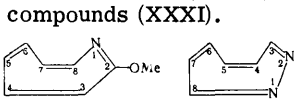
(25)

(XXXIIIa) (XXXIIIb)

Here one ring, which was previously planar, is bent, while the previously bent ring is converted into the planar form. The activation energy for this transition is 16–17 kcal mole^{-1}. It is extremely significant that the observed value is comparable to the one stated above for the inversion of cyclo-octatetraene[102,104] via reaction (18).

The abstraction of an electron from cyclo-octatetraene leads to a radical-cation whose ESR spectrum indicates a non-planar structure[129]. Calculations[106] also predict a non-planar form of this radical. The cyclo-octatetraene dication contains six π-electrons. If this dication had a planar structure, then, according to the Hückel rule, it would be aromatic and would exhibit an enhanced stability. So far such a dication has not been obtained, but it has been shown[130] that the ion $C_8H_8^{2+}$, formed under the influence of electron impact in a mass-spectrometer, is stable.

Azacyclo-octatetraene[102] has C=C vibration frequencies[131] and ultra-violet spectra[132] surprisingly similar to those of the nitrogen-free analogue (XXVIII). Hence one may conclude, according to Paquette and Kakihana[102], that the nitrogen-containing ring has, like cyclo-octatetraene, a strain-free boat form of type (XXXIV). According to the conditions of synthesis[102], all the azacyclo-octatetraene derivatives investigated contained a methoxy-group in the 2-position; in THF, DME, or liquid ammonia these compounds combine with two equivalents of potassium, forming dianions[133]. The NMR spectra show that the dianions are planar and contain delocalised ten-electron systems, i.e. have the structure (XXXV).[134] These are aza-analogues of compounds (XXXI).

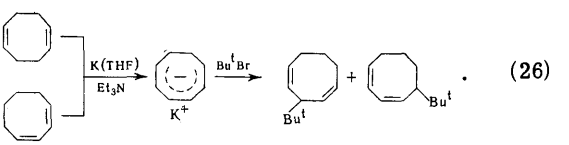


(XXXIV) (XXXVI)

The equalisation of the charge is also indicated by the formation of 3,4-, 3,6-, and 7,8-dihydro-derivatives on reaction of (XXXV) with proton donors and the interconversions of the dihydro-derivatives are impossible under the reaction conditions[133,134]. The electrochemical reduction of (XXXIV) at mercury or platinum electrodes in DMF or THF in the presence of tetra-n-butylammonium salts as carrier electrolytes[135–137] also leads to the dianion (XXXV). We may note that, according to data from the same laboratory[117], the electrochemical reduction of cyclo-octatetraene in an aprotic medium is arrested at the stage involving the formation of the radical-anion (XXX). This difference between (XXVIII) and (XXXIV) also follows from the calculation of the corresponding π-electron energy levels[138]. According to the authors, the transfer of the first electron to azacyclo-octatetraene is coupled with a change in its configuration (XXXIV) to an almost planar form, actually more planar than in the case of compound (XXX). This process requires such a high energy expenditure that the capture of a second electron, required to complete the decet ($4n + 2$; $n = 2$), proceeds without additional activation. This implies that the reduction of the radical-anion in a polarographic experiment should proceed more readily than that of the initial azacyclo-octatetraene and that, after the attainment of the potential corresponding to the transfer of the first electron, the second electron should also be transferred. It follows from the analysis of polarographic data[136] that the two-electron reduction of (XXXIV) to (XXXV) does indeed consists of two simultaneous one-electron stages.

Recently it proved possible to obtain also the diaza-analogue of cyclo-octatetraene for which the authors suggest the structure (XXXVI).[139] It would be interesting to show whether this compound is capable of undergoing a change in geometry in electron transfer reactions.

Electron transfer might also induce the isomerisation of non-conjugated cyclo-olefins to conjugated forms. Thus metallation of cyclo-octa-1,3-diene and cyclo-octa-1,5-diene leads [see reaction (26)] to the same anion, which on treatment with t-butyl iodide gives rise to a mixture of equal amounts of 3-t-butylcyclo-octa-1,4-diene and 5-t-butylcyclo-octa-1,3-diene[140].



(26)

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The data discussed in this review permit the conclusion that the geometry of organic compounds can change on electron transfer. The cause of such changes have been discussed. They may determine the stereochemical structure of the products obtained as a result of reactions involving an electron transfer stage. Consequently the detection of the stereochemical changes induced by electron transfer is important for the investigation of the mechanisms of many organic reactions. In particular, it is important to study the relation between the geometry of the repeat units in high-molecular-weight compounds and the method used to initiate polymerisation. On the other hand, it would be useful to take into account more fully the role of electron exchange processes in biochemical reactions. Indeed, many biomolecules with unsaturated bonds are involved in reactions associated with electron transfer. Here one may include the chemical changes arising, for example, in the processes involved in vision[141] or in the isomerisation of unsaturated aliphatic acids under the influence of enzymes[142,143]. The capacity to undergo a change in configuration on electron transfer might be used to select new biologically active substances; no doubt other no less important applications are also possible. The aim of the present review is to attract attention to the stereochemical results of electron transfer.

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